

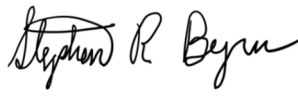
**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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

**DECLARATION OF DR. STEPHEN BYRN**

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

Date: \_\_November 25, 2025\_\_

By:   
Stephen Byrn, Ph.D.

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## **I. ASSIGNMENT**

1. I have been retained on behalf of NJOY LLC and NJOY Holdings to offer technical opinions in an *inter partes* review (“IPR”) challenging U.S. Patent No. 12,156,533 (“the ’533 patent”) (EX1001).

2. I have been asked to provide my independent analysis of nicotine salt formulations and the chemistry underlying the formation of nicotine salts.

3. I am not and never have been, an employee of NJOY LLC, NJOY Holdings, or any related company. I have received no compensation for this declaration beyond my normal hourly compensation based on my time actually spent providing analysis for this declaration, and I will not receive any additional compensation based on the outcome of this IPR or any other proceeding involving the ’533 patent.

## **II. QUALIFICATIONS AND BACKGROUND INFORMATION**

4. My qualifications are summarized here and explained in more detail in my curriculum vitae, which is attached as Appendix A to this Declaration. Appendix A also includes a list of my publications and the cases in which I have testified at deposition, hearing, or trial within the past four years.

5. I received a Ph.D. in Organic and Physical Chemistry from the University of Illinois in 1970 and was a post-doctoral fellow in Physical Chemistry at UCLA from 1970 to 1972. In 1972, I became a professor of Medicinal Chemistry

at Purdue University. I was Head of the Department of Medicinal Chemistry and Pharmacognosy at Purdue University in the School of Pharmacy and Pharmaceutical Sciences from 1988-1994. I was the Director of the Center for AIDS Research at Purdue from 1988 until 1998, and I was the Head of the Department of Industrial and Physical Pharmacy from 1994 to 2009. I became the Charles B. Jordan Professor of Medicinal Chemistry in 1992.

6. I am an author of over 235 peer reviewed publications in technical journals on topics that include salt chemistry, physical chemistry, organic chemistry, and medicinal chemistry, manufacturing of pharmaceuticals and analysis of pharmaceuticals, including papers on nicotine salts.

7. I have organized and taught over one-hundred courses in chemistry, manufacturing, analysis and related areas. I have also taught at the federal Food and Drug Administration (“FDA”), and have given over 270 invited lectures and symposium talks and presentations on chemistry and related topics.

8. Under my supervision, over 50 students and post-doctoral associates have published numerous papers and theses on many different compounds, formulations, many of them involving salts. I have taught many courses throughout my career including medicinal analysis, advanced medicinal analysis, computers in pharmacy, solid state chemistry, pharmaceuticals, formulation, molecular basis of

manufacturing, sterile products, drug development, and devices. Currently, I am lecturing on a range of topics in our Doctor of Pharmacy curriculum.

9. I have founded or co-founded several academic and industrial programs/companies including Purdue's Center for AIDS Research, CAMP (Consortium for the Advancement of Manufacturing in Pharmacy), Purdue's MS program in regulatory sciences, SSCI, Inc., which is now owned by AMRI, and Improved Pharma, LLC, a research and information company located in the Purdue Research Park that provides innovative problem-solving and analytical research to a broad range of companies. Improved Pharma performs crystallizations, prepares salts, performs X-ray analysis, and Synchrotron-based X-ray analysis. Improved Pharma also performs polymorph screening on salts to search for new polymorphs, solvates, and hydrates and to analyse mixtures of solids.

10. I also co-founded the Sustainable Medicines in Africa Program which is now part of Purdue's Biotechnology Innovation and Regulatory Sciences Center where I am co-director. This Africa program currently is supported by the Bill and Melinda Gates Foundation and I typically travel to Africa two times per year to help present the on-site portion of this blended distance education program.

11. I have used a wide range of analytical methods to characterize chemical compounds including X-ray diffraction, NMR spectroscopy, environmental

scanning electron microscopy, differential scanning calorimetry, thermal gravimetric analysis, IR spectroscopy, Raman spectroscopy, moisture sorption analysis, thermal microscopy, dissolution, and HPLC.

12. I have received numerous awards including the AAPS David Grant Research Achievement Award in Physical Pharmacy. In 2010, a Special Issue of the Journal of Pharmaceutical Sciences was dedicated to me based on my work as a Scientist, Educator and Visionary. I was also awarded the AAPS Dale E. Wurster Research Award as the top formulation expert in pharmaceutical sciences in 2016, the AAPS Global Health Award in 2018, the Chaney Award for the outstanding research in the College of Pharmacy in 2022, the Pharmaceutical Sciences Teacher of the Year Award, and the Morrill Award for the most outstanding faculty member at Purdue University in 2018.

13. I have received numerous grants as the Principal Investigator for research relating to the chemistry of pharmaceutical drugs and medicinal chemistry. The grants I have received during my tenure at Purdue University total roughly \$50 million and have been sponsored by government research organizations and pharmaceutical companies, including the National Institutes of Health, the U.S. FDA, Eli Lilly & Co., Merck & Co., Bristol-Myers Squibb, Boehringer, Pfizer, Sandoz, Glaxo, and Upjohn.

14. I have served as a consultant for many companies in the United States and abroad. Among the companies for which I have consulted are Pfizer, GlaxoSmithKline, Merck, Genentech, Bristol-Myers Squibb, Johnson & Johnson, Wyeth, Eli Lilly, Roche, and Abbott. In addition, I served as the head of the Scientific Advisory Board for Aptuit.

15. My curriculum vitae, included as Appendix A to this Declaration, includes a list of publications on which I am a named author. It contains further details regarding my experience, education, publications, and other qualifications to render an expert opinion in connection with this proceeding.

16. In writing this Declaration, I have considered the following: my own knowledge and experience, including my work experience in the fields of chemistry and in salt chemistry in particular; my experience in teaching those subjects; and my experience in working with others involved in those fields. In addition, I have analyzed the following publications and materials, in addition to the other materials I cite in my Declaration:

- U.S. Patent No. 12,156,533 (“the ’533 patent”)
- U.S. Patent Application No. 2014/0000638 titled “Reservoir and Heater System for Controllable Delivery of Multiple Aerosolizable Materials in an Electronic Smoking Article” (“Sebastian”)

- U.S. Patent Application No. 2006/0018840 titled titled, “Aerosolizable Formulation Comprising Nicotine” (“Lechuga-Ballesteros”)

17. I have no financial interest in the outcome of this proceeding. I am being compensated for my work as an expert on an hourly basis. My compensation is not dependent on the outcome of these proceedings or the content of my opinions.

18. My opinions, as explained below, are based on my education, experience, and expertise in chemistry.

### III. ACID-BASE INTERACTIONS AND SALT FORMATION

19. When present in water or other solvents, chemical compounds are either neutral, acidic or basic in nature. EX1007, 516. An acidic compound can be characterized by its ability to donate a proton ( $H^+$ ) to its surroundings and a basic compound can be characterized by its ability to accept a proton from its surroundings. EX1007, 140-142. When an acid donates its proton to a base, it becomes a negatively charged molecule called an *anion*. When the base accepts the proton, it becomes a positively charged molecule called a *cation*. EX1007, 147. Due to their opposite charges, the anion and cation will attract each other and form an ionic compound, which in generic terms, *is a salt*, as will be discussed in more detail below. EX1007, 61. The constituents of the resulting salt molecule, are “ionically bonded”, which refers to the fact that they are held together solely by their

opposite charges, i.e., electrostatic attraction. EX1011, 96. Therefore, when an acid and base react, a compound—specifically, a salt—forms.

20. Acids and bases have different strengths. EX1007, 144-149. For example, hydrochloric acid is a strong acid, whereas acetic acid, the active ingredient in vinegar, is a weak acid. EX1007, 145-147. Similarly, sodium hydroxide is an example of a strong base and ammonia is an example of a weak base. EX1007, 145, 149. The strength of an acid is determined by its tendency to donate its proton; a strong acid readily donates its proton, whereas a weak acid binds to its proton more tightly. By contrast, the strong base attracts protons very strongly, whereas a weak base exhibits less attraction to protons. EX1007, 144. The tendency of an acid to donate a proton and the tendency of a base to accept a proton explains why acids and bases react to form new compounds.

21. The strength of acids and bases are measured on a logarithmic scale, known as the  $pK_a$  scale.<sup>1</sup> EX1011, 194-195. The *lower* the  $pK_a$ , the *stronger* the acid. *Id.* In contrast, the *higher* the  $pK_a$ , the *stronger* the base. EX1011, 195. For example, in water, hydrochloric acid is a stronger acid ( $pK_a$  value of less than 1)

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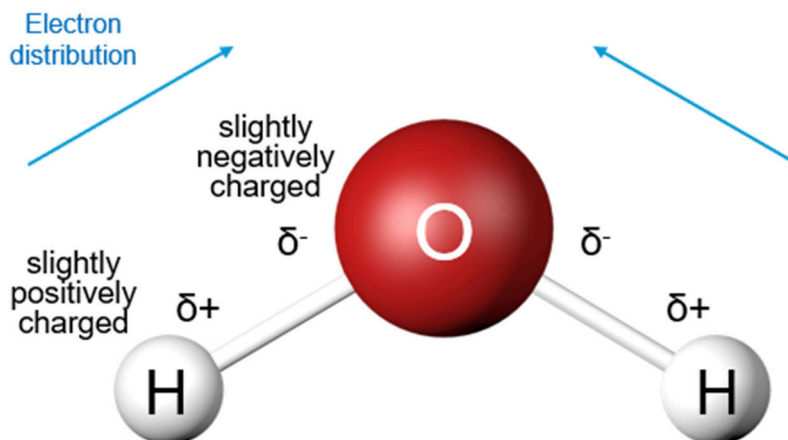
<sup>1</sup> Note that some textbooks and articles refer to the  $pK_a$  scale as the  $pK_b$  scale when referring to this value for bases. *See, e.g.*, EX1011, 195. Regardless, the value is calculated the same way for both acids and bases. EX1011, 194. Herein, I will use  $pK_a$  for both acids and bases.

compared to acetic acid ( $pK_a$  of 4.74). EX1019, 14; EX1011, 195. The  $pK_a$  values of different acids and bases in water are generally well established, and the  $pK_a$  values in other solvents can be experimentally or computationally determined.

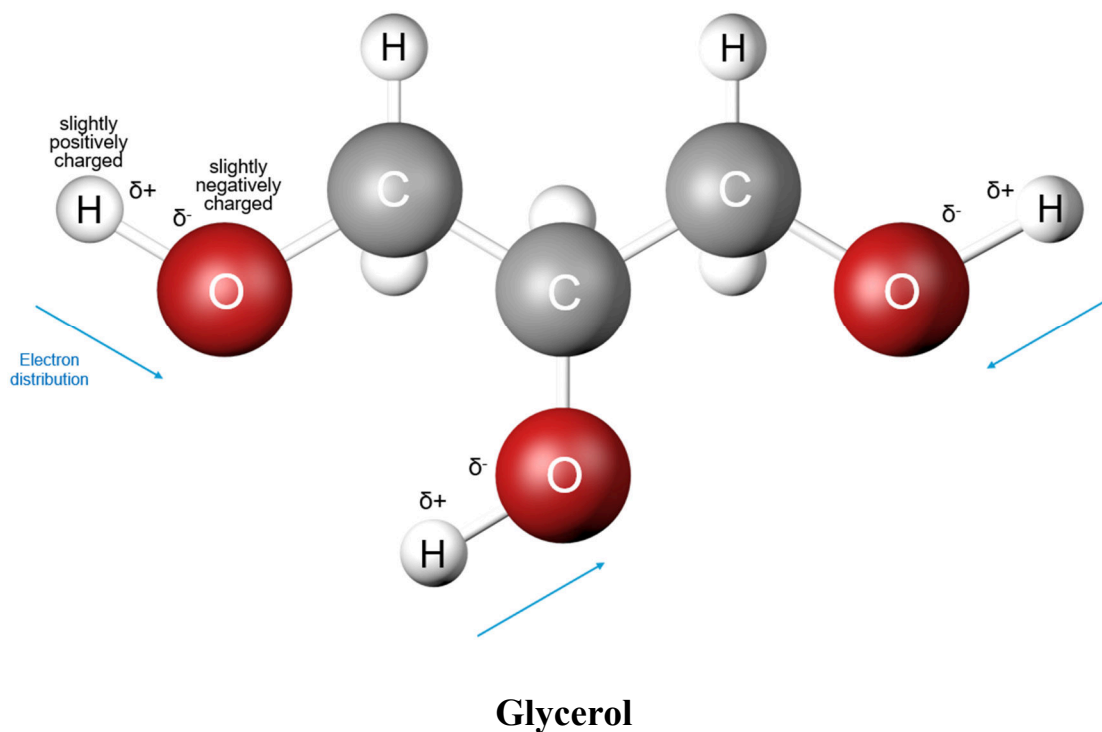
22. The  $pK_a$  of a chemical compound will vary depending, in part, on the polarity of the solvent it is dissolved in. EX1020, 4. “Polarity” refers to the asymmetric distribution of electron density when two different atoms with different attractive forces are chemically bonded to form a compound. EX1011, 55-56. A compound simply refers to any substance formed when two or more atoms are chemically joined together in a fixed ratio. EX1007, 13. The asymmetric distribution of electrons results in one part of the compound being more negatively or positively charged than the other part of the compound. EX1011, 71.

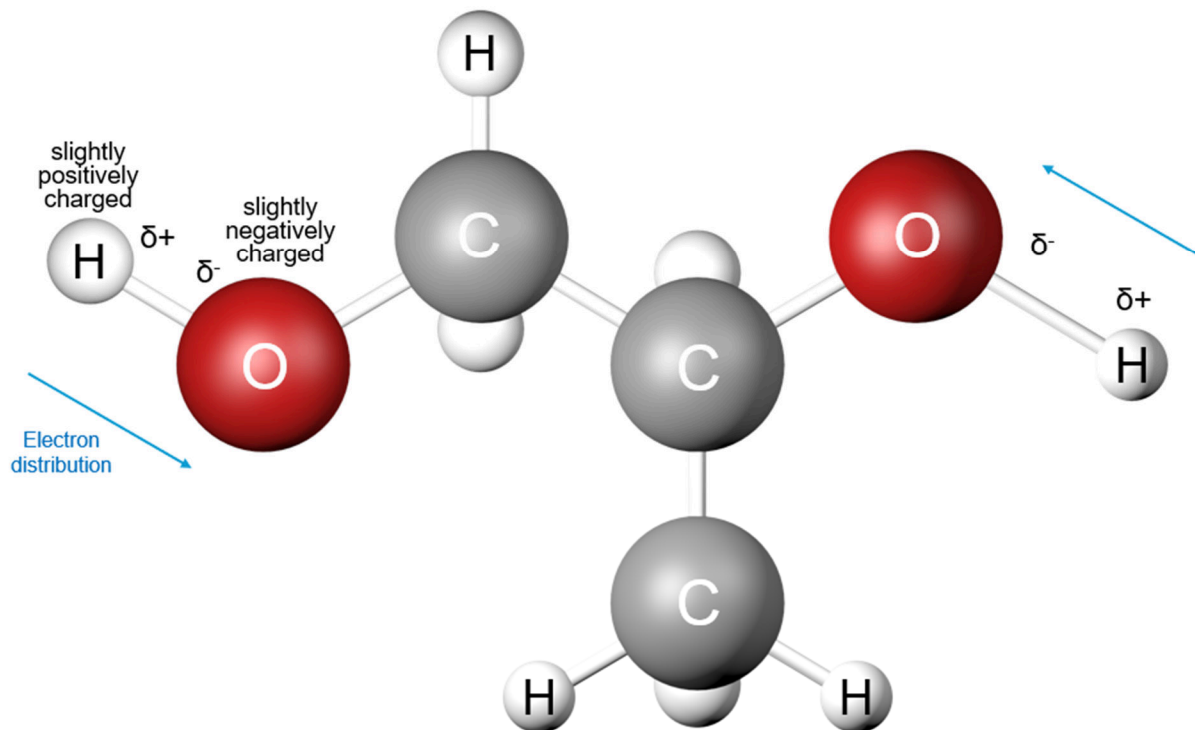
23. Polarity is easy to understand through an example. Take water, for instance. Water—which is comprised of one oxygen atom and two hydrogen atoms—is a polar compound because the oxygen atom has a much stronger affinity for electrons than hydrogen, resulting in the oxygen atom being partially negatively charged and the hydrogen atoms being partially positively charged. The structure of a water molecule illustrating the partially positively charged hydrogen atoms ( $\delta^+$ ) and partially negatively charged oxygen atoms ( $\delta^-$ ) is shown below, with the arrows indicating the unequal sharing of electrons between the oxygen atom and each

hydrogen atom to which the oxygen atom is bonded:



Similarly, other solvents, like propylene glycol and glycerol, are also polar because of similar polar hydrogen-oxygen bonds:





### Propylene Glycol

24. The partial positive and negative charges present in polar solvents such as water, propylene glycol, and glycerol affect whether a reaction is more or less favored to occur—i.e., if a compound will be formed. The stronger the partial positive and negative charges of the solvent, the better they are able to stabilize charged atoms formed by dissolving an acid or base, thereby allowing them to form a compound.

25. To break this down even further, as described previously, acids generally donate protons and bases accept protons to form compounds. That means when a neutrally charged acid donates a positively charged proton to a base, it will

then generally possess a *negative* charge in solution (having lost its positively charged proton). This newly formed, negatively charged ion in solution can interact with and be stabilized by the partially *positively* charged hydrogen atoms of polar solvents like water, glycerol, and propylene glycol. The presence of a polar solvent lowers the energy required for an acid to donate a proton to a base, thus making the acid-base reaction more energetically favorable. This increase in the strength of an acid can be quantified, as the  $pK_a$  of a chemical compound will typically decrease as the polarity of the solvent increases. EX1020, 4. As such, the  $pK_a$  of an acid is dependent on the polarity of the solvent, among other factors. EX1020, 4.

26. At that same time, because bases generally accept protons, that means that when a neutrally charged base accepts that positively charged proton that the acid donated, it will then generally possess a *positive* charge in solution. This newly formed, positively charged ion in solution can interact with and be stabilized by the partially *negatively* charged atoms of polar solvents like water, glycerol, and propylene glycol. Just as with the acid, the presence of the polar solvent similarly lowers the energy required for a base to accept a proton from an acid, thus making the acid-base reaction more energetically favorable.

27. The formation of a salt can be predicted using the  $pK_a$  value of the acid and the  $pK_a$  value of the base. Specifically, if the difference in the  $pK_a$  values

( $\Delta$  pK<sub>a</sub>) of the acid and base is three units or more, a salt will form when the acid and base interact. EX1018, 1; EX1016, 14-15. This is generally referred to as the pK<sub>a</sub> rule. EX1018, 1.

#### **IV. ANALYSIS OF SEBASTIAN'S LIQUID AEROSOL PRECURSOR COMPOSITION**

##### **A. Sebastian Discloses a Nicotine Salt Formulation**

28. Based on my review of Sebastian, I understand that Sebastian describes a liquid aerosol precursor composition. EX1004, [0015], [0055], [0057]. I understand that this composition is housed in a single cartridge which functions as a reservoir for the liquid aerosol precursor composition. EX1004, [0012], [0069], [0116].

29. It is my further understanding that Sebastian's liquid aerosol precursor composition includes nicotine, one or more organic acids such as lactic acid, and one or more liquid materials such as water, propylene glycol, and glycerol. EX1004, [0055], [0057], [0059]-[0061].

30. Looking specifically at the disclosure of the combination of nicotine and organic acid, I understand that Sebastian states that its liquid aerosol precursor composition can include organic acid and nicotine—a base—in “up to being equimolar” amounts. EX1004, [0059]; *see also* EX1004, [0059] (disclosing ratio of “about 0.5 moles of lactic acid per one mole of nicotine”). “Equimolar” means that

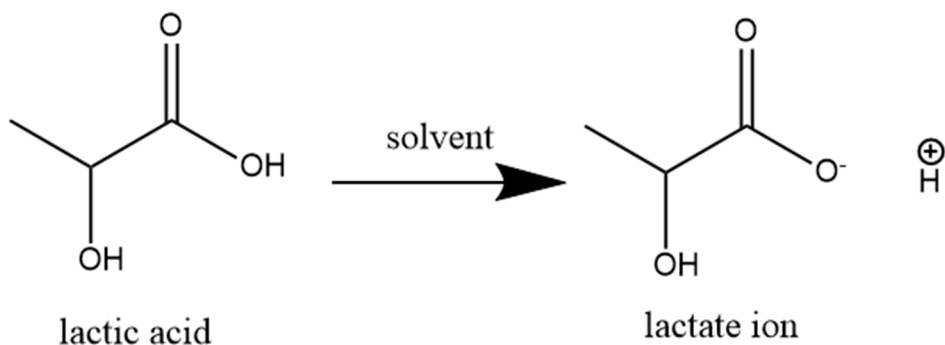
nicotine and organic acid are present in equal stoichiometric amounts. “Stoichiometric” amounts refer to the amount of reactants in a chemical reaction. EX1011, 17. Put a simpler way—equimolar means that for every molecule of nicotine, there is a corresponding molecule of organic acid with which it can react.

31. I further understand that Sebastian discloses the concentration of nicotine in the liquid aerosol precursor composition being anywhere between 0.1% to 5% by weight percentage, and in another example, describes that nicotine can be present in a concentration up to about 10%. EX1004, [0060]-[0061].

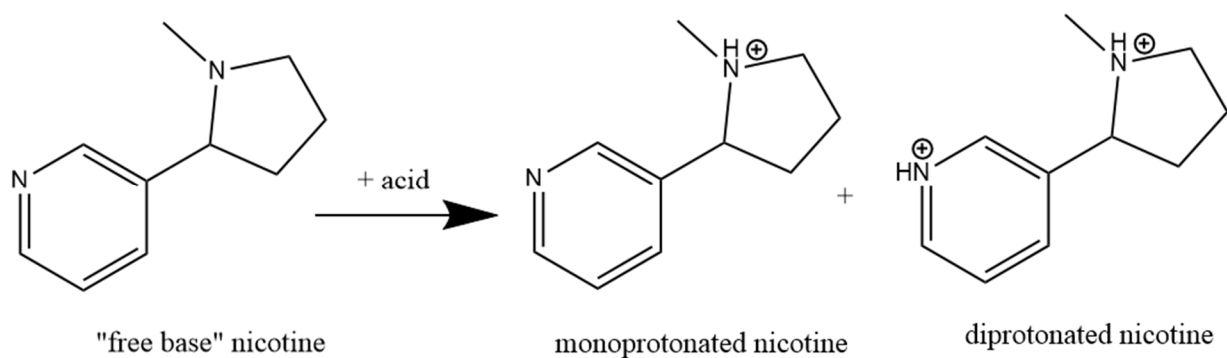
32. Based on my knowledge and experience in salt chemistry over the past fifty years, it is my opinion that a nicotine salt, such as nicotine lactate, is present in Sebastian’s liquid aerosol precursor composition because of the inherent *basic* properties of nicotine and inherent *acidic* properties of lactic acid, as well as how these two chemical compounds will necessarily behave in a polar solvent like water, propylene glycol, glycerol, or a mixture thereof.

33. To illustrate the inevitable formation of nicotine lactate, lactic acid will dissociate into its negatively charged ionic form, the lactate ion, when placed in solution such as water, propylene glycol, or glycerol, or a mixture of these solvents, due to the polarity of these solvents. Specifically, the carboxylic acid group (COOH), represented below by the double bond to oxygen and the single bond to

the OH group, will ionize and partially lose its hydrogen atom to become a negatively charged lactate **anion**:



34. When nicotine ( $C_{10}H_{14}N_2$ ) is added to this solution, it will react with the free positively charged hydrogen molecules, creating a mono-positively charged **monoprotonated cation** form and partly create a di-positively charged deprotonated cation form.:



When nicotine exists in its unprotonated form (left, above), I understand that it is colloquially referred to in the tobacco industry as in "free base" form, when it is at its most basic pH. When combined with an organic acid, nicotine can exist with both a single charged nitrogen ("mono-protonated") or two charged nitrogens ("di-

protonated”). Notably, the nitrogen atom on the 5-membered “pyrrolidine” ring is a stronger base than the nitrogen atom on the 6-membered “pyridine” ring, and as such it accepts a proton more easily. The pyridine nitrogen is a much weaker base and will accept a proton only at low pH. EX1008, 1-2; EX1022, 3-4.

35. Therefore, as a result of being present in solution together, the negatively charged lactate ions and the positively charged nicotine ions will electrostatically interact, due to their opposing charges, and will react to form a salt, i.e., nicotine lactate. Put another way, the base nicotine will react with the acid lactic acid to form a salt. In my opinion, this formation of nicotine lactate inevitably and necessarily occurs in Sebastian’s aerosol precursor that contains lactic acid and nicotine in a polar solvent such as water, propylene glycol, glycerol, or mixtures thereof.

36. My opinion that nicotine lactate will form is further grounded in empirical data that I have reviewed with respect to the  $pK_a$  values of nicotine and lactic acid and the rule discussed previously. Specifically, it is well understood that, in water, the  $pK_a$  of lactic acid is 3.86. EX1023, 19. As was shown previously, nicotine—a base—possesses two nitrogen atoms that can potentially accept a proton from an acid, resulting in either mono-protonated nicotine or di-protonated nicotine. The  $pK_a$  of the first nitrogen atom is 8.0 and the  $pK_a$  of the second nitrogen atom is

3.1.<sup>2</sup> EX1022, 4. This means that the difference, in  $pK_a$  ( $\Delta pK_a$ ) between the first “basic” site of nicotine and lactic acid is 4.14. As such, based on the  $pK_a$  rule, a  $\Delta pK_a$  of 4.14 between the first basic site of nicotine and lactic acid will necessarily result in an electrostatic interaction between the ionic forms of nicotine and lactic acid, forming a salt. When conditions are such that there is not an excessive amount of acid over nicotine (i.e., in less than equimolar amounts), or if the protonating acid is weak, the second nitrogen atom will not accept a proton. In other words, the nicotine lactate salt that forms under most pH conditions will predominantly have the mono-protonated form of nicotine.

37. While these  $pK_a$  values are based on measurements in water as the solvent, I would expect the  $pK_a$  of nicotine and lactic acid to be similar in other polar solvents like propylene glycol and glycerol such that the  $\Delta pK_a$  would indicate that a salt forms. I would expect that the  $pK_a$  values for both nicotine and lactic acid would increase slightly, as propylene glycol and glycerol are slightly less polar than water. Nevertheless, I would expect nicotine and lactic acid would have approximately the same relative difference such that the  $\Delta pK_a$  would be highly similar, and in any event not less than 3, therefore satisfying the  $pK_a$  rule.

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<sup>2</sup> I note that the literature, such as EX1022, reports a very narrow range of  $pK_a$  values for the two nitrogen atoms. For example, EX1022 reports a range of 8.0-8.11 for the first nitrogen and 3.0-3.22 for the second nitrogen.

Specifically, I note that water, propylene glycol, and glycerol are all considered strong polar solvents, and have similar polarity parameters. EX1024, 5 (Table 1, deriving polarity parameters for each polar solvent from Hansen, C.M., *Hansen Solubility Parameters: A User's Handbook*, CRC Press (2007)).

38. Additionally, I note that Sebastian discloses that its aerosol precursor solution, in addition to containing glycerol and propylene glycol, can also contain water “in an amount of about 10% to about 20% by weight[.]” EX1004, [0061]. In my view, the presence of 10% or 20% water—generally considered the most polar solvent—would also strongly favor salt formation in the aerosol precursor solution.

39. Thus, it is my opinion that Sebastian’s liquid aerosol precursor composition includes a salt of nicotine and an organic acid, i.e., nicotine lactate based on the inherent characteristics of nicotine as a base and lactic acid as an acid in solution, and the necessary electrostatic interactions that occur between the nicotine ion and lactate ion to produce a salt in solution.

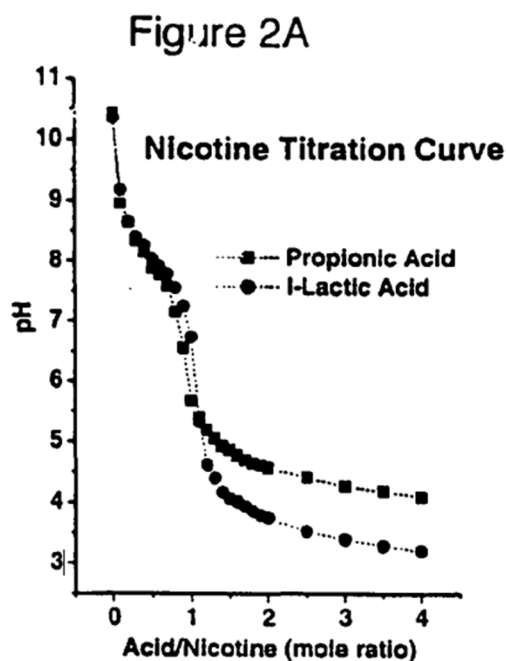
**B. The Formation of a Nicotine Salt in Sebastian is Further Supported by Lechuga-Ballesteros**

40. Based on my review of Lechuga-Ballesteros, I see that Lechuga-Ballesteros describes an aerosolizable liquid formulation containing a salt of nicotine and an organic acid, such as nicotine lactate. EX1005, [0012], [0023], [0084].

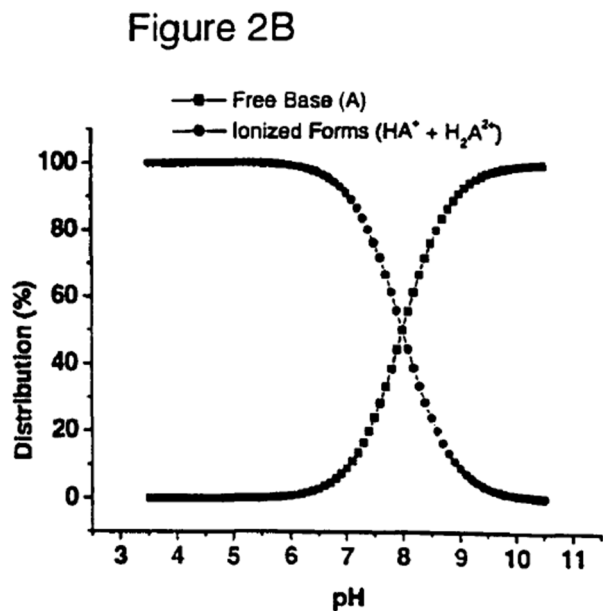
41. Lechuga-Ballesteros, through a titration experiment, expressly

demonstrates the formation of nicotine lactate. EX1005, [0066], [0089]-[0091]. In the experiment, Lechuga-Ballesteros explains that similar stoichiometric amounts of nicotine and lactic acid were combined in water. EX1005, [0066].

42. As the lactic acid was added to the nicotine, pH measurements were taken, shown in Figure 2A below. EX1005, Fig. 2A. As explained in Lechuga-Ballesteros, the pH of the solution is shown on the vertical axis as more and more lactic acid is added to the nicotine. EX1005, Fig. 2A, [0089]. This increasing ratio of lactic acid to nicotine is shown along the horizontal axis. EX1005, Fig. 2A. Specifically, according to Lechuga-Ballesteros, his experiment shows a majority of unprotonated nicotine (i.e., free base nicotine) was converted to nicotine lactate at an approximate ratio of 1.2:1 of acid to nicotine. EX1005, [0091].



43. Additionally, I note that Lechuga-Ballesteros converted the results of this titration experiment to a plot showing the distribution of the unprotonated, free base nicotine compounds to the nicotine ions. EX1005, Fig. 2B, [0090]. In the plot below, the squares represent nicotine in the free base form (“Free Base (A)”), and the circles represent the ionized (i.e. protonated) forms (“Ionized Forms ( $\text{HA}^+ + \text{H}_2\text{A}^{2+}$ )”):



EX1005, Fig. 2B. Starting at the right of this plot, it shows that when the pH is highest, i.e. ~pH 10.5, the solution is entirely free base nicotine. EX1005, Fig. 2B. As the acid is added to the mixture, the percentage of free base nicotine *decreases* as the protons from the acid bond with the free base nicotine to form the ionized form—i.e., the salt—thereby lowering the pH. EX1005, Fig. 2B. Inversely, the

percentage of nicotine lactate—represented by circles (“Ionized Forms ( $\text{HA}^+ + \text{H}_2\text{A}^{2+}$ ), *increases* as more acid is added to the mixture, and more salt is formed. EX1005, Fig. 2B. In other words, as soon as lactic acid is added to the solution, the nicotine lactate salt is formed, and as additional acid is added, even more salt is formed.

44. Additionally, these experimental results show that when the distribution of nicotine is equal between free base nicotine and ionized nicotine (i.e. 50% distribution, where the two lines cross), the pH is around 8. Moreover, one can easily tell by drawing a vertical line at a pH of 7 on the horizontal axis that about 10% of the nicotine was present as the free base nicotine while the other about 90% was ionized (i.e., in salt form) at pH 7.

45. Additionally, I note that Lechuga-Ballesteros further discloses that its aerosolizable formulation comprises “said organic acid is present in a mole ratio with said nicotine in a range of about 0.25:1 (organic acid:nicotine) to about 4:1 (organic acid:nicotine)[.]” EX1005, [0012]; *see also* EX1005, [0013]-[0014] (same). As we see above, Figure 2A of Lechuga-Ballesteros shows that, for example, at a mole ratio of 4:1, the pH of lactic acid is below 4. Figure 2B, then, demonstrates that at pH below 4, nearly 100% of the nicotine is in the ionized forms. EX1005, FIG. 2A-2B.

46. Finally, I understand that, in addition to simply forming a nicotine salt, claim 1 of the '533 patent requires specifically that “the salt is present in an amount that forms a nicotine concentration of 0.5% (w/w) to 20% (w/w) in the nicotine salt liquid formulation.” EX1001, cl. 1. In applying my understanding as a chemist, I understand this limitation to be disclosed in Sebastian by the express disclosure that “nicotine can be present in an amount of about 0.1% to about 5% by weight” in the “aerosol precursor according to the invention[.]” EX1004, [0061]; *see also* EX1004, [0060] (disclosing that “[f]lavors and the like (which can include medicaments, such as nicotine) can comprise up to about 10%...of the aerosol precursor.”).

47. To the extent only the protonated nicotine is considered, while I disagree with such an interpretation, I nevertheless have calculated the percentage of nicotine that would be in protonated nicotine form as compared to nicotine base form, using standard equations well-known in this field. *See, e.g.*, EX1008, 1-2; EX1011, 215; EX1022, 4. I calculate that within a broad pH range of 3 to 9, in water a disclosure of 5% nicotine results in a weight percentage falling between 0.5% and 5% protonated nicotine. Certainly, when nicotine and organic acid are “equimolar,”—a concentration Sebastian expressly discloses, (EX1004, [0059]),—as the curve in Lechuga-Ballesteros demonstrates, I calculate that greater than 0.5% of the nicotine is present in the protonated nicotine form. Additionally, at higher

organic acid to nicotine molar ratios, like the ones described in Lechuga-Ballesteros, an even greater percentage of nicotine would be protonated. For example, at a molar ratio of 4:1, approximately 4% of the nicotine would be protonated.

## V. CONCLUSION

48. For all the reasons I have noted in the foregoing paragraphs, by disclosing a liquid aerosol precursor composition that contains nicotine, lactic acid, propylene glycol, and glycerol, Sebastian necessarily discloses a nicotine salt—i.e., nicotine lactate.

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

# **APPENDIX A**



**Stephen R. Byrn, Ph.D.**  
*NJOY, et al. v. JUUL*

Prepared for Joseph R. Dorris, Esq.  
of Fish & Richardson P.C.

IMS Project No. 64358-01 | October 8, 2025

### Expert in Nicotine Salt Formulation

Dr. Stephen Byrn is a professor of medicinal chemistry at Purdue University and co-founder of the solid-state chemistry consultancy SSCI, Inc. (now part of Aptuit). He serves as a principal investigator on multiple studies focused on solid-state pharmaceuticals and manufacturing processes. With nearly 50 years of experience in chemistry and stability of pharmaceutical salts, Dr. Byrn has contributed his expertise to numerous litigations involving compounds such as clopidogrel (bisulfate salt), paroxetine (HCl salt) and amlodipine (benzenesulfonate salt). He earned his Ph.D. in organic and physical chemistry from the University of Illinois and is a fellow of the American Association of Pharmaceutical Scientists.

### Litigation Support Summary

Dr. Byrn has extensive experience as an expert witness in pharmaceutical patent litigations and inter partes reviews. A list of cases in which he has testified within the past four years is included in this presentation.

**50+**  
Cases

**200+**  
Depositions

**25+**  
Trials

### Rate Schedule

\$1,000 per hour for all work and travel time

**General:** The quoted rate includes both the expert's fee and IMS Legal Strategies' fee but excludes reimbursement for customary travel, lodging, and business expenses.

**Contact your executive account manager or expert services consultant to discuss this candidate or schedule an interview.**

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- Home Address:** 824 Barlow Street, West Lafayette, Indiana 47906
- Marital Status:** Married, ten children
- Education:** DePauw University, Greencastle, Indiana, B.A., 1962-1966, Chemistry
- University of Illinois, Urbana, Illinois, Ph.D., 1966-1970, Organic and Physical Chemistry
- University of California, Los Angeles, California, Postdoctoral, 1970-1972, Physical Chemistry
- Professional Experience:** Assistant Professor of Medicinal Chemistry, Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, Indiana, July 1, 1972 to June 30, 1976
- Associate Professor of Medicinal Chemistry, Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, Indiana, July 1, 1976 to June 30, 1981
- Professor of Medicinal Chemistry, Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, Indiana, July 1, 1981 to present
- Associate Department Head of Medicinal Chemistry, Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, Indiana, 1979 to 1988
- Assistant Dean of the Graduate School, Purdue University, West Lafayette, Indiana, 1984 to 1988
- Head, Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, Indiana, 1988 to 1994
- Founder and Director, Purdue University Center for AIDS Research, September 30, 1988 to March 1, 1998
- Head, Department of Industrial and Physical Pharmacy, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, Indiana, September 1, 1994 to June 30, 2009
- Charles B. Jordan Professor of Medicinal Chemistry, 1992 to present.
- Co-Director, Center for Biotechnology Innovation and Regulatory Science, Discovery Park and Agricultural and Biochemical Engineering Department, 2014-present
- Director, NIPTE Center of Excellence for Abuse Deterrent Formulations, March, 2017-present

## **Memberships:**

Phi Eta Sigma, Rho Chi, Phi Lambda Upsilon, Phi Kappa Phi, Sigma Xi  
American Chemical Society  
American Crystallographic Association  
American Association of Pharmaceutical Scientists

## **Awards, Honors:**

Rector Scholar, DePauw University, 1962-1966  
Sinclair Oil Company Fellow, University of Illinois, 1967-1968  
National Science Foundation Graduate Fellow, University of Illinois, 1968-1971  
National Institutes of Health Postdoctoral Fellow, University of California, 1971-1972  
Elected Fellow, American Association of Pharmaceutical Scientists, 1989  
Elected Member, United States Pharmacopeia Revision Committee, 1990-1995 & 1995-2000 & 2000-2005.  
Council of Experts 2000-2005, Member of several subcommittees including chemistry, dissolution, excipients and PAT.  
Purdue University Representative to the USP, 2000, 2005, 2010.  
Alumni Citation, DePauw University, 1991  
Thomas W. Binford Memorial Award for Outstanding Contributions to Entrepreneurial Development, World of Difference Award, State of Indiana, 2000  
FDA Advisory Committee Service Award, October 31, 2001  
AAPS Outstanding Paper Award, 2008, APQ Section (With L. Taylor)  
Purdue University, Outstanding Faculty Commercialization Award, 2008-09  
AAPS David Grant Research Achievement Award in Physical Pharmacy, 2009  
Special Issue (September 2010) of the Journal of Pharmaceutical Sciences was dedicated to Stephen R. Byrn, based on his contributions to the field of solid state pharmaceuticals.  
FDA Honor Award. Stephen Byrn as Member of FDA/Kilimanjaro School of Pharmacy Regulatory Collaboration, 2013  
AAPS Dale Wurster Award In Pharmaceutics, November 16, 2016.  
LSAMP Faculty Mentor of the Year Award, Purdue University, 2018  
Pharmaceutical Sciences Teacher of the Year Award, Purdue University, 2018  
Purdue University Morrill Award, Most Outstanding Faculty Member, 2018  
AAPS Pharmaceutical Global Health Award, November 2018  
Chaney Faculty Scholar Award, College of Pharmacy, Purdue University 2022

## **Memberships, Editorial Boards and Major Committees:**

Pharmaceuticals, Editorial Advisory Board, 2021-present  
Journal of Pharmaceutical Sciences Editorial Advisory Board - 1994-present.  
AAPS Pharm. Sci. Tech. Editorial Advisory Board – 2007 – present.  
Pharmaceutics Editorial Advisory Board - 2009 – 2014  
Journal of Validation Technology, Editorial Advisory board – 2010 – 2012  
Crystal Growth and Design Editorial Advisory Board – 2002 to 2007  
Journal of Drug Targeting, 1993-1995.  
Journal of Pharmaceutical and Biomedical Analysis, 1998-2002  
Pharmaceutical Sciences Advisory Committee, FDA 1997-2001, Chair 2000-2001  
Controlled Substances Advisory Committee, State of Indiana 1982-1998 (Chair 1995-8)  
Drug Substance Technical Committee, FDA-PQRI, 1997-present (Chair 1997-2001)  
National Academies of Sciences, Engineering, and Medicine, Topical Pain Creams, March 1, 2019 - present

## **Professional Service:**

American Chemical Society, Secretary-Treasurer, Vice-Chairman and Chairman Purdue Section, 1976-1982  
Controlled Substances Advisory Committee, 1982-1998, Secretary, 1987-1994, Chair, 1994-1998  
American Society of Pharmacognosy, Program Committee, 1977

Symposium Organizer American Chemical Society, Division of Medicinal Chemistry, 1987

Organizer, First and Third Midwest Organic Solid State Chemistry Symposia, 1988 (University of Illinois), 1990 (Purdue University), 2005 (Purdue University, with Ken Morris). Co-organizer, 2016 (Purdue University)

Organizer of a Short Course, entitled "Polymorphs and Solvates of Drugs," 1988 (Bradford, England), 1990 (Purdue University), 1992 (Bradford, England)

Reviewer numerous journals including JACS, J. Org. Chem., Acc. Chem. Res., J. Pharm. Sci., Pharm. Res., Crystal Growth and Design

Chair, NIPTE Abuse Deterrent Center of Excellence 2017 - present

### **University Committees:**

Athletic Affairs Committee, 1979-1984  
Computer Center Policy Committee, 1983-1988  
Commencement Committee, 1984-1989  
Development Committee, 1991-2  
Vision (Long Range Planning) Committee, 1993  
University Promotions Committee 1995-1998.  
Purdue University Faculty Senate 2007-2010 and 2012-2016.  
Global Academic Committee, 2018-Present

### **Departmental Committees:**

As Chair of two departments I have served on numerous departmental committees.

### **Graduate School Committees:**

M.D.-Ph.D., 1984-1988  
Area Committee, 1984-1988  
Computer Committee, 1984-1988  
Residency Review Committee, 1984-1988  
David Ross Fellowship Committee, 1984

### **Teaching Effort:**

#### **Courses Taught – Pharmacy and Doctor of Pharmacy Curriculum**

Pharmaceutical Solids, 1998-2001.

Regulatory Affairs, 1998-present.

MDCH 310 - Analytical Medicinal Chemistry, 1972-1997

MDCH 418 - Computers in Pharmacy, 1978-1988

IPPH 471 – Sterile Products – Instructor in Charge 2004-05, 2014

IPPH 363 – Industrial Pharmacy - 2008-2012 (Instructor in charge, 2010)

PHRM 898 – Dosage Forms I – Solid state, Tablets, Capsules – 2012-present, course coordinator 2017

PHRM 461 – Drug Discovery and Development II –Course coordinator or co-coordinator, 2014-present

#### **Courses Taught - Graduate Curriculum**

MDCH 614 - Advanced Medicinal Analysis, 1972-1997

IPPH 590/587 - Pharmaceutical Solids 2004 – 2018

MDCH 698, 699 - Directed research for M.S. and Ph.D. graduate students and post-doctoral associates. 1972 - Present

IPPH 521– Drug Development 2004 - 2014

IPPH 522 – Good Regulatory Practices 2004 – 2014

IPPH 562 – Pharmaceutical Manufacturing 2010

PHRM 46100 – Drug Discovery and Development II, 2013-present

ABE 52100 – Drug Development 2015 - present

ABE 52200 – Good Regulatory Practices, 2015-present

IT 50800 - Quality and Productivity in Industry and Technology

IT 57100 Project Management in Industry and Technology

**Teaching Programs Co-Founded – MS Degree in Biotechnology Innovation and Regulatory Sciences in the US and Africa (Joint with Professor Kari Clase, Ph. D.) originally Program in Regulatory and Quality Compliance, cofounded jointly with M. Schmidt, Ph. D.:**

This new area of specialization in the Agricultural and Biochemical Engineering Department focuses on creating leaders in biotechnology innovation and regulatory science, especially relating to pharmaceuticals. The curricula also addresses topics of innovation and integrates emerging technologies.

The program consists of 10 courses and a special project for a total of 30 credit hours. The array of courses will provide:

- an understanding of all aspects of quality
- an understanding of biotechnology innovation and regulatory science
- in-depth knowledge related to biotechnology and pharma
- knowledge on how to lead and manage operations within the industry

The degree format is tailored to student needs:

- Traditional, on-campus degree program in West Lafayette
- Blended online and weekend program
- In Africa in collaboration with Kilimanjaro School of Pharmacy, Moshi, Tanzania and Nelson Mandela, African Institute of Science and Technology, Arusha, Tanzania

**Sustainable Medicines in Africa (Joint with Sr. Zita Ekeocha, M.S. and Professor Kari Clase)**

The sustainable medicine program in Africa is aimed at addressing the problem of lack of access to high quality medicines in Africa. This program consists of: (1) Master’s degree in Biotechnology Innovation and Regulatory Science (Sr. Zita Ekeocha); (2) an actual GMP-level pharmaceutical manufacturing facility (2008 – 2020), and (3) a quality medicines laboratory equipped with HPLCs. The educational programs are aimed at providing source of well-trained manufacturing scientists for pharmaceutical industry in Tanzania and Africa. The GMP-level facility and GMP courses are used to teach manufacturing under strict quality control. The GMP facility served as a model for other such facilities throughout Sub-Saharan Africa. The feasibility of establishing a

sustainable medicine program in Tanzania is supported by the experience of the former Infusion Units Project in Tanzania, now known as Saint Luke Foundation (SLF). This program has manufactured and distributed infusion solutions throughout Tanzania since 1983. Additionally, the availability of trained personnel and a model facility will combat several current problems especially those related to counterfeited/poor quality medicines.

This Master's degree in Biotechnology Innovation and Regulatory Science is supported by Bill and Melinda Gates Foundation as an ANDi (African National Drug Innovation) Center for Pharmaceutical Manufacturing and Regulatory Training. This center is one of less than 50 centers in Africa.

### **Graduate Students and Postdoctoral Associates:**

M.S. (thesis) - E. Kreutzer (1976), S. VanEss (1977), B. Stewart (1978), G. Migliaccio (1979), G. Gibson-Clay (1979), J. Gomes (1979), P. Hoyos (1982), L. Morales (1991), H. Tat (1998), R. Alajlouni

Ph.D. - G. Dolch (1976), M.D. Tsai (1978), R. Clay (1979), J. Gomes (1981), H. Martinez (1983), I. Lassalle (1984), P. Sutton (1984), P. Toren (1985), J. Chaber (1986), D. Kessler (1986), P. Hoyos (1986), E. Kolodziej (1986), D. Carlson (1989), C. Chan (1990), P. Saindon (1991), K. Ray (1992), N. Sipahimalani (1992), Wu-Po Ma (1993), D. Nugyen (1993), P. Toma (1993), G. Stephenson (1994), M. Wahle (1997), W. Xu (1997), T. Borchardt (1997), V. Joshi (1998), X. He (1999), R. Te (2000), X. Chen (2000), Y. Hu (2000), Zhihui Qui (2001); Hui Li (2002); T. Davis (2003), A Gupta (2005), Chen Mao (2007), Faraj Atassi (2007), EunHee Lee (2007), Yuerong Hu (With L. Taylor) (2008); Niraj Trasi (2011), Ziyang Su (2011); Sumana Penumetcha (2011); Xin Chen (2012); Y. Song (2015), H. Nie (2017); Salma Salem (2019)

Postdoctoral Associates - P.Y. Siew (1976), C.T. Lin (1980), P. Perrier (1981), J. Stowell (1984), B. Tobias (1988), C. Chan (1990), C. Cox (1990), Kin-shan Huang (1995), R. Schlam (1999); N. Poendaev (2001-2003), D. Smith (2003-2006), Eun Hee Lee (2007-2010), Salma Salem 2020 - present

Current Graduate Students - None

Current Senior Research Associate – Daniel Smith, Ph. D.

### **Undergraduate Student Activities:**

Counselor for Pharmacy Students, 1978-1996.  
Faculty Fellow (Shreve Hall & Hillenbrand Hall), 1982-1997.  
Senior Faculty Fellow (Shreve Hall), 1986-1990.  
Senior Faculty Fellow (Hillenbrand Hall) 1993-1995  
Adopt a Student Program, College of Pharmacy, 2009-10

### **Research Interests:**

#### **Solid State Chemistry of Drugs/Pharmaceutical Solids**

Investigators: S. Byrn, Amrinder Singh

The overall goal of our research is to develop the field of Solid State Chemistry of Drugs so that all of the principles and factors governing solid state chemistry are understood. This knowledge is then used to predict and analyze all behaviors of solids observed during the drug development process and in formulations. Thus, the solid state chemistry of drugs is being studied to improve knowledge of the factors which affect this chemistry and to develop new methods of studying these reactions. At present, our group is focusing solid state structure using PDF function analysis of data from Argonne National Laboratory, and stability. We are also interested solid state desolvation reactions, solid state decarboxylation reactions, solid-solid reactions, and solid state rearrangements. These studies are important in that they will lead to better understanding of the mechanism of drug degradation and eventually to new approaches to stabilizing drugs. By carrying out research on the solid state chemistry of drugs it is hoped that new approaches and ideas for drug analysis including solid state NMR spectroscopy and X-ray diffraction will be developed. In addition, this research is aimed at providing new insight into drug stability and at developing methods for predicting drug stability. Furthermore, approaches to the production via crystallization of the desired drug form are an important component of these studies.

## **Processing and Manufacturing of Pharmaceuticals**

Investigators: S. Byrn

Approaches to understanding the molecular basis of pharmaceutical manufacturing are being developed. These approaches which include Raman mapping and EDS can in favorable cases provide information on the spatial location of all components in tablets and capsules. The effect of processing on the solid state chemistry of drugs and the stability of formulations is also being investigated. Particular emphasis is placed on the wet granulation and coating. Continuous manufacturing and manufacturing design are also being investigated especially for protease inhibitors and fixed dose combination drugs. The regulatory aspects of processing and manufacturing are also being emphasized.

## **Analysis of Amorphous Pharmaceuticals**

Investigators: S. Byrn

The structure of amorphous pharmaceuticals is not known and poorly understood. Pair distribution functions derived from X-ray powder diffraction measurements made at Argonne National Laboratories Synchrotron as well as solid state NMR measurements along with more conventional studies can provide phase diagrams and information on the functional groups and atom-atom distances involved in drug-drug and drug-polymer interactions present in amorphous materials. These methods will lead to the establishment of a rational design method for amorphous compositions. This bottom-up design approach focuses on amorphous protease inhibitors since these are the most bioavailable compositions. This new method will determine structural details of amorphous compositions by providing atom-atom distances and other structural parameters. We will use the atomic distances, and other parameters determined, to predict properties of these compositions including stability (failure to crystallize), dissolution rate, and bioavailability. This method is particularly important since amorphous drugs are now being used to cure HCV and as potential treatments for a range of other viral diseases besides HIV.

## **Abuse Deterrent Formulations of Opioids**

Investigators: Dan Smith

The goal of the abuser is to alter the opioid dosage from such that it provides a plasma concentration that is sufficient to induce euphoria. The abuse-deterrent dosage form is designed to minimize the feeling of euphoria when taken as prescribed by a patient, i.e. when using the medication as intended. However, a prescription drug abuser would try to modify the dosage form in a manner to increase the plasma concentration to a level that would induce euphoria. They can achieve this by increasing the rate of drug uptake. For example, they could crush a controlled release tablet, which would induce dose dumping when swallowed. They could change the route of administration. For example the abuser could crush a tablet and then try and inject or snort the contents of the crushed tablet. Thus, abuse deterrent formulations are investigated to identify the failure modes. This knowledge will lead to second generation formulations that are even more difficult to abuse than those currently on the market.

## **Engagement Program Co-Founded – Chao Center now Purdue GMP Center:**

The Chao Center is a self-supporting manufacturing facility located in the Purdue Research Park. A major donor, Dr. Allan Chao, established the Center with a very substantial gift of \$5.0 million. The Chao Center is involved in contract research and manufactures the anti-tuberculosis drug Seromycin for Lilly.

## **Publications (Books):**

Byrn, S.R., "Solid State Chemistry of Drugs," Academic Press, New York, New York, 1982.

Knevel, A.M., DiGangi, F.E., and Byrn, S.R., "Quantitative Pharmaceutical Chemistry," 7th Edition, Waveland Press, Inc., Prospect Heights, Illinois, 1983.

Byrn, S.R., Stowell, J.G., and Pfeiffer, R.R., "Solid State Chemistry of Drugs," 2<sup>nd</sup> Edition, SSCI Press, West Lafayette, IN, 1999

Byrn, S.R., Zografis, G., Chen, Xiaoming (Sean), "Solid State Properties of Pharmaceutical Materials," John Wiley and Co., Hoboken, NJ, 2017

### Publications (Book Co-Edited)

Templeton, Allen; Byrn, Stephen R.; Haskell, Roy J.; Prisinzano, Thomas E., "Discovering and Developing Molecules with Optimum Drug-Like Properties", AAPS Press, Springer, NY, NY 2016

### Publications:

1. Weingarten, H., Miles, M.G., Byrn, S.R., and Hobbs, C.F., *J. Am. Chem. Soc.*, 1967, **89**, 5874, "Amination of  $\beta$ -Dicarbonyl Compounds with Tetrakis (dimethylamino) Titanium."
2. Curtin, D.Y. and Byrn, S.R., *J. Am. Chem. Soc.*, 1969, **91**, 1865, "Stereoisomerism at the Oxygen:Carbon Single Bond Due to Hydrogen Bonding. Structures of the Yellow and White Crystalline Forms of Dimethyl 3,6-Dichloro-2,5-Dihydroxy-terephthalate."
3. Curtin, D.Y. and Byrn, S.R., *J. Am. Chem. Soc.*, 1969, **91**, 6102, "Structures in Solution of the Yellow and White Forms of Dimethyl 3,6-Dichloro-2,5-Dihydroxyterephthalate."
4. Curtin, D.Y., Byrn, S.R., and Pendergrass, D.B., Jr., *J. Org. Chem.*, 1969, **34**, 3345, "Thermal Rearrangement of Arylazotribenzoyl-methanes in the Solid State. Examination with Differential Thermal Analysis."
5. Byrn, S.R., Maverick, E., Muscio, O.J., Trueblood, K.N., and Jacobs, T.L., *J. Am. Chem. Soc.*, 1971, **93**, 6680, "The Structure of Two Head to Head Allene Dimers."
6. Byrn, S.R., Curtin, D.Y., and Paul, I.C., *J. Am. Chem. Soc.*, 1972, **94**, 890, "The X-Ray Crystal Structure of the Yellow and White Forms of Dimethyl 3,6-Dichloro-2,5-Dihydroxyterephthalate and a Study of the Conversion of the Yellow Form to the White Form in the Solid State."
7. Wang, A.H.J., Misavage, R.J., Byrn, S.R., and Paul, I.C., *J. Am. Chem. Soc.*, 1972, **94**, 7100, "The Crystal and Molecular Structure of 1-Azabicyclo (3.3.3) Undecane Hydrochloride. Correlation of Molecular Dimensions with Spectroscopic Properties."
8. Byrn, S.R., *Biochemistry*, 1974, **13**, 5186, "The Cation-Binding Properties of Gramicidin."
9. Byrn, S.R., *Indiana Pharmacist*, 1974, **79**, "Caution Advised in Handling Neutral Red Dye."
10. Byrn, Stephen R., *Amer. Jour. Pharm. Ed.*, 1975, **40**, 295, "Combined BS:MS Programs: Alternatives for Pharmacy Students."
11. Byrn, S.R., *J. Pharm. Sci.*, 1976, **65**, 1-22, "Mechanisms of Solid-State Reactions of Drugs."
12. Byrn, S.R. and Lin, C.T., *J. Am. Chem. Soc.*, 1976, **98**, 4004, "The Effect of Crystal Packing and Defects on the Desolvation of Hydrate Crystals of Caffeine and L(-)-1,4-cyclohexadiene-1-alanine."
13. Byrn, S.R., Graber, C.W., and Midland, S.L., *J. Org. Chem.*, 1976, **41**, 2283, "Comparison of the Solid State and Solution Conformation of Methapyriline, Tripeleminamine, Diphenhydramine, Histamine and Choline. The IR-X-Ray Method for Determination of Solution Conformation."
14. Byrn, S.R. and Siew, P.Y., *J. Chem. Soc.*, 1977, Perkin II, 144, "The Structure and Conformation of  $\beta$ -Thiodan in the Solid State and in Solution. Application of the IR-X-Ray Method."

15. Weintraub, H.J.R., Tsai, M.D., Byrn, S.R., Chang, C.-j., and Floss, H.G., *Int. J. Quantum Chem., Quantum Biology Symp.*, 1976, **3**, 99, "Conformational Analysis of Some Pyridoxal Amino Acid Schiff Bases."
16. Stamos, I.K., Howie, G.A., Manni, P.E., Haws, W.J., Byrn, S.R., and Cassady, J.M., *J. Org. Chem.*, 1977, **42**, 1703, "Synthesis and Structures of Dilactones Related to Anemonin."
17. Otten, J.G., Yeh, C.S., Byrn, S.R., and Morrison, H.A., *J. Amer. Chem. Soc.*, 1977, **99**, 6353, "Solution Phase Photodimerization of Tetramethyl Uracil. Further Studies of Ground-State Aggregates."
18. Byrn, S.R. and Dolch, G.D., *J. Pharm. Sci.*, 1978, **67**, 688, "Analysis of the Binding of Daunomycin and Doxorubicin to DNA Using Computerized Curve Fitting Procedures."
19. Lin, C.T., Siew, P.Y., and Byrn, S.R., *J. Chem. Soc.*, 1978, Perkin II, 957, "Solid State Dehydrochlorination and Decarboxylation Reactions I. Reactions of *p*-Aminosalicylic Acid Hydrochloride and *p*-Aminosalicylic Acid and the Crystal Structure of *p*-Aminosalicylic Acid."
20. Lin, C.T., Siew, P.Y., and Byrn, S.R., *J. Chem. Soc.*, 1978, Perkin II, 963, "Solid State Dehydrochlorination and Decarboxylation Reactions II. Reactions of Three Crystal Habits of *p*-Aminosalicylic Acid Hydrochloride and the Crystal Structure of *p*-Aminosalicylic Acid Hydrochloride."
21. Tsai, M.D., Weintraub, H.J.R., Byrn, S.R., Chang, C.-j., Floss, H.G., *Biochemistry*, 1978, **17**, 3183, "Conformational-Reactivity Relationships for Pyridoxal Schiff's Bases of Amino Acids."
22. Tsai, M.D., Byrn, S.R., Chang, C.-j., Floss, H.G., and Weintraub, H.J.R., *Biochemistry*, 1978, **17**, 3177, "Conformational Analysis of Pyridoxal Schiff's Bases. NMR Studies of the Conformation about the C<sub>4</sub>-C<sub>4'</sub>, C-C, and N-C Bonds of the Pyridoxal Schiff's Bases of Amino Acids."
23. Cassady, J.M., Byrn, S.R., Stamos, I.K., Evans, S.M., and McKenzie, A., *J. Med. Chem.*, 1978, **21**, 815, "Potential Antitumor Agents. Synthesis, Reactivity and Cytotoxicity of Alpha-Methylene Carbonyl Compounds."
24. Lin, C.T. and Byrn, S.R., *Tetrahedron Letters*, 1978, **1975**, "Solvolysis of Hydrazobenzene in Methyl Iodide."
25. Lin, C.T. and Byrn, S.R., *Mol. Cryst. and Liq. Cryst.*, 1979, **50**, 99, "Desolvations of Solvated Organic Crystals."
26. Lin, C.T. and Byrn, S.R., *Tet. Lett.*, 1979, **4623**, "Solid Gas Reaction of Hydrazobenzene with Methyl Iodide."
27. Migliaccio, G.P. and Byrn, S.R., *J. Pharm. Sci.*, 1981, **70**, 284, "Comparisons of the Rotamer Populations of Nialamide, Chloroquine and Azaperone in the Solid State and in Solution."
28. Siew, P.Y. and Byrn, S.R., *J. Pharm. Sci.*, 1981, **70**, 280, "The Crystal Structure and Solid State Behavior of Aspirin Anhydride."
29. Pyne, S.G., Hensel, M.J., Byrn, S.R., McKenzie, A.T., and Fuchs, P.L., *J. Amer. Chem. Soc.*, 1980, **102**, 5960, "Cytochalasin Support Studies, Chiral and Stereochemical Control via an Intramolecular Diels-Alder Reaction of a (Z)-Diene."
30. Migliaccio, G.P., Shieh, T.L., Byrn, S.R., Hathaway, B.A., and Nichols, D.E., *J. Med. Chem.*, 1981, **70**, 284, "Comparison of Solution Conformational Preferences for the Hallucinogens Bufotenin and Psilocin using 360 MHz Proton NMR Spectroscopy."
31. Chang, C.-j., Gomes, J.D., and Byrn, S.R., *J. Amer. Chem. Soc.*, 1981, **103**, 2892, "Chemical Modification of Deoxyribonucleic Acids: A Direct Study by NMR Spectroscopy."
32. Clay, G.G., Byrn, S.R., and Heinstein, P.H., *J. Pharm. Sci.*, 1982, **71**, 467, "The Interaction of Gramacitin with Nucleic Acids and Pyruvate Decarboxylase."

33. Perrier, P. and Byrn, S.R., *J. Org. Chem.*, 1982, **47**, 4671, "The Influence of Crystal Packing on the Desolvation of Purine and Pyrimidine Hydrates."
34. Perrier, P. and Byrn, S.R., *J. Org. Chem.*, 1982, **47**, 4677, "Dehydration of Glucuronamide Hydrate. Confirmation of the Predicted Influence of Crystal Packing on Dehydration Reactions."
35. Lin, C.T., Perrier, P., Clay, G.G., Sutton, P.A., and Byrn, S.R., *J. Org. Chem.*, 1982, **47**, 2978, "Solid State Photooxidation of Cortisol-21-tert-butylacetate to Cortisone-21-tert-butylacetate."
36. Shieh, T.L. and Byrn, S.R., *J. Med. Chem.*, 1982, **25**, 403, "The Solution Conformation of the Thermolysin Inhibitors Carbobenzoxy-L-phenylalanine and  $\beta$ -Phenylpropionyl-L-phenylalanine and Comparison of the Solution Conformation to the Enzyme Bound Conformation."
37. Clay, R.J., Knevel, A.M., and Byrn, S.R., *J. Pharm. Sci.*, 1982, **71**, 1289, "The Desolvation and Oxidation of Crystals of Dialuric Acid Monohydrate."
38. Shieh, T.L., Lin, C.T., McKenzie, A.T., and Byrn, S.R., *J. Org. Chem.*, 1983, **26**, 3103, "Relationship Between the Solid State and Solution Conformations of  $\beta$ -benzylaminocrotonate."
39. Donaldson, R.E., Saddler, J.C., Byrn, S.R., McKenzie, A.T., and Fuchs, P.L., *J. Org. Chem.*, 1983, **48**, 2167, "A Triply Convergent Total Synthesis of L-(-)-Prostaglandin E<sub>2</sub>."
40. Chang, C.J., DaSilva Gomes, J., and Byrn, S.R., *J. Org. Chem.*, 1983, **48**, 5151, "Chemical Modification of Deoxyribonucleic Acids: A Direct Study by Carbon-13 Nuclear Magnetic Resonance Spectroscopy."
41. Stewart, B.S., Midland, S.L. and Byrn, S.R., *J. Pharm. Sci.*, 1984, **73**, 1322-1323, "Degradation of Crystalline Ergocalciferol."
42. Ebrahim El-Zayat, A.A., Ferringni, N.R., McCloud, T.G., McKenzie, A.T., Byrn, S.R., Cassady, J.M., Chang, C.-j., and McLaughlin, J.L., *Tetrahedron Letters*, 1985, **26**, 955, "Goniothalenol: A Novel, Bioactive, Tetrahydrofurano-2-pyrone from *Goniothalamus giganteus* (Annonaceae)."
43. Mossa, J.S., Cassady, J.M., Antoun, M.D., Byrn, S.R., McKenzie, A.T., Kozlowski, J.F. and Main, P., *J. Org. Chem.*, 1985, **50**, 916-918, "Saudin, a Hypoglycemic Diterpenoid with a Novel 6,7-Secolabdane Carbon Skeleton, from *Cluytia richardiana*."
44. Byrn, S.R., Gray, G., Frye, J., and Pfeiffer, R.R., *J. Pharm. Sci.*, 1985, **73**, 565-568, "Analysis of Solid-State Carbon-13 NMR Spectra of Polymorphs (Benoxaprofen and Nabilone) and Pseudopolymorphs (Cefaclor)."
45. Byrn, S.R., Chapter 29. Solid State Organic Chemistry and Drug Stability, Annual Reports in Medicinal Chemistry, 1986, 287-294.
46. Byrn, S.R., McKenzie, A.T., Hassan, M.M.A., and Al-Badr, A.A., *J. Pharm. Sci.*, 1986, **75**, 596-600, "Conformation of Glyburide in the Solid State and in Solution."
47. Byrn, S.R. and Kessler, D.W., *Tetrahedron*, 1987, **43**, 1335-1343, "The Solid State Reactivity of the Crystal Forms of Hydrocortisone Esters."
48. Sutton, P.A. and Byrn, S.R., *J. Pharm. Sci.*, 1987, **76**, 253-258, "The Crystal Structure of Two Crystal Forms of 9 $\alpha$ -Fluorocortisol Acetate. Variation of the Conformation of the A Ring of Steroids due to Crystal Packing."
49. Byrn, S.R., Perrier, P., Lin, C.T., Martinez, H., and Pfeiffer, R.R., *Pharmaceutical Research*, 1987, **4**, 137-141, "The Solid State Decarboxylation of the Diammonium Salt of Moxalactam."
50. Ho, D.K., McKenzie, A.T., Byrn, S.R., and Cassady, J.M., *J. Org. Chem.*, 1987, **52**, 342-347, "O<sup>5</sup>-Methyl-(q)-2'R,3'S-Psorospermin."
51. Hedstrand, D.M., Byrn, S.R., McKenzie, A.T. and Fuchs, P.L., *J. Org. Chem.*, 1987, **52**, 592-598, "Use of an Axial  $\beta$ -Face Thiomethyl Control Element in Intramolecular Conjugate Additions. Synthesis of a Tricyclic Bruceantin Precursor."

52. Byrn, S.R., Sutton, P.A., and Tobias, B., *J. Am. Chem. Soc.*, 1988, **110**, 1609-1614, "The Crystal Structure, Solid State NMR Spectra, and Oxygen Reactivity of Five Crystal Forms of Prednisolone tert-butylacetate."
53. Riggs, Robert M., McKenzie, Ann T., Byrn, Stephen R., Nichols, David E., Foreman, Mark M., and Truex, Lewis L., *J. Med. Chem.*, 1987, **30**, 1914-18, "Effect of  $\beta$ -Alkyl Substitution on D-1 Dopamine Agonist Activity: Absolute Configuration of  $\beta$ -Methyldopamine."
54. Habib, A.M., Ho, David K., Masuda, S., McCloud, T., Reddy, K.S., Aboushoer, M., McKenzie, A., Byrn, S. R., Chang, Ching Jer, and Cassady, John M. *J. Org. Chem.*, 1987, **52**, 412-18, "Structure and Stereochemistry of Psorospermin and Related Cytotoxic Dihydrofuranoxanthenes from *Psorospermum febrifugum*."
55. Mossa, Jaber S., Cassady, John M., Kozlowski, John F., Zennie, Thomas M., Antoun, Mikhail D., Pellechia, Marianne G., McKenzie, Ann T., and Byrn, Stephen R., *Tetrahedron Lett.*, 1988, **29**, 3627-30, "Novel 6,7-seco-6,11-cyclolabdane Diterpenes from *Cluytia richardiana*."
56. Lassalle, I., Hoyos, P.H., Byrn, S.R., Weith, H.L., *Nucleosides and Nucleotides*, 1989, **6**, 1071, "Sequence Preference of Acridine Interaction with Single and Double Stranded Octadeoxyribonucleotides."
57. Cushman, M., Patrick, D., Toma, P., Byrn, S.R., *Tetrahedron Letters*, 1989, **30**, 7161-7164, "A Novel ring System from Intramolecular Oxidative Cyclization of 8-(4-Pentenyl)dihydroberberine."
58. Martinez, H., Byrn, S. R., Pfeiffer, R.R., *Pharm. Res.*, 1990, **7**, 147-153, "Solid State Chemistry and Crystal Structure of Cefaclor Dihydrate."
59. Shieh, T.L., Hoyos, P., Kolodziej, E., Stowell, J.G., Baird, W.M., Byrn, S. R., *J. Med. Chem.*, 1990, **33**, 1225-1230, "Properties of the Nucleic Acid Photoaffinity Labeling Agent, 3-Azido-Amsacrine."
60. Byrn, S.R., Ray, K., Stowell, J.G., Toma, P., *Acta Cryst., Sect. C*, 1990, **C46**, 1573-1576, "Crystal Structure of Acridinyl Ethanol."
61. Alkofahi, A., Ma, W.W., McKenzie, A.T., Byrn, S.R., McLaughlin, J.L., *J. Natural Products*, 1989, **52**, 1371-1373.
62. Ma, W.W., Anderson, J.E., McKenzie, A.T., Byrn, S.R., McLaughlin, J.L., and Hudson, M.S., *J. Nat. Prod.*, 1990, **63**, 1009-1014, "Tubulosine: An Antitumor Constituent of *Pogonopus speciosus*."
63. Pidgeon, C., Weith, H.L., Darbishire-Weith, D., Cushman, M., Byrn, S.R., Chen, J.-K., Stowell, J.G., Ray, K., and Carlson, D., *Anal. New York Acad. Sci.*, 1991, **616**, 593-596, "Synthesis and Liposome Encapsulation of Antisense Oligonucleotides-Intercalator Conjugates."
64. Byrn, S.R., Tobias, B., Kessler, D., Frye, J., Sutton, P. Saindon, P., and Kozlowski, J., *Trans. Amer. Cryst. Assoc.*, 1989, **24**, 41-54, "Relationship Between Solid State NMR and Crystal Structures of Polymorphs and Solvates of Drugs."
65. Byrn, S.R., Carlson, D.V., Chen, J.K., Cushman, M.S., Goldman, M.E., Ma, W.P., Pidgeon, C.L., Ray, K.A., Stowell, J.G., and Weith, H.L., *Adv. Drug. Delivery Rev.*, **6**, 1991, 287-308, "Drug-Oligonucleotide Conjugates."
66. Stowell, J.G., Toma, P.H., and Byrn, S.R., *Acta Cryst.*, **C47**, 1991, 1635-1637, "9,10-Dihydro-9-methylacridine."
67. Stowell, J.G., Toma, P.H., and Byrn, S.R., *Acta Cryst.*, **C47**, 1991, 1637-1640, "9-Phenylacridine and 9-Phenylacridine Hydrochloride."
68. Stowell, J.G., Toma, P.H., and Byrn, S.R., *Biorg. and Med. Chem. Letters*, **2**, 1992, 185-190, "The Structure of MK-571 (Form I) at 170K and Conformational Analysis by Molecular Modeling."
69. Saindon, P.J., Cauchon, N.S., Sutton, P.A., Chang, C.J., Peck, G.E., and Byrn, S.R., *Pharm. Res.*, **10**, 1993, 197-203, "Solid-State NMR Spectra of Pharmaceutical Dosage Forms."

70. Dalla Riva Toma, J.M., Toma, P.H., Fanwick, P.E., Bergstrom, D.E., Byrn, S.R., *J. Cryst. and Spect. Res.*, **23**, 1993, 41-47. Photochemical Synthesis and Crystal Structure of two Potentially Useful Metal Carbonyl Complexes: Pentacarbonyl ( $\eta^2$ -*cis*-cyclooctene)-tungsten(0) and tetracarbonylbis ( $\eta^2$ -*cis*-cyclooctene)-tungsten(0).
71. Toma, P.H., Nguyen, D.N., Byrn, S.R., *Acta Cryst.*, **C49**, 1993, 914-916. 9-Chloro-2-ethoxy-6-nitroacridine.
72. Stephenson, G.A., Stowell, J.G., Toma, P.A., Dorman, D.E., Greene, J.R., and Byrn, S.R., *J. Am. Chem. Soc.*, **116**, 5766 (1994). Solid-state analysis of Polymorphs, Isomorphs, and Solvated Forms of Dirithromycin.
73. Ma, Wu Po, Hamilton, S.E., Stowell, J.G., Byrn, S.R., and Davisson, V.J., *Biorg. & Med. Chemistry*, **2**, 169-179 (1994). Sequence Specific Cleavage of Messenger RNA by a Modified Ribonuclease H.
74. Byrn, S.R., Pfeiffer, R.R., Stephenson, G., Grant, D.J.W., and Gleason, W.B., *Chemistry of Materials*, **6**, 1148 (1994). Solid-State Pharmaceutical Chemistry.
75. Toma, P.H., Kelley, M.P., Borchardt, T.B., Byrn, S.R., and Kahr, B., *Chemistry of Materials*, **6**, 1317 (1994). Chromoisomers and Polymorphs of 9-Phenylacridinium Hydrogen Sulfate.
76. Huang, K.-S., Britton, D., Etter, M.C., and Byrn, S.R., *J. Materials Chemistry*, 1995, **5**, 379-383. Polymorphic Characterization and Structural Comparisons of the NLO Active and Inactive Forms of Two Polymorphs of 1,3-Bis(m-nitrophenyl)urea.
77. Byrn, S.R., Pfeiffer, R.R., Ganey, M., Hoiberg, C., and Poochikian, G., *Pharm Res.* **12**, 945-954 (1995). Pharmaceutical Solids: A Strategic approach to Regulatory Considerations.
78. Saleki-Gerhardt, A., Stowell, J.G., Byrn, S.R., and Zografis, G., *J. Pharm. Sci.* **84**, 318-323 (1995). Hydration and Dehydration of Crystalline and Amorphous Forms of Raffinose.
79. Byrn, S. R. and J. G. Stowell *J. Drug Targeting* **3**(4): 239-41 (1995). "Drug targeting using conjugates: the importance of pharmaceutical chemistry."
80. Akers, M. J., N. Milton, et al. *Pharm. Res* **12**(10): 1457-61 (1995). "Glycine crystallization during freezing: the effects of salt form, pH, and ionic strength."
81. Huang, K. S., D. Britton, Etter, M.C., and Byrn, S.R.; *J. Mater. Chem* **5**(3): 379-83 (1995). "Polymorphic characterization and structural comparisons of the non-linear optically active and inactive forms of two polymorphs of 1,3-bis(m-nitrophenyl)urea."
82. Huang, K. S., D. Britton, Etter, M.C., and Byrn, S.R.; *J. Mater. Chem* **6**(2): 123-9 (1996). "Synthesis, polymorphic characterization and structural comparisons of the non-linear optically active and inactive forms of polymorphs of 3-(nitroanilino)cycloalk-2-en-1-ones."
83. Morales, L., Stowell, J.G, and Byrn, S.R.; *Rev. Boliv. Quim* **12**(1): 59-67(1995). "Alkyl substituted acridine synthesis. I. Organometallic synthesis."
84. Stephenson, G. A., Borchardt, T. B., Bunnell, C., Snorek, S., Bowyer, J., Yu, L., and Byrn, S, *J. Pharm. Sci* **84**(11): 1385-6. (1995). "Conformational and Color Polymorphism of 5-Methyl-2-[(2- nitrophenyl)amino]-3-thiophenecarbonitrile."
85. Wahle, M.C., Stowell, J.G., and Byrn, S.R., *Acta Crystallogr., Sect. C, Cryst. Struct. Commun.*, **c52**, 325-8 (1996). "Sodium 3 $\alpha$ , 7 $\alpha$ , 12 $\alpha$ -trihydroxy-5 $\beta$ -cholan-24-oate ethanolate (sodium cholate ethanolate)."
87. Wahle, M.C., and Byrn, S.R., *Acta Crystallogr., Sect. C, Cryst. Struct. Commun.*, **C52**, 2495-2499 (1996). "Sodium Cholate Methanolate and Sodium Cholate 2-Propanolate."
88. Wahle, M.C. and Byrn, S.R., *Acta Crystallogr., Sect. C, Cryst. Struct. Commun.*, **C52**, 2500-2502 (1996). "3 $\alpha$ , 7 $\alpha$ , 12 $\alpha$ -Trihydroxy-5 $\beta$ -cholan-24-oic Acid Methyl Ester Ethanolate (Methyl Cholate Ethanolate)."

89. Stephenson, G.A., Wozniak, T.J., Stowell, J.G., and Byrn, S.R., *J. Mol. Struct.*, 380, 93-100 (1996). "Nizatidine, N-[2-[[[2[(dimethylamino)methyl]-4-thiazoyl]methyl]thio]ethyl]-N'-methyl-2-nitro-1,1-ethenediamine."
90. Stephenson, Gregory A.; Pfeiffer, Ralph R.; Byrn, Stephen R., *Int. J. Pharm.*, 146(1), 93-99 (1997). Solid-state investigation of the tautomerism of acetohexamide.
91. Wahle, Mark C. and Byrn, Stephen R., *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, C53(3), 334-339 (1997). Hydrated structures of N-methylated cholamide derivatives.
92. Kim, Chinpal; MacKellar, Warren C.; Cho, NaMi; Byrn, Stephen R. ; Morre, D. James, *Biochim. Biophys. Acta*, 1324(2), 171-181 (1997). Impermeant antitumor sulfonylurea conjugates that inhibit plasma membrane NADH oxidase and growth of HeLa cells in culture. Identification of binding proteins from sera of cancer patients.
93. Wahle, Mark C.; Fanwick, Phillip E.; Byrn, Stephen R., *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, C53(4), 480-482 (1997). Cholamide dihydrate.
94. Shalaev, Evgenyi Yu.; Byrn, Stephen R.; Zografis, George, *Int. J. Chem. Kinet.*, 29(5), 339-348 (1997). Single-phase and heterophase solid-state chemical kinetics of thermally induced methyl transfer in tetraglycine methyl ester.
95. Huang, Kin-Shan; Britton, Doyle; Etter, Margaret C.; Byrn, Stephen R., *J. Mater. Chem.*, 7(5), 713-720 (1997). A novel class of phenol-pyridine co-crystals for second harmonic generation.
96. Stahly, G. Patrick; McKenzie, Ann T.; Andres, Mark C.; Russell, Catherine A.; Byrn, Stephen R.; Johnson, Pete , *J. Pharm. Sci.*, 86(8), 970-971 (1997). Determination of the Optical Purity of Ibuprofen Using X-ray Powder Diffraction.
97. Shalaev, Evgenyi Yu.; Shalaeva, Marina; Byrn, Stephen R.; Zografis, George, *Int. J. Pharm.*, 152(1), 75-88 (1997). Effects of processing on the solid-state methyl transfer of tetraglycine methyl ester.
98. Stephenson, Gregory A.; Stowell, Joseph G.; Toma, Pascal H.; Pfeiffer, Ralph R.; Byrn, Stephen R., *J. Pharm. Sci.*, 86(11), 1239-1244 (1997). Solid-State Investigations of Erythromycin A Dihydrate Structure, NMR Spectroscopy, and Hygroscopicity.
99. Xu, Wei; Wahle, Mark C.; Stowell, Joseph G.; Byrn, Stephen R., *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, C53(12), 1917-1919 (1997). Spirapril hydrochloride hydrate.
100. Joshi, Vidya; Stowell, Joseph G.; Byrn, Stephen R. *Mol. Cryst. Liq. Cryst. Sci. Technol., Sect. A*, 313, 265-270 1998. Solid-state stability of indomethacin solvates.
101. Borchardt, Thomas B.; Stowell, Joseph G.; Byrn, Stephen R. *Mol. Cryst. Liq. Cryst. Sci. Technol., Sect. A*, 313, 271-276 (English) 1998. The crystallization of 5-methyl-2-[(2-nitrophenyl)amino]-3-thiophenecarbonitrile in the presence of structurally similar compounds.
102. Morris, K.R., Nail, S.L., Peck, G.E., Byrn, S.R., Griesser, U.J., Stowell, J.G., Hwang, S-J, Park, K, "Advances in pharmaceutical materials and processing", Pharmaceutical Science and Technology Today, Volume 1, No. 6, September 1998.
103. Smith, Jay; MacNamara, Ernesto; Raftery, Daniel; Borchardt, Thomas; Byrn, Stephen J. *Am. Chem. Soc.*, 120(45), 11710-11713 (English) 1998. Application of Two-Dimensional <sup>13</sup>C Solid-State NMR to the Study of Conformational Polymorphism.
104. Chongprasert, Suchart; Griesser, Ulrich J.; Bottorff, Arthur T.; Williams, N. Adeyinka; Byrn, Stephen R., Nail, Steven L. *J. Pharm. Sci.*, 87(9), 1155-1160 Effects of Freeze-Dry Processing Conditions on the Crystallization of Pentamidine Isethionate.

105. Yu, Lian; Stephenson, Gregory A.; Mitchell, Christine A.; Bunnell, Charles A.; Snorek, Sharon V.; Bowyer, J. Joe; Borchardt, Thomas B.; Stowell, Joseph G.; Byrn, Stephen R. J. *Am. Chem. Soc.*, 122(4), 585-591, 2000. Thermochemistry and Conformational Polymorphism of a Hexamorphic Crystal System.
106. Guo, Yushen; Byrn, Stephen R., Zografi, George; *Pharm. Res.*, 17(8), 930-935 2000. Effects of lyophilization on the physical characteristics and chemical stability of amorphous quinapril hydrochloride.
107. Guo, Yushen; Byrn, Stephen R., Zografi, George; *J. Pharm. Sci.*, 89, 128-143, 2000. Physical characteristics and chemical degradation of amorphous quinapril hydrochloride.
108. Morris, Kenneth R.; Stowell, Joseph G.; Byrn, Stephen R.; Placette, Allen W.; Davis, Tiffani D.; Peck, Garnet E.; *Drug Dev. Ind. Pharm.*, 26(9), 985-988, 2000. Accelerated fluid bed drying using NIR monitoring and phenomenological modeling.
109. Zografi, Z., Byrn, S.R., [Symposium on the Properties of Water in Foods], Helsinki, Finland, May 30-June 4, 1998, Meeting Date 1998, 397-410. Editor(s): Roos, Yrjo H.; Leslie, R. B.; Lillford, Peter J. Technomic Publishing Co., Inc.: Lancaster, Pa. (English) 1999. The effects of residual water on solid-state stability of drugs and drug products.
110. He, Xiaorong; Griesser, Ulrich J.; Stowell, Joseph G.; Borchardt, Thomas B.; Byrn, S.R. ; *J. Pharm. Sci.*, 90, 371, 2001. Conformational color polymorphism and control of crystallization of 5-methyl-2-[(4-methyl-2-nitrophenyl)amino]-3-thiophenecarbonitrile.
111. He, Xiaorong; Stowell, Joseph G.; Morris, Kenneth R.; Pfeiffer, Ralph R.; Li, Hui; Stahly, G. Patrick; Byrn, Stephen R.; Stabilization of a Metastable Polymorph of 4-Methyl-2-nitroacetanilide by Isomorphic Additives. *Crystal Growth and Design*, 1, 305-312, 2001.
112. Byrn, S. R.; Xu, W.; Newman, A. W.; Chemical reactivity in solid-state pharmaceuticals: formulation implications. *Advanced Drug Delivery Reviews*, 48(1), 115-136, 2001.
113. Pagola, S.; Stephens, P. W.; He, X.; Byrn, S. R.; Crystal structure solution of the dark red, light red and orange polymorphs of 5-methyl-2-[(2-nitro-4-methylphenyl)amino]-3-thiophenecarbonitrile by high resolution X-ray powder diffraction and simulated annealing techniques. *Materials Science Forum*, 378-381(Pt. 2, EPDIC 7, Part 2), 789-794 (English) 2001.
114. Reutzel-Edens, Susan M.; Bush, Julie K.; Magee, Paula A.; Stephenson, Greg A.; Byrn, Stephen R.; Anhydrates and Hydrates of Olanzapine: Crystallization, Solid-State Characterization, and Structural Relationships. *Growth & Design*, 3(6), 897-907, 2003
115. Griesser, Ulrich J.; Morris, Kenneth R.; Byrn, Stephen R.; Stowell, Joseph G. X-ray Diffraction and Solid-State NMR Investigation of the "Single-Crystal to Single-Crystal Dehydration of Thiamine Hydrochloride." *Crystal Growth & Design*, 3(6), 997-1004, 2003
116. Tishmack, Patrick A.; Bugay, David E., Byrn, Stephen R., "Solid-state nuclear magnetic resonance spectroscopy-pharmaceutical applications." *Journal of Pharmaceutical Sciences*, 92(3), 441-474 (English) 2003
117. Chen, Xiaoming; Morris, Kenneth R.; Griesser, Ulrich J.; Byrn, Stephen R. ; Stowell, Joseph G. "Reactivity Differences of Indomethacin Solid Forms with Ammonia Gas." *Journal of the American Chemical Society*, 124(50), 15012-15019, 2002.
118. Newman, Ann W.; Byrn, Stephen R., "Solid-state analysis of the active pharmaceutical ingredient in drug products." *Drug Discovery Today*, 8(19), 898 -905.

119. Davis, Tiffani D.; Morris, Kenneth R.; Huang, Huapeng; Peck, Garnet E.; Stowell, Joseph G.; Eisenhauer, Bradley J.; Hilden, Jon L.; Gibson, David; Byrn, Stephen R., "In situ Monitoring of Wet Granulation Using Online X-Ray Powder Diffraction," *Pharmaceutical Research*, 20(11), 1851-1857, 2003.
120. Davis, Tiffani D.; Peck, Garnet E.; Stowell, Joseph G.; Morris, Kenneth R.; Byrn, Stephen R., "Modeling and Monitoring of Polymorphic Transformations During the Drying Phase of Wet Granulation." *Pharmaceutical Research*, 21 (5), 860-866, 2004.
121. Stephen R. Byrn, Simon Bates, and Igor Ivanisevic. Regulatory Aspects of X-ray Powder Diffraction, Part I. *American Pharmaceutical Review*, 8(3), 55-59 May/June 2005.
122. Stephen R. Byrn, Simon Bates, and Igor Ivanisevic. Regulatory Aspects of X-ray Powder Diffraction, Part II. *American Pharmaceutical Review*, 8(4), 137-141 Jul/Aug 2005.
123. Stephen Byrn, Kenneth Morris, Shawn Comella, Reducing Time to Market with A Science-Based Product Management Strategy, *Pharmaceutical Technology*, Aug. 1, 2005.
124. Terakita, Akira; Byrn, Stephen R., Structure and physical stability of hydrates and thermotropic mesophase of calcium benzoate. *Journal of Pharmaceutical Sciences*, 95(5), 1162-1172, 2006.
125. McBride, Jennifer M.; Smith, Daniel T.; Byrn, Stephen R.; Borgens, Richard B.; Shi, Riyi Dose responses of three 4-aminopyridine derivatives on axonal conduction in spinal cord trauma. *European Journal of Pharmaceutical Sciences*, 27(2-3), 237-242, 2006.
126. Qiu, Zhihui; Stowell, Joseph G.; Cao, Wenjin; Morris, Kenneth R.; Byrn, Stephen R.; Carvajal, M. Teresa. Effect of milling and compression on the solid-state Maillard reaction. *Journal of Pharmaceutical Sciences*, 94(11), 2568-2580, 2005.
127. Qiu, Zhihui; Stowell, Joseph G.; Morris, Kenneth R.; Byrn, Stephen R.; Pinal, Rodolfo Kinetic study of the Maillard reaction between metoclopramide hydrochloride and lactose. *International Journal of Pharmaceutics*, 303(1-2), 20-30, 2005.
128. Chen, Xiaoming; Griesser, Ulrich J.; Te, Ruth L.; Pfeiffer, Ralph R.; Morris, Kenneth R.; Stowell, Joseph G.; Byrn, Stephen R., Analysis of the acid-base reaction between solid indomethacin and sodium bicarbonate using infrared spectroscopy, X-ray powder diffraction, and solid-state nuclear magnetic resonance spectroscopy. *Journal of Pharmaceutical and Biomedical Analysis*, 38(4), 670-677, 2005.
129. Smith, Daniel T.; Shi, Riyi; Borgens, Richard B.; McBride, Jennifer M.; Jackson, Kevin; Byrn, Stephen R. Development of novel 4-aminopyridine derivatives as potential treatments for neurological injury and disease. *European Journal of Medicinal Chemistry*, 40(9), 908-917, 2005.
130. Byrn, Stephen R.; Pfeiffer, Ralph R.; Stowell, Joseph G. Polymorphs, regulations, crystallization, and solid-state chemistry. *American Pharmaceutical Review*, 5(3), 92, 94, 96-99, 2002.
131. Hu, Yuerong; Wikstrom, Hakan; Byrn, Stephen R.; Taylor, Lynne S. Analysis of the effect of Particle size on Polymorphic Quantitation by Raman spectroscopy. *Applied Spectroscopy*, 60(9), 977-984, 2006.
132. Atassi, Faraj; and Byrn, Stephen R. General Trends in the Desolvation Behavior of Calcium Salts. *Pharmaceutical Research*, 23(10), 2405-2412, 2006.
133. Li, Hui; Stowell, Joseph G.; Borchardt, Thomas B.; Byrn, Stephen R. Synthesis, Conformational Polymorphism, and Construction of a G-T Diagram of 2-[(2-Nitrophenyl)amino]-3-thiophenecarbonitrile. *Crystal Growth & Design*, 6(11), 2469-2474, 2006.
134. Mao, Chen; Chamarthy, Sai Prasanth; Byrn, Stephen R. ; Pinal, Rodolfo A Calorimetric Method to Estimate Molecular Mobility of Amorphous Solids at Relatively Low Temperatures. *Pharmaceutical Research*, 23(10), 2269-2276, 2006.
135. Crooks, Peter A.; Kottayil, Santosh G.; Al-Ghananeem, Abeer M.; Byrn, Stephen R.; Butterfield, D. Allan Opiate receptor binding properties of morphine-, dihydromorphine-, and codeine 6-O-sulfate ester congeners. *Bioorganic & Medicinal Chemistry Letters*, 16(16), 4291-4295, 2006.

136. Henck, Jan-Olav; and Byrn, Stephen R., Designing a Molecular Delivery System in a Preclinical Timeframe, *Drug Discovery Today*, 12, 189-199 (2007)
137. Li, Hui; Stowell, Joseph G.; He, Xiaorong; Morris, Kenneth R.; Byrn, Stephen R., Investigations on solid-solid phase transformation of 5-methyl-2-[(4-methyl-2-nitrophenyl)amino]-3-thiophenecarbonitrile. *Journal of Pharmaceutical Sciences* 96(5), 1079-1089 (2007).
138. McBride, J. M.; Smith, D. T.; Byrn, S. R.; Borgens, R. B.; Shi, R. 4-Aminopyridine derivatives enhance impulse conduction in guinea-pig spinal cord following traumatic injury. *Neuroscience*, 148(1), 44-52 (2007).
139. Liang, Jessica K.; Byrn, Stephen. On-line Raman spectroscopy in pharmaceutical process development: application and future prospects. *American Pharmaceutical Review* 10(4), 45-51 (2007).
140. Hu, Yuerong; Wikstroem, Hakan; Byrn, Stephen R.; Taylor, Lynne S. Estimation of the transition temperature for an enantiotropic polymorphic system from the transformation kinetics monitored using Raman spectroscopy. *Journal of Pharmaceutical and Biomedical Analysis*, 45(4), 546-551 (2007).
141. Chongcharoen, Wanchai; Byrn, Stephen; Sutanthavibul, Narueporn; Solid state interconversion between anhydrous norfloxacin and its hydrates, *Journal of pharmaceutical Sciences*, 97 (1), 473-489 (2007).
142. Lee, Eun Hee; Boerrigter, Stephan X.; Rumondor, Alfred C.; Chamarchy, Sai P.; and Byrn, Stephen R., Formation and Solid-State Characterization of a Salt-Induced Metastable Polymorph of Flufenamic Acid, *Crystal Growth and Design*, 8 (1), 91-97 (2008).
143. Byrn, Stephen; Liang, Jessica; Bates, Simon; Newman, Ann; PAT – Process Understanding and Control of Active Pharmaceutical Ingredients; *PAT – The Journal of Process Analytical Technology*, 3 (6), 14-19 (2006).
144. Lee, EunHee; Byrn, Stephen; Carvajal, Teresa; Additive Induced Metastable Single Crystal of Mefenamic Acid; *Pharmaceutical Research*, 23 (10), 2375-2380 (2006).
145. Joshi, Vidya; Morris, Kenneth R.; Byrn, Stephen R.; Carvajal, M. Teresa, Evaluation of the Use of Ea (Activation Energy) as a Quantitative Indicator of Physical Stability of Indomethacin Solvates: Methanolate and Tertiary Butyl Alcohol Solvate, *Crystal Growth & Design* 9(8), 3359-3366. (2009).
146. Chen, Xiaoming; Stowell, Joseph G.; Morris, Kenneth R.; Byrn, Stephen R., Quantitative study of solid-state acid-base reactions between polymorphs of flufenamic acid and magnesium oxide using X-ray powder diffraction. *Journal of Pharmaceutical and Biomedical Analysis* (2010), 51(4), 866-874.
147. Lee, Eun Hee; Boerrigter, Stephan X. M.; Byrn, Stephen R., Epitaxy of a Structurally Related Compound on the (100) Faces of Flufenamic Acid Form I and III Single Crystals. *Crystal Growth & Design* (2010), 10(2), 518-527.
148. Lee, Eun Hee; Smith, Daniel T.; Fanwick, Phillip E.; Byrn, Stephen R., Characterization and Anisotropic Lattice Expansion/Contraction of Polymorphs of Tenofovir Disoproxil Fumarate. *Crystal Growth & Design* (2010), 10(5), 2314-2322.
149. Trasi, Niraj S.; Boerrigter, Stephan X. M.; Byrn, Stephen Robert, Investigation of the Milling-Induced Thermal Behavior of Crystalline and Amorphous Griseofulvin. *Pharmaceutical Research* (2010), 27(7), 1377-1389.
150. Atassi, Faraj; Mao, Chen; Masadeh, Ahmad S.; Byrn, Stephen R., Solid-state characterization of amorphous and mesomorphous calcium ketoprofen. *Journal of Pharmaceutical Sciences* (2010), 99(9), 3684-3697.

151. Byrn, Stephen R.; Zograf, George; Chen, Xiaoming. . Accelerating proof of concept for small molecule drugs using solid-state chemistry. From *Journal of Pharmaceutical Sciences* (2010), 99(9), 3839-3848.
152. Li, Hui; Wen, Hong; Stowell, Joseph G.; Morris, Kenneth R.; Byrn, Stephen R., Crystal quality and physical reactivity in the case of flufenamic acid (FFA). *Journal of Pharmaceutical Sciences* (2010), 99(9), 3839-3848.
153. Engers, David; Teng, Jing; Jimenez-Novoa, Jonathan; Gent, Philip; Hossack, Stuart; Campbell, Cheryl; Thomson, John; Ivanisevic, Igor; Templeton, Alison; Byrn, Stephen; et al., A solid-state approach to enable early development compounds: selection and animal bioavailability studies of an itraconazole amorphous solid dispersion. *Journal of Pharmaceutical Sciences* (2010), 99(9), 3901-3922.
155. Ripin, David H. Brown; Teager, David S.; Fortunak, Joseph; Basha, Shaik Mahaboob; Bivins, Nylea; Boddy, Christopher N.; Byrn, Stephen; Catlin, Kelly K.; Houghton, Stephen R.; Jagadeesh, S. Tirumala; et al., Process Improvements for the Manufacture of Tenofovir Disoproxil Fumarate at Commercial Scale. *Organic Process Research & Development* (2010), 14(5), 1194-1201.
156. Emeje, Martins; Olaleye, Olajide; Isimi, Christiana; Fortunak, Joseph; Byrn, Stephen; Kunle, Olobayo; Ofoefule, Sabinus, Oral sustained release tablets of zidovudine using binary blends of natural and synthetic polymers. *Biological & Pharmaceutical Bulletin* (2010), 33(9), 1561-1566.
157. Mao, Chen; Prasanth Chamarthy, Sai; Byrn, Stephen R.; Pinal, Rodolfo, Theoretical and Experimental Considerations on the Enthalpic Relaxation of Organic Glasses using Differential Scanning Calorimetry. *Journal of Physical Chemistry B* (2010), 114(1), 269-279.
158. Lee, Eun Hee; Byrn, Stephen R., Stabilization of metastable flufenamic acid by inclusion of mefenamic acid: solid solution or epilayer., *Journal of Pharmaceutical Sciences* (2010), 99(9), 4013-4022.
158. Trasi, Niraj S.; Boerrigter, Stephan X. M.; Byrn, Stephen R.; Carvajal, Teresa M., Investigating the effect of dehydration conditions on the compactibility of glucose. *International Journal of Pharmaceutics*(2011), 406(1-2), 55-61.
159. Yamauchi, Masahiro; Lee, Eun Hee; Otte, Andrew; Byrn, Stephen R.; Carvajal, M. Teresa, Contrasting the Surface and Bulk Properties of Anhydrate and Dehydrated Hydrate Materials. *Crystal Growth & Design*(2011), 11(3), 692-698.
160. Ito, Takanori; Byrn, Stephen; Chen, Xin; Carvajal, M. Teresa. Thermal insight of mechanically activated bile acid powders, *International Journal of Pharmaceutics* (2011), 420(1), 68-75.
161. Emeje, Martins; Isimi, Christiana; Byrn, Stephen; Fortunak, Joseph; Kunlun, Olobayo; Ofoefule, Sabinus. Extraction and physicochemical characterization of a new polysaccharide obtained from the fresh fruits of *Abelmoschus esculentus* . *Iranian Journal of Pharmaceutical Research* (2011), 10(2), 237-246
162. Byrn, Stephen R.; Tishmack, Patrick A.; Milton, Mark J.; Velde, Helgi, Analysis of Two Commercially Available Bortezomib Products: Differences in Assay of Active Agent and Impurity Profile. *AAPS PharmSciTech* (2011), 12(2), 461-467.
163. Su, Ziyang; Luthra, Suman; Krzyzaniak, Joseph F.; Agra-Kooijman, Dena M.; Kumar, Satyendra; Byrn, Stephen R.; Shalaev, Evgenyi Y. Crystalline, liquid crystalline, and isotropic phases of sodium deoxycholate in water. *Journal of Pharmaceutical Sciences* (2011), 100(11), 4836-4844.

164. Weber, R.J.K., Benmore, C.J., Tumber, S.K., Taylor, A.N., Rey, C.A., Taylor, L.S., and Byrn, S. R., Acoustic levitation: recent developments and emerging opportunities in biomaterials research, *Eur. Biophys. J.*, (2012) 41, 397-403.
165. Byrn, Stephen R.; Henck, Jan-Olav, Optimizing Physical Form – opportunities and limitations, *Drug Discovery Today: Technologies* (2012), 9(2), e73-e78.
166. Trasi, Niraj S.; Byrn, Stephen R, Mechanically Induced Amorphization of Drugs: A Study of the Thermal Behavior of Cryomilled Compounds, *AAPS PharmSciTech* (2012), 13(3), 772-784.
167. Lee, Eun Hee; Byrn, Stephen R.; Pinal, Rodolfo, The solution properties of mefenamic acid and a closely related analogue are indistinguishable in polar solvents but significantly different in nonpolar environments, *Journal of Pharmaceutical Sciences* (2012), 101(12), 4529-4539.
168. Fortunak, Joseph MD; Byrn, Stephen R.; Dyson, Brandon; Ekeocha, Zita; Ellison, Tiffany; King, Christopher L.; Kulkarni, Amol A.; Lee, Mindy; Conrad, Chelsea; Thompson, Keeshaloy, An efficient, green chemical synthesis of the malaria drug, piperazine, *Tropical Journal of Pharmaceutical Research* (2013), 12(5), 791-798.
169. Lee, Jangmi; Boerrigter, Stephan X. M.; Jung, Young Woo; Byun, Youngjoo; Yuk, Soon Hong; Byrn, Stephen R.; Lee, Eun Hee, Organic vapor sorption method of isostructural solvates and polymorph of tenofovir disoproxil fumarate, *European Journal of Pharmaceutical Sciences* (2013), 50(3-4), 253-262.
170. Weber, J. K. R.; Benmore, C. J.; Taylor, A. N.; Tumber, S. K.; Neufeind, J.; Cherry, B.; Yarger, J. L.; Mou, Q.; Weber, W.; Byrn, S. R., A neutron-X-ray, NMR and calorimetric study of glassy Probuco synthesized using containerless techniques, *Chemical Physics* (2013), 424, 89-92.
171. Benmore, Chris J.; Weber, J. K. R.; Taylor, Amit N.; Cherry, Brian R.; Yarger, Jeffery L.; Mou, Qiushi; Weber, Warner; Neufeind, Joerg; Byrn, Stephen R., Structural characterization and aging of glassy pharmaceuticals made using acoustic levitation, *Journal of Pharmaceutical Sciences* (2013), 102(4), 1290-1300.
172. Gurvich Vadim J; Byrn Stephen R, NIPTE: a multi-university partnership supporting academic drug development, *Drug Discovery Today* (2013), 18(19-20), 916-21.
173. Byrn, Stephen; Futran, Maricio; Thomas, Hayden; Jayjock, Eric; Maron, Nicola; Meyer, Robert F.; Myerson, Allan S.; Thien, Michael P.; Trout, Bernhardt L., Achieving Continuous Manufacturing for Final Dosage Form: Challenges and How to Meet Them. 2014 Continuous Symposium, May 20-21, *Journal of Pharmaceutical Sciences* (2015), 104(3), 792-802.
174. Song, Yang; Yang, Xinghao; Chen, Xin; Nie, Haichen; Byrn, Stephen; Lubach, Joseph W., Investigation of Drug-Excipient Interactions in Lapatinib Amorphous Solid Dispersions Using Solid-State NMR Spectroscopy, *Molecular Pharmaceutics* (2015), Ahead of Print. DOI:10.1021/mp500692a
175. Song, Yang; Zemlyanov, Dmitry; Chen, Xin; Nie, Haichen; Su, Ziyang; Fang, Ke; Yang, Xinghao; Smith, Daniel; Byrn, Stephen; Lubach, Joseph W, Acid-Base Interactions of Polystyrene Sulfonic Acid in Amorphous Solid Dispersions Using a Combined UV/FTIR/XPS/ssNMR Study; *Molecular Pharmaceutics* (2016), 13(2), 483-492. Language: English, DOI:10.1021/acs.molpharmaceut.5b00708
176. Nie, Haichen; Mo, Huaping; Zhang, Mingtao; Song, Yang; Fang, Ke; Taylor, Lynne S.; Li, Tonglei; Byrn, Stephen R., Investigating the Interaction Pattern and Structural Elements of a Drug-Polymer Complex at the Molecular Level. *Molecular Pharmaceutics* (2015), 12(7), 2459-2468. Language: English, DOI:10.1021/acs.molpharmaceut.5b00162

177. Penumetcha, Sai Sumana; Byrn, Stephen R.; Morris, Kenneth R., Relaxation Kinetic Study of Eudragit NM30D Film Based on Complex Modulus Formalism, *AAPS PharmSciTech* (2015), 16(5), 1180-1189.
178. Nie, Haichen; Xu, Wei; Ren, Jie; Taylor, Lynne S.; Marsac, Patrick J.; John, Christopher T.; Byrn, Stephen R., Impact of Metallic Stearates on Disproportionation of Hydrochloride Salts of Weak Bases in Solid-State Formulations, *Molecular Pharmaceutics* (2016), 13(10), 3541-3552.
179. Song, Yang; Zemlyanov, Dmitry; Chen, Xin; Su, Ziyang; Nie, Haichen; Lubach, Joseph W.; Smith, Daniel; Byrn, Stephen; Pinal, Rodolfo, Acid-base interactions in amorphous solid dispersions of lumefantrine prepared by spray-drying and hot-melt extrusion using X-ray photoelectron spectroscopy *International Journal of Pharmaceutics* (Amsterdam, Netherlands) (2016), 514(2), 456-464. Language: English, \,DOI:10.1208/s12249-015-0289-x
180. Benmore, C. J.; Mou, Q.; Benmore, K. J.; Robinson, D. S.; Neufeind, J.; Ilavsky, J.; Byrn, S. R.; Yarger, J. L., A SAXS-WAXS study of the endothermic transitions in amorphous or supercooled liquid itraconazole *Thermochimica Acta* (2016), 644, 1-5.
181. Nie, Haichen; Su, Yongchao; Zhang, Mingtao; Song, Yang; Leone, Anthony; Taylor, Lynne S.; Marsac, Patrick J.; Li, Tonglei; Byrn, Stephen, Solid-State Spectroscopic Investigation of Molecular Interactions between Clofazimine and Hypromellose Phthalate in Amorphous Solid Dispersions, *Molecular Pharmaceutics* (2016), 13(11), 3964-3975.
182. de Araujo, Gabriel L. B.; Zeller, Matthias; Smith, Daniel; Nie, Haichen; Byrn, Stephen R, Unexpected Single Crystal Growth Induced by a Wire and New Crystalline Structures of Lapatinib, *Crystal Growth & Design* (2016), 16(10), 6122-6130
183. Braun, Doris E.; Nartowski, Karol P.; Khimiyak, Yaroslav Z.; Morris, Kenneth R.; Byrn, Stephen R ; Griesser, Ulrich J., Structural Properties, Order-Disorder Phenomena, and Phase Stability of Orotic Acid Crystal Forms, *Molecular Pharmaceutics* (2016), 13(3), 1012-1029.
184. Byrn, S. R.; Ekeocha, Z.; Clase, K. L., An Education Strategy to Respond to Medicine Inequality in Africa. *J. Pharm. Sci.* 2017, 106 (7), 1693-1696.
185. de Araujo, G. L. B.; Benmore, C. J.; Byrn, S. R., Local Structure of Ion Pair Interaction in Lapatinib Amorphous Dispersions characterized by Synchrotron X-Ray diffraction and Pair Distribution Function Analysis. *Sci. Rep.* 2017, 7, 46367.
186. Kalra, A.; Tishmack, P.; Lubach, J. W.; Munson, E. J.; Taylor, L. S.; Byrn, S. R.; Li, T., Impact of Supramolecular Aggregation on the Crystallization Kinetics of Organic Compounds from the Supercooled Liquid State. *Mol. Pharmaceutics* 2017, 14 (6), 2126-2137.
187. Nie, H.; Byrn, S. R.; Zhou, Q., Stability of pharmaceutical salts in solid oral dosage forms. *Drug Dev. Ind. Pharm.* 2017, 43 (8), 1215-1228.

188. Nie, H.; Xu, W.; Taylor, L. S.; Marsac, P. J.; Byrn, S. R., Crystalline solid dispersion-a strategy to slowdown salt disproportionation in solid state formulations during storage and wet granulation. *Int. J. Pharm.* (Amsterdam, Neth.) 2017, 517 (1-2), 203-215.
189. Weber, J. K. R.; Benmore, C. J.; Suthar, K. J.; Tamaloni, A. J.; Alderman, O. L. G.; Sendelbach, S.; Kondev, V.; Yarger, J.; Rey, C. A.; Byrn, S. R., Using containerless methods to develop amorphous pharmaceuticals. *Biochim. Biophys. Acta, Gen. Subj.* 2017, 1861 (1\_Part\_B), 3686-3692.
190. Zeller, M.; Barros de Araujo, G. L.; Parker, T.; Singh Rai, A.; Byrn, S. R., A new solvate of afatinib, a specific inhibitor of the ErbB family of tyrosine kinases. *Acta Crystallogr., Sect. E: Crystallogr. Commun.* 2017, 73 (3), 417-422.
191. Nie, Haichen; Mo, Huaping; Byrn, Stephen R., Investigating the Physicochemical Stability of Highly Purified Darunavir Ethanolate Extracted from PREZISTA Tablets, *AAPS PharmSciTech* (2018), 19(5), 2407-2417.
192. Boyce, Heather; Smith, Dan; Byrn, Steve; Saluja, Bhawana; Qu, Wen; Gurvich, Vadim J.; Hoag, Stephen W. In Vitro Assessment of Nasal Insufflation of Comminuted Drug Products Designed as Abuse Deterrent Using the Vertical Diffusion Cell, *AAPS PharmSciTech* (2018), 19(4), 1744-1757.
193. de Araujo, Gabriel L. B.; Ferreira, Fabio Furlan; Bernardes, Carlos E. S.; Sato, Juliana A. P.; Gil, Otavio M.; de Faria, Dalva L. A.; Loebenberg, Raimar; Byrn, Stephen R. ; Ghisleni, Daniela D. M.; Bou-Chacra, Nadia A.; et al, A new thermodynamically favored flubendazole/maleic acid binary crystal form: Structure, energetics, and in silico PBPK model-based investigation, *Crystal Growth & Design* (2018), 18(4), 2377-2386.
194. Kalra, Arjun; Luner, Paul; Taylor, Lynne S.; Byrn, Stephen R.; Li, Tonglei, Gaining Thermodynamic Insight From Distinct Glass Formation Kinetics of Structurally Similar Organic Compounds, *Journal of Pharmaceutical Sciences* (Philadelphia, PA, United States) (2018), 107(1), 192-202.
195. Nie, Haichen; Byrn, Stephen R., Edited By: Li, Tonglei; Mattei, Alessandra, Polymorphism and phase transitions, *Pharmaceutical Crystals* (2019), 169-221.
196. Byrn, Stephen R.; Chen, Xiaoming Sean; Smith, Pamela A., Predictive and Accelerated Formulation Design Using Synchrotron Methods, *AAPS PharmSciTech* (2019), 20(5), 1-11.
197. Lavan, Monika; Byrn, Stephen R.; Knipp, Gregory, Pediatric Formulations: Knowledge Gaps Limiting the Expedited Preclinical to Clinical Translation in Children, *AAPS PharmSciTech* (2019), 20(2), 1-7. .
198. Barbosa, E. J.; Gubitoso, M. R.; Bou-Chacra, N. A.; Byrn, S. R.; Carvalho, F. M. S.; Barros de Araujo, G. L., Contribution to the improvement of an oral formulation of niclosamide, an antihelmintic drug candidate for repurposing in SARS-CoV-2 and other viruses. *ChemRxiv* **2020**, 1-7.
199. Boyce, H. J.; Dave, V. S.; Scoggins, M.; Gurvich, V. J.; Smith, D. T.; Byrn, S. R.; Hoag, S. W., Physical Barrier Type Abuse-Deterrent Formulations: Mechanistic Understanding of Sintering-Induced Microstructural Changes in Polyethylene Oxide Placebo Tablets. *AAPS PharmSciTech* **2020**, 21 (3), 86.

200. Byrn, S. R.; Dan, S.; Smith, P. A.; Tian, F.; Zimmerman, A.; Gao, M. Composition with improved dissolution properties. CN111467501A, 2020.
201. Lu, X.; Huang, C.; Li, M.; Skomski, D.; Xu, W.; Yu, L.; Byrn, S. R.; Templeton, A. C.; Su, Y., Molecular Mechanism of Crystalline-to-Amorphous Conversion of Pharmaceutical Solids from 19F Magic Angle Spinning NMR. *J. Phys. Chem. B* **2020**, *124* (25), 5271-5283.
202. Lu, X.; Li, M.; Huang, C.; Lowinger, M. B.; Xu, W.; Yu, L.; Byrn, S. R.; Templeton, A. C.; Su, Y., Atomic-Level Drug Substance and Polymer Interaction in Posaconazole Amorphous Solid Dispersion from Solid-State NMR. *Mol. Pharmaceutics* **2020**, *17* (7), 2585-2598.
203. Lu, X.; Tsutsumi, Y.; Huang, C.; Xu, W.; Byrn, S. R.; Templeton, A. C.; Buevich, A. V.; Amoureux, J.-P.; Su, Y., Molecular packing of pharmaceuticals analyzed with paramagnetic relaxation enhancement and ultrafast magic angle spinning NMR. *Phys. Chem. Chem. Phys.* **2020**, *22* (23), 13160-13170.
204. Okezue, M.; Smith, D.; Zeller, M.; Byrn, S. R.; Smith, P.; Bogandowich-Knipp, S.; Purcell, D. K.; Clase, K. L., Crystal structures of salts of bedaquiline. *Acta Crystallogr., Sect. C: Struct. Chem.* **2020**, *76* (11), 1010-1023.
205. Okezue, M. A.; Clase, K. L.; Okezue, M. A.; Adeyeye, M. C.; Abiola, V. O.; Byrn, S. J., Impact of ISO/IEC 17025 laboratory accreditation in sub-Saharan Africa: a case study. *BMC Health Serv Res* **2020**, *20* (1), 1065.
206. Su, Y.; Lu, X.; Huang, C.; Xu, W.; Byrn, S. R.; Templeton, A. In *Molecular packing of posaconazole in crystalline-to-amorphous conversion*, American Chemical Society: 2020; pp PHYS-0753.
207. Yang, M.; Clase, K. L.; Byrn, S. R., An Analytic Investigation of the Drug Formulation- Based Recalls in the USA: See More Beyond the Literal. *AAPS PharmSciTech* **2020**, *21* (5), 198.
208. Barbosa, E. J., Andrade, M. A. B., Gubitoso, M. R., Bezzon, V. D. N., Smith, P. A., Byrn, S. R., Bou-Chacra, N. A., Carvalho, F. M. S., & de Araujo, G. L. B. (2021). Acoustic levitation and high-resolution synchrotron X-ray powder diffraction: A fast screening approach of niclosamide amorphous solid dispersions [10.1016/j.ijpharm.2021.120611]. *Int. J. Pharm.* (Amsterdam, Neth.), 602, 120611. <https://doi.org/10.1016/j.ijpharm.2021.120611>
209. Benmore, C. J., Benmore, S. R., Edwards, A. D., Shrader, C. D., Bhat, M. H., Cherry, B. R., Smith, P., Gozzo, F., Shi, C., Smith, D., Yarger, J. L., Byrn, S. R., & Weber, J. K. R. (2022). A High Energy X-ray Diffraction Study of Amorphous Indomethacin [10.1016/j.xphs.2021.12.003]. *J. Pharm. Sci.* (Philadelphia, PA, U. S.), Ahead of Print. <https://doi.org/10.1016/j.xphs.2021.12.003>
210. Benmore, C. J., Benmore, S. R., Edwards, A. D., Shrader, C. D., Bhat, M. H., Cherry, B. R., Yarger, J. L., Smith, P., Gozzo, F., Shi, C., Smith, D., Byrn, S. R., & Weber, J. K. R. (2021). A High Energy X-ray Diffraction Study of Amorphous Indomethacin. *J Pharm Sci.*
211. Bezzon, V. D. N., Ferreira, F. F., Smith, P., Benmore, C. J., Byrn, S. R., & de Araujo, G. L. B. (2021). Amorphous dispersions of flubendazole in hydroxypropyl methylcellulose: Formulation stability assisted by pair distribution function analysis [10.1016/j.ijpharm.2021.120500]. *Int. J. Pharm.* (Amsterdam, Neth.), 600, 120500. <https://doi.org/10.1016/j.ijpharm.2021.120500>

212. Kerstiens, E. A., Clase, K. L., Kerstiens, E. A., Byrn, S. R., Clase, K. L., & Byrn, S. R. (2021). The Identification of Quality Risk Factors for Non-biological Complex Drugs and Epilepsy Drugs Using Statistical Analysis of Formulation-Based Recalls in the USA. *AAPS PharmSciTech*, 23(1), 19.
213. Lavan, M., Wang, X., McCain, R., Jannasch, A., Cooper, B., Hostetler, S., Byrn, S., & Knipp, G. (2021). Development of a Pediatric Mini-Tablet Formulation for Expedited Preclinical Studies [10.1208/s12249-020-01891-x]. *AAPS PharmSciTech*, 22(1), 40. <https://doi.org/10.1208/s12249-020-01891-x>
214. Okezue, M., Bogdanowich-Knipp, S., Smith, D., Zeller, M., Byrn, S., Smith, P., Purcell, D. K., & Clase, K. (2021). Salts and Polymorph Screens for Bedaquiline [10.1208/s12249-021-02106-7]. *AAPS PharmSciTech*, 22(7), 228. <https://doi.org/10.1208/s12249-021-02106-7>
215. Yu, D., Seelam, R. R., Zhang, F., Byrn, S. R., & Hoag, S. W. (2021). Evaluation of tableting performance of Poly (ethylene oxide) in abuse-deterrent formulations using compaction simulation studies [10.1016/j.xphs.2021.03.008]. *J. Pharm. Sci. (Philadelphia, PA, U. S.)*, 110(7), 2789-2799. <https://doi.org/10.1016/j.xphs.2021.03.008>
216. Zeller, M., Bogdanowich-Knipp, S., Smith, P., Purcell, D. K., Okezue, M., Clase, K. L., Okezue, M., Clase, K. L., Smith, D. T., Byrn, S. R., & Byrn, S. R. (2021). Maleate salts of bedaquiline. *Acta Crystallogr E Crystallogr Commun*, 77(Pt 4), 433-445.
217. Zeller, M., Bogdanowich-Knipp, S., Smith, P., Purcell, D. K., Okezue, M., Smith, D. T., Byrn, S. R., & Clase, K. L. (2021). Maleate salts of bedaquiline [10.1107/s2056989021002991]. *Acta Crystallogr., Sect. E: Crystallogr. Commun.*, 77(4), 433-445. <https://doi.org/10.1107/s2056989021002991>.
218. Benmore, C.J., et al., *A High Energy X-ray Diffraction Study of Amorphous Indomethacin*. *Journal of Pharmaceutical Sciences*, 2022. **111**(3): p. 818-824.
219. Ekeigwe, A., et al., *Describing competency requirements for competency-based regulatory sciences education in sub-Saharan Africa—A qualitative systematic review*. *Pharmacy Education*, 2022. **22**(4): p. 42-62.
220. Kerstiens, E.A., S.R. Byrn, and K.L. Clase, *The Identification of Quality Risk Factors for Non-biological Complex Drugs and Epilepsy Drugs Using Statistical Analysis of Formulation-Based Recalls in the USA*. *AAPS PharmSciTech*, 2022. **23**: p. 1-9.
221. Okezue, M.A., S.J. Byrn, and K.L. Clase, *Determining the solubilities for benzoate, nicotinate, hydrochloride, and malonate salts of bedaquiline*. *International Journal of Pharmaceutics*, 2022. **627**: p. 122229.
222. Okezue, M.A., S.J. Byrn, and Z. Ekeocha, *Efforts at building capacity for manufacturing and testing the quality of medicines in Sub-Saharan Africa: Historical evidence from the BIRS programme*. *Pharmacy Education*, 2022. **22**(1): p. 872-894.
223. Salem, S., et al., *Impact assessment of the variables affecting the drug release and extraction of polyethylene oxide based tablets*. *Journal of Drug Delivery Science and Technology*, 2022. **71**: p. 103337.
224. António, C. T., Évora, A. O., Bernardes, C. E., Diogo, H. P., de Araujo, G. L., Smith, P., Byrn, S. R., Fausto, R., & Minas da Piedade, M. E. (2023). Polymorphism in Erlotinib Hydrochloride: New Insights into Relative Stability, Thermal Behavior, and Structural Differences of Forms A and B. *Crystal Growth & Design*, 23(10), 7374-7384.

225. Benmore, C., Benmore, S., Wilke, S., Menon, V., Byrn, S., & Weber, J. (2023). X-ray Diffraction of Water in Polyvinylpyrrolidone. *Molecular Pharmaceutics*, 20, 3645-3652
226. Chen, Z., Nie, H., Benmore, C. J., Smith, P. A., Du, Y., Byrn, S., Templeton, A. C., & Su, Y. (2023). Probing Molecular Packing of Amorphous Pharmaceutical Solids Using X-ray Atomic Pair Distribution Function and Solid-State NMR. *Molecular Pharmaceutics*, 20(11), 5763-5777.
227. Okezue, M. A., & Byrn, S. R. (2023). Synthesis, Characterization, and Stability Assessment for the Benzoate, Hydrochloride, Malonate, and Nicotinate Salts of Bedaquiline. *Pharmaceutics*, 16(2), 257.
228. Salem, S., Smith, D. T., & Byrn, S. R. (2023). Degradation products of the abuse deterrent agent Poly (ethylene) oxide under thermal manipulation conditions. *Journal of Drug Delivery Science and Technology*, 84, 104450.

### **Patents**

1. Pyridines for treating injured mammalian nerve tissue, Borgens; Richard B. (Delphi, IN), Shi; Riyi (West Lafayette, IN), Byrn; Stephen R. (West Lafayette, IN), Smith; Daniel T. (Lafayette, IN), US Patent 8,729,107, Sept. 9, 2010.
2. Pyridines for treating injured mammalian nerve tissue, Borgens; Richard B. (Delphi, IN), Shi; Riyi (West Lafayette, IN), Byrn; Stephen R. (West Lafayette, IN), Smith; Daniel T. (Lafayette, IN), US 8,097,638, July 16, 2007.
3. Pyridines for treating injured mammalian nerve tissue, Borgens; Richard B. (Delphi, IN), Shi; Riyi (West Lafayette, IN), Byrn; Stephen R. (West Lafayette, IN), Smith; Daniel T. (Lafayette, IN), US 7,244,748, Dec. 5, 2003.
4. Crystalline forms of [R-(R\*,R\*)]-2-(4-fluorophenyl)-.beta.,.delta.-dihydroxy-5-(1-methylethyl)- -3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrole-1-heptanoic acid calcium salt (2:1), Byrn; Stephen Robert (West Lafayette, IN), Coates; David Andrew (West Lafayette, IN), Gushurst; Karen Sue (Lafayette, IN), Krzyzaniak; Joseph Francis (Pawcatuck, CT), Li; Zheng Jane (Quaker Hill, CT), Morrison, II; Henry Grant (Lafayette, IN), Park; Aeri (West Lafayette, IN), Vlahova; Petinka Ivanova (Lafayette, IN), US 7,144,915, June 6, 2003.
5. NADH oxidase assay for neoplasia determination, Morr e; D. James (West Lafayette, IN), Byrn; Steven R. (West Lafayette, IN), Crane; Frederick L. (West Lafayette, IN), Morre; Dorothy M. (West Lafayette, IN), US 5,605,810, April 5, 1994.

### **Book Chapters**

Solid State Structure of Chiral Organic Pharmaceuticals, Stahly, G.P.; and Byrn, S. R., in *Molecular Modeling Applications in Crystallization*, 313-345, Allan Myerson, Ed., Cambridge Univ., Press

Structural aspects of polymorphism. Brittain, Harry G.; Byrn, Stephen R. *Drugs Pharm. Sci.*, 95(Polymorphism in Pharmaceutical Solids), 73-124

The solid-state structure of chiral organic pharmaceuticals. Stahly, G. Patrick; Byrn, Stephen R. *Mol. Model. Appl. Cryst.*, 313-345. Editor(s): Myerson, Allan S. Cambridge University Press: Cambridge, UK.(English) 1999.

### **Papers Presented or Co-Authored:**

A large number of papers have been presented at various conferences since 1974.

### **Invited Lectures, Seminars, and Courses:**

"The Mechanisms of Action of Ion Transporting Antibiotics," DePauw Univ., Greencastle, Indiana, October, 1974.

"The Solid State and Solution Conformational Isomerism of Drugs," Commercial Solvents Corporation, Terre Haute, Indiana, May, 1975.

"Solid State Reactions of Drugs," Indiana State University, Terre Haute, Indiana, April, 1975.

"Desolvations of Organic Molecular Crystals and their Pharmaceutical Applications," Chemistry Department, University of Illinois, Urbana Illinois, November, 1977.

"Desolvations of Organic Molecular Crystals and their Pharmaceutical Applications," Department of Medicinal Chemistry, University of Illinois at the Medical Center, Chicago, Illinois, March, 1978.

"Solid State Reactions of Drugs," Eli Lilly and Co., Indianapolis, Indiana, June, 1979.

"Relationship between the Solid State and Solution Conformation of Drugs," Youngstown State University, Youngstown, Ohio, Oct., 1980.

"Solid State Reactions in Medicinal Chemistry," Rose Polytechnical Institute, March, 1980.

"Solid State NMR Spectra of Drugs," Eli Lilly and Co., June, 1982.

"Solid State Chemistry of Drugs," DePauw University, Greencastle, Indiana, October, 1983.

"Polymorphism and the Solid State Chemistry of Drugs," McNeil Laboratories, Fort Washington, Pennsylvania, January, 1984.

"Structure Elucidation of Natural Products Using X-Ray Crystallography," King Saud University, Riyadh, Saudi Arabia, A series of 4 lectures presented in February, 1984.

"Mode of Action of AMSA," Drug Dynamics Institute, School of Pharmacy, University of Texas, Austin, Texas, May, 1984.

"Solid State Chemistry of Drugs," Eli Lilly-Tippecanoe Labs, May 10, 1985.

"Methods for the Analysis of Drugs," Hewlett Packard Short Course, Purdue University, West Lafayette, Indiana, June 19, 1985.

"Solid State Chemistry of Drugs," Chemistry Department, University of Kentucky, Lexington, Kentucky, October, 1984.

"Chemistry of Drug-DNA Interactions," Phi Lambda Upsilon Lecture, DePauw-Wabash Chapter, DePauw University, Greencastle, Indiana, March 20, 1986.

"Desolvation of Drug Crystal Forms" and "Crystallographic Study and Solid State NMR Spectra of Crystalline Drugs," both Seminars presented at Merck-Frosst Pharmaceuticals, Montreal, Canada, May 4-6, 1986.

"Solid State Chemistry of Drugs, Desolvation, Oxidation, and Solid State NMR Spectra of Steroid Crystal Forms," Merck Sharp and Dohme Research Laboratories, West Point, Pennsylvania, June 10, 1986.

"Solid State Stability of Drug Substances," Burroughs Wellcome Company, Research Triangle Park, North Carolina, October 1, 1986.

"Solid State Oxidation Reactions," Merck Sharpe and Dohme Research Laboratories, West Point, Pennsylvania, May 8, 1987

"Polymorphs and Solvates of Drugs," Ortho Lecture Series, Ortho Pharmaceutical, Raritan, New Jersey, April 22, 1987.

"Solid State Chemistry of Drugs," K. N. Trueblood Retirement Symposium, University of California, Los Angeles, California, March 18, 1989.

"Residential School: Polymorphs and Solvates of Drugs," Short Course, Royal Society of Chemistry, University of Bradford, London, June 24-26, 1989.

"Solid State Oxidation Reactions," University of Wisconsin, Madison, Wisconsin, June 12, 1989.

"Solid State Chemistry of Drugs," Land-of-Lakes Conference, Madison, Wisconsin, June 13, 1989.

"Solid State Chemistry of Steroids," Upjohn Company, Kalamazoo, Michigan, November 6, 1989.

"Solid State Chemistry of Drugs," Wyeth-Ayerst Pharmaceuticals, Rouses Point, New York, February 20, 1990.

"Solid State Chemistry of Drugs," Smith Kline Beecham, King of Prussia, Pennsylvania, April 11, 1990.

X-Ray Crystallographic Analysis of Pharmaceuticals," Land of Lakes Conference, Madison, Wisconsin, August 1, 1990.

"Solid State Oxidation Reactions," Pfizer Central Research, Groton, Connecticut, August 18, 1989.

"Solid State Chemistry of Drugs," Glaxo, Inc., Research Triangle Park, North Carolina, August 22, 1990.

"Polymorphs and Solvates of Drugs," Short Course presented to Hoffmann LaRoche, Nutley, New Jersey, September 11 and 12, 1990.

"Stability of Solvated Crystals," Abbott Laboratories, Abbott Park, Illinois, April 17, 1991.

"Powder Diffraction Analysis of Pharmaceuticals," Parke-Davis/Warner Lambert, Holland, Michigan, May 3, 1991.

"Anticancer Drug Design," American Cancer Society, Indianapolis, Indiana, February 25, 1989.

"Polymorphs and Solvates of Drugs," Short Course, Purdue University, June 5-7, 1990.

"Crystal Hydrates and Water in Crystalline Pharmaceuticals," Eino Nelson Conference, Phoenix, Arizona, November 27, 1990.

"Polymorphs and Solvates of Drugs," Burroughs-Wellcome, Inc., Greenville, North Carolina, April 9, 1991.

"Pharmaceutical Solids Short Course," Rhone-Poulenc Rorer, Collegeville, Pennsylvania, January 22-23, 1992.

"Pharmaceutical Solids Short Course," Eli Lilly and Company, Indianapolis, Indiana, February 13-14, 1992.

"Regulatory Issues for Pharmaceutical Solids," Merck Research Laboratories, West Point, Pennsylvania, February 28, 1992.

"Pharmaceutical Solids Short Course," Sandoz Pharmaceutical, East Hanover, New Jersey, March 2-3, 1992.

"Pharmaceutical Solids Short Course," Meadowlands Hilton, Secaucus, New Jersey, April 21-22, 1992.

"Pharmaceutical Solids Short Course," UNIGOV, University of Puerto Rico, San Juan, Puerto Rico, April 30-May 1, 1992.

"Pharmaceutical Solids Short Course," Abbott Laboratories, Chicago, Illinois, May 15, 1992

"Pharmaceutical Solids Short Course," Sterling, Inc., Rensselaer, NY, June 4-5, 1992

"Residential School: Polymorphs and Solvates of Drugs," Short Course, Royal Society of Chemistry, University of Bradford, London, July, 27-29, 1992.

"Pharmaceutical Solids Short Course," Burroughs Wellcome, Greenville, NC, August 11-12, 1992

"Pharmaceutical Solids Short Course," Washington Marriott, Washington, DC, October 27-28, 1992

"Polymorphs and Solvates Short Course," AAPS Short Course, San Antonio, TX, November 15, 1992

"Drug-Excipient Interactions in the Solid State," UNIGOV Conference on Excipients, San Juan, PR, Jan. 28, 1993

"Pharmaceutical Solids Short Course," Rhône-Poulenc Rorer, Paris, France, Feb. 9-10, 1993

"Pharmaceutical Solids Short Course," Meadowlands Hilton, Secaucus, NJ, April 27-30, 1993

"Pharmaceutical Solids Short Course," Syntex, Inc., Palo Alto, CA, May 6-7, 1993

"Mobility in Pharmaceutical Solids," G.D. Searle, Chicago, Illinois, May 12, 1993

"Solid State Chemistry of Drugs," Parke-Davis Warner/Lambert, Morris Plains, NJ, June 21, 1993

"Pharmaceutical Solids Short Course," Washington Marriott, Washington D.C., September 30, 1993

"Solid-State Pharmaceutical Chemistry," PR&D Building Dedication, Merck Research Laboratories, West Point, PA, October 8, 1993

"AIDS Research at Purdue University," Northeast Missouri State University, Kirksville, MO December 7, 1993.

"Mobility in Pharmaceutical Solids," Hoffmann-LaRoche, Nutley, NJ December 9, 1993.

"Solid State Chemistry of Drugs," Parke-Davis Warner/Lambert, Holland, MI, February 24, 1994.

"Mobility in Pharmaceutical Solids," Pfizer Central Research, Groton, CT, February 9, 1994.

"Solid State Pharmaceutical Chemistry," University of Minnesota, Minneapolis, MN, April 4, 1994.

"Pharmaceutical Solids Short Course," Pfizer, Inc., Groton, CT, April 11-12, 1994.

"Pharmaceutical Solids Short Course," Meadowlands Hilton, Secaucus, NJ, April 27-30, 1994.

"Pharmaceutical Solids Short Course," Geneva, Pharmaceuticals, Broomfield, CO, May 4-5, 1994.

"Pharmaceutical Solids Short Course," Crystal City Marriott, Washington, D.C., October 5-7, 1994.

"Instrumental Methods of Characterizing Bulk Drug Substances" Pharmaceutical Seminars, Wilmington, N.C., June, 1994

"Pharmaceutical Solids," R.W. Johnson, August 10, 1995.

"Pharmaceutical Solids," Upjohn Co., December 7, 1995.

"Pharmaceutical Solids Short Course," Crystal City Marriott, Washington, D.C., April, 1995.

"Solid State Chemistry of Drugs," Syntex Chemicals, Inc., Boulder, CO, February 2, 1996

"Intersection of Laws, Regulations, and Scientific Principles," Burkett Lectures, DePauw University, Greencastle, IN April 2, 1996.

"Organic Solid State Chemistry and Pharmaceutical Materials Science," Burkett Lectures, DePauw University, Greencastle, IN April 2, 1996.

"Pharmaceutical Solids Short Course," Crystal City Marriott, Washington, D.C., April 30-May 2, 1996.

“Practical Consequences of Polymorphism,” McNeil Consumer Products, Ft. Washington, PA May 7, 1996.

“Practical Consequences of Polymorphism,” Biogen, Cambridge MA, June 12, 1996.

“Practical Consequences of Polymorphism,” Genentech, S. San Francisco, CA, June 19, 1996.

“Pharmaceutical Solids Short Course,” Crystal City Marriott, Washington, D.C., April 28 -May 1, 1998.

“Pharmaceutical Solids,” Short Course at the DuPont-Merck, June 12-13, 1997.

“Pharmaceutical Solids,” Short Course at the FDA, September 29, 1997.

“Pharmaceutical Solids Short Course,” Crystal City Marriott, Washington, D.C., April 29-May 1, 1998.

“Pharmaceutical Solids,” Proctor and Gamble Pharmaceuticals, Norwich, N.Y., July 27-28, 1998

“Pharmaceutical Solids Short Course,” Sanofi Pharma, September 21-23, 1998

“Pharmaceutical Solids Short Course,” Novartis, Feb. 4-5, 1999

“CAMP Technologies, J&J, Spring House,” PA April 13-15, 1999

“Pharmaceutical Solids, SSCI Course,” Washington, DC, April 28-30, 1999

“Solid-state Chemistry of Drugs and Analysis,” University of Michigan, College of Pharmacy and Engineering, Ann Arbor, MI 2-10-00.

“Solid-state Chemistry of Drugs,” University of Minnesota, College of Pharmacy, 3-30-00.

“Polymorphism and Solid-state Chemistry of Drugs,” Ball State University, Chemistry Department, Muncie, IN 11-11-99.

“Particle Formation and Crystallization of Pharmaceuticals,” London, England and Crystal City, VA, June and Sept 9-10. 1999

“Pharmaceutical Solids Short Course,” Roche, August 12-13, 1999

“Pharmaceutical Solids Short Course,” Searle, October 10-13, 1999

“Pharmaceutical Solids Short Course,” Warner-Lambert, November 1-3, 1999

“Pharmaceutical Solids Short Course,” Warner-Lambert, Feb. 23-25, 2000

“Pharmaceutical Solids Short Course,” Pfizer, March 20-22, 2000

“Pharmaceutical Solids,” SSCI Course, Washington, DC, May 9-11, 2000

“Pharmaceutical Solids,” SSCI Course, Fremont, CA, May 23-25, 2000

“Pharmaceutical Solids,” SSCI Course, J&J, July 29-31, 2000.

“Pharmaceutical Materials Science and Research,” AAPS Head’s Meeting, Indianapolis, IN, October 27, 2000.

“Dimensions of Pharmaceutical Solids,” IIT Seminar, November, 2000.

“Pharmaceutical Solids,” SSCI Course, Schering, May, 2001.

“Pharmaceutical Solids,” SSCI Course, Washington, DC, May 2001.

“Pharmaceutical Solids,” SSCI Course, Pfizer, May, 2001.

“Six Dimensions of Pharmaceutical Solids,” Wyeth Ayerst, January 2001.

“Polymorphism and Stability of Drugs,” Univ. of Kentucky, February 7, 2001.

“Pharmaceutical Solids, SSCI Course,” Washington, DC, May 8-10, 2001

“New Technologies for Process Analytical Technologies,” FDA, Washington, DC, April 1, 2002.

“PAT,” Watson Pharmaceuticals, Corona, CA, March 3-4, 2003

“Pharmaceutical Solids, SSCI Course,” Washington, DC, May 9-11, 2002

“Pharmaceutical Solids, SSCI Course,” Washington, DC, May 10-12, 2003

“Solid State Chemistry of Biologicals,” SSCI Course, South San Francisco, Nov. 16-17, 2003

“Pharmaceutical Solids, SSCI Course,” Washington, DC, May 5-7, 2004

“PAT: Achieving Mechanistic Understanding through Solid State Chemistry,” SSCI Short Course, Princeton, NJ, September, 2004

“Midwest Organic Solid State Chemistry Symposium” June 2-4, 2005, Purdue University.

“Pharmaceutical Solids, SSCI Course,” Washington, DC, May 9-11, 2005

“Biological Solids,” South San Francisco, CA, February 15-16, 2005

“Pharmaceutical Solids, SSCI Course,” Washington, DC, March 29-31, 2006.

“Pharmaceutical Solids, SSCI Course,” Merck and Co., West Point, PA, September 16-17, 2006.

“Biopharmaceutical Solids, Aptuit/SSCI Course,” San Francisco, CA, February, 27-28, 2007.

“Pharmaceutical Solids, SSCI Course,” Washington, DC, April 10-12, 2007.

“Pharmaceutical Solids, SSCI Course,” Washington, DC, April 8-10, 2008.

“Pharmaceutical Solids, SSCI Course,” San Francisco, CA, May 14-15, 2008.

“Processing and Formulation Approaches for Improving the Apparent Solubility Controlled Release, Glatt Controlled Release Symposium, Sept. 18-20, 2007, Mahwah, NJ.

“Solid State Properties in Drug Development,” Howard University, Washington, DC, Sept. 10, 2007.

“Pharmaceutical Solids, SSCI Course,” Washington, DC, April 22-24, 2008.

“Forced Degradation Testing To Improve Stability Prediction and Reduce Time to Market”, Forced Degradation of Small Molecules Conference, Philadelphia, PA, February 25-27, 2008

“Solid Phase Characterization Short Course,” EAS, Nov. 11, 2008

“Pharmaceutical Solids, SSCI Course,” Washington, DC, April 21-23, 2009.

“Pharmaceutical Solids, SSCI Course,” San Francisco, CA, May 13-14, 2009.

“Drug Discovery”, Kilimanjaro School of Pharmacy/St. Luke Foundation Course, Moshi, Tanzania, March 17 - 28, 2008

“Drug Development”, Kilimanjaro School of Pharmacy/St. Luke Foundation Course, Moshi, Tanzania, December 1-12, 2008

“Drug Development”, Kilimanjaro School of Pharmacy/St. Luke Foundation Course, Moshi, Tanzania, May 18-29, 2009

“Pharmaceutical Manufacturing,” Kilimanjaro School of Pharmacy/St. Luke Foundation Course, Moshi, Tanzania, August 3-14, 2009.

“Drug Discovery”, Kilimanjaro School of Pharmacy/St. Luke Foundation Course, Moshi, Tanzania, March 17 - 28, 2010

“Pharmaceutical Solids, SSCI Course,” Washington, DC, April 13-15, 2010.

“Drug Development”, Kilimanjaro School of Pharmacy/St. Luke Foundation Course, Moshi, Tanzania, March 10-19, 2010

“Physical Characterization and Methods of Analysis”, Short Course,” EAS, Nov. 14, 2010

“Drug Development”, Kilimanjaro School of Pharmacy/St. Luke Foundation Course, Moshi, Tanzania, March 14-25, 2011

“Physical Characterization and Methods of Analysis”, Short Course,” EAS, Nov. 12-13, 2011

“Sustainable Medicines in Africa,” University of Kansas, Oct. 10, 2011

“Drug Development”, Kilimanjaro School of Pharmacy/St. Luke Foundation Course, Moshi, Tanzania, March 14-25, 2011

“Manufacturing”, Kilimanjaro School of Pharmacy/St. Luke Foundation Course, Moshi, Tanzania, August 8-19, 2011

“Documents”, Kilimanjaro School of Pharmacy/St. Luke Foundation Course, Moshi, Tanzania, March 5-16, 2012

“Drug Development”, Kilimanjaro School of Pharmacy/St. Luke Foundation Course, Moshi, Tanzania, August 6-17, 2012

“Drug Registration: US FDA Approaches to Reviewing Generic Drug Applications and PEPFAR Reviews.” Short course taught by US FDA, Kilimanjaro School of Pharmacy, Purdue University, and Howard University, Moshi, Tanzania , Sept. 24-28, 2012.

“Pharmaceutical Solids,” SSCI Short Course, Chicago, IL, Oct. 18-19, 2012

“Pharmaceutical Solids,” EAS Short Course, Somerset, NJ, November 4, 2013

“Solid State Properties of Pharmaceutical Materials”, Eastern Analytical Symposium, Sommerset, NJ, Nov. 12 and 13, 2015

"Molecular Structure of Medicines," Wagner Lecture, University of Michigan, Sept. 26, 2016.

“Solid State Chemistry of Drugs Impact and Regulatory Awareness,” Short Course, Bangkok, Thailand, August 11, 2017.

“Pharmaceutical Solids,” EAS Short Course, Somerset, NJ, November 11, 2018

**Invited Symposium Talks at National or International Meetings:**

"The Purdue BS-MS Program," AACP Meeting, Boston, Massachusetts, July, 1980.

"Polymorphism and the Solid State Chemistry of Drugs," FACSS Meeting, Philadelphia, Pennsylvania, September, 1983.

"CP/MAS Spectra of Drugs, A New Method for the Investigation of Polymorphs and Solvates," 25th Annual Medicinal Chemistry Symposium, SUNY Buffalo, Buffalo, New York, June 11-14, 1984.

"Polymorphism and the Solid State Chemistry of Drugs," Eastern Analytical Symposium, New York, New York, November 15, 1984.

"Structure-Reactivity Correlations in Crystalline Solids," 132nd Annual A.Ph.A. Meeting, San Antonio, Texas, February 19, 1985.

"Solid State Chemistry of Drugs," A.Ph.A. Acad. Pharm. Sci., Short Course on Materials Characterization, San Francisco, California, March 16, 1986.

"Solid State Chemistry of Polymorphs, Solvates, and Metastable Crystal Forms of Drugs," North Eastern Regional Pharmaceutics Association Seventh Annual Meeting, New Haven, Connecticut, June 27, 1986.

"Correlation of Crystal Structure and Solid State NMR Spectra of Steroid Polymorphs," 44th Pittsburgh Diffraction Conference, Pittsburgh, Pennsylvania, October 29-31, 1986.

"Polymorphism of Drugs," Annual Meeting of the American Crystallographic Association, University of Texas, Austin, Texas, March 15-20, 1987.

"Overview - Current Status of Basic Research in Pharmaceutical Solids," Second Annual Meeting, American Association of Pharmaceutical Sciences, Boston, Massachusetts, June 7-12, 1987.

"X-ray Crystallography and Solid-State NMR," American Crystallographic Association Symposium, Philadelphia, Pennsylvania, June 1988.

"Hepa Filtration and Biosafety Training of Pharmacy Students," Biomedical Safety Conference, Indianapolis, Indiana, June 1989.

"Design of Anti-AIDS Drugs," 17th International Symposium of the Controlled Release Society, Reno, Nevada, July 22-25, 1990.

"Structure and Stability of Crystal Solvates," American Association of Pharmaceutical Scientists, Las Vegas, Nevada, November 6, 1990.

"Structure and Behavior of Crystal Hydrates," Eino Nelson Conference, Phoenix, Arizona, November 27, 1990.

"Structure and Mobility of Polymorphs and Solvates of Pharmaceuticals," 4th Computational Methods in Chemical Design, Kloster Irsee, Germany, May 15-20, 1994.

"Solid State Chemical Instability: Mechanistic and Kinetic Issues" 36th Annual International Industrial Pharmaceutical Research Conference, Merrimac, Wisconsin, June 6-10, 1994.

"Solid State Pharmaceutical Chemistry: Applications of Solid State NMR," PharmAnalysis Conference, Atlantic City, NJ, June 21, 1994.

"Solid State Pharmaceutical Chemistry," 25th Meeting, Fine Particle Society and Second International Conference, New Brunswick, NJ, July 26, 1994.

“Solid State Pharmaceutical Chemistry,” Am. Cryst. Assoc., July, 27, 1995, Montreal, Canada

“Chemical Reactions in Amorphous or Disordered Pharmaceutical Solids,” Fine Particle Society, Chicago, IL, August 23, 1995

“Color Dimorphism from 1905 To 1995,” COGM International Meeting, Washington, DC, August 30, 1995

“Practical Consequences of Polymorphism,” FDA-AAPS Workshop on Polymorphism, Washington, D.C., February 26-28, 1996

“New Developments in Solid State NMR,” AAPS-USP Meeting, Washington, D.C., April 25-6, 1996.

“Solid State NMR Spectra of Drugs, Eastern Analytical Symposium, Somerset, N.J., Nov. 8, 1996

“Solid-state Chemical Reactions of Drugs,” Higuchi Conference, Lake of the Ozarks, Mo., March 9-11, 1997.

“Assessment: Impact of Bulk Drug Manufacturing Changes on Physical Properties”, AAPS-FDA BACPAC Conference, Washington D.C., March 25, 1997

“Practical Consequences of Polymorphism,” ACT Meeting, St. Louis, Mo., April 7-9, 1997.

“Characterization of Polymorphic Behavior: Research and Regulatory Perspective,” AAPS Eastern Regional Meeting, New Brunswick, N.J., June 9-10, 1997.

“Overview - What is Polymorphism and How Important is it?” British Pharmaceutical Conference, Scarborough England, September 18, 1997.

“Chemical Reactivity in the Solid State,” AAPS National Meeting, Boston, Mass., Nov. 2-6, 1997

“Solid State Chemistry – Regulations and Reactions” MSI International Symposium, San Diego, CA, February 18-20, 1998

“Physical Transformations of Solvated Pharmaceuticals,” Royal Society of Chemistry National Meeting, Polymorphism Symposium, Durham, England, April 7, 1998

“Stability of Solid Pharmaceuticals,” AAPS Western Regional Meeting, South San Francisco, CA. June 1, 1998

“Crystallization and Polymorphism Issues in Controlled Release Dosage Forms,” Organized and presented at a one day short course, Controlled Release Society International Meeting, Las Vegas, NV., June 25, 1998.

“BACPAC,” World Pharm Conference, Philadelphia, PA, Sept 22, 1998

“BACPAC and PQRI,” DIA Conference, Washington, D.C., Nov. 9, 1998

“PQRI”, AAPS National Meeting, San Francisco, CA, Nov. 17, 1999

“Energy-temperature Diagrams,” PhaTA4, Karlsruhe, Germany, March 24, 1999

“BACPAC, An Update, SUPAC Conference, Washington, DC, 5-4-99

“BACPAC, Bulk Active Post Approval Changes,” World Pharm., Philadelphia, PA, 10-28-00.

“Transformation During Processing,” AAPS National Meeting, New Orleans, LA 11-15-99

“PQRI, Drug Substances Technical Committee,” AAPS National Meeting, New Orleans, LA 11-15-99

“Impurities and Stability of Pharmaceuticals,” GMP-API Course, Univ. of Wisconsin Continuing Ed., Jan 20, 2000 and May 19, 2000.

“Crystallization of Pharmaceuticals,” Alun Bowen Lecture, British Crystallographic Association Meeting, April 4, 2000, Edinburgh, Scotland

“Computational Approaches to Solid State Chemistry,” Millennium Pharmaceutical Sciences Meeting, San Francisco, CA April 18, 2000

“Chemical Stability of Pharmaceuticals,” Land of Lakes Conference, Devils Lake, WI, June, 2000.

“Solid State NMR of Pharmaceuticals,” SMASH NMR Conference, Argonne, IL July 16, 2000.

“Polymorphism,” Land of Lakes Analytical Conference, Devils Lake, WI, July 31, 2000.

“Fundamentals of Solid State Reactions,” AAPS National Meeting, Indianapolis, IN, Oct. 26, 2000.

“NIR and LIF Methods of Monitoring Blend Homogeneity,” AAPS National Meeting, Indianapolis, IN 2000.

“Strategies for Metastable Phases,” AAPS Congress of Americas Short Course, March 2000.

“Implications of Solid State Chemistry for Process Development,” Rhodia International Conference on Process Development, Amelia Island, FL, April 2001

“Raman Mapping and Physical Transformations,” EAS, September 2001, Atlantic City, NJ

“Using Crystal Engineering to Predict Stability and Reduce Time to Market,” Higuchi Research Seminar, May 2001, Lawrence, KA.

Polymorphism & Crystallization Conference, Chairperson and Presenter on Regulatory Aspects, Philadelphia, PA June 20-21, 2002.

“Crystallization and Solid State Chemistry of Pharmaceuticals”, Aminoff Symposium, Royal Academy of Sciences, Stockholm, Sweden, September 12, 2002.

“Validation of Process Analytical Technologies”, IVT PAT Conference, Gaithersberg, MD, Oct. 24, 2002

“Engineering Sameness: Polymorphism, Crystallization, and Stability of Solid Pharmaceuticals”, AIChE Plenary Lecture, AIChE National Meeting, Indianapolis, IN, November 4, 2002

“Solid State Analysis of API in Drug Product,” AAPS National Meeting, November 6, 2002

“Validation of NIR Methods for the Pharmaceutical Industry,” AAPS National Meeting, November 6, 2002

“Achieving Sameness, USP, Washington, DC, December 18, 2002.

“Strategies for Incorporating NIR into PAT, “ IIR Conference, Washington, DC, Feb 4-6, 2003.

“Overview of Particle Manufacture and Blending,” Particle Size analysis Workshop, AAPS, April 30, 2003.

“Reactivity of Polymorphs, Predicting Stability,” ACS Prospectives Conference, Tampa, FL Feb 23, 2003

“Regulatory Aspects of Polymorphism,” APV Course, Bonn, Germany, May 12, 2003

“Approaches to PAT using In-line Sensors,” PAT Summit, Washington, DC, September 29, 2003

“Solid State Characterization Technologies for Online Analysis,” AAPS National Meeting, Salt Lake City, UT, October 30, 2003

“National GMP Curriculum, “AAPS National Meeting, Salt Lake City, UT, October 28, 2003

Enz Lectures, University of Kansas, August, 2004

“Solid State Chemistry of Amorphous Materials,” ACS Prospectives Symposium, Feb 8-11, 2004

“Polymorphism and Pharmaceuticals,” Stephen R. Byrn, IUCR Intl. School of Crystallography, Diversity Amidst Similarity, Erice, Italy

“Strategies to Improve Solubility Using Amorphous Materials and Co-crystals,” Barnett Improving Solubility Conference, Philadelphia, PA, June 3, 2005.

“Polymorphs of API and Implications in Drug Development,” CVG Conference, Toronto, CA, Sept. 27, 2004

“Implementing Quality by Design,” IIR PAT Conference, Princeton, NJ, Dec. 13, 2004.



“Novel Approaches to Characterization,” AAPS National Meeting, Baltimore, MD, November 2005.

“Busse Lectures” (1. Solid State Pharmaceutical Chemistry; 2. Regulated Pharmaceutical Industry in 2010), University of Wisconsin, Madison, Wisconsin.

“Achieving Mechanistic Understanding through Solid State Chemistry,” PAT Workshop, J. Liang and S. Byrn, PAT Conference, June 14-17, 2005, Philadelphia, PA.

“Regulatory Applications of Patent-Derived Analytical Methods,” PITTCON, March 4, 2005, Orlando FL,

“Using PAT to Reduce Time to Market” Academic and Industrial Research in PAT, Wyeth Scientific Symposium, Pearl River, NY, Feb. 27, 2005.

“PAT Process Understanding and Control of APIs” PAT Workshop, J. Liang and S. Byrn, PAT Conference, June 14-17, 2005, Philadelphia, PA.

“Novel Approaches to Characterization. Accelerating the Drug Development Process” AAPS National Meeting, November 11 2004, Baltimore, MD.

“Polymorphs in API, Implications for Drug Development”, CVG Meeting, Toronto, CA, Sept. 27-28, 2005.

“Building a Start-up Knowledge Based Company” ACS National Meeting, August 2004, Philadelphia, PA.

“Design and Characterization of Pharmaceutical Solids for Quality Product Development, Strategies for the 21<sup>st</sup> Century,” Keynote Lecture, Stephen R. Byrn, Ph. D., Department of Industrial and Physical Pharmacy, Purdue University and SSCI, Inc. West Lafayette, Indiana, Land of Lakes 48<sup>th</sup> Conference, Merrimac Wisconsin, June 2006.

“Physical Characterization of Pharmaceutical Solids,” NIST Meeting on Organic Materials, NIST, Rockville, MD, April 5-7, 2006.

“What does this all mean to a Formulator,” AAPS National Meeting, Nashville, TN, Nov. 6-11, 2006.

“New Opportunities in Solid State Characterization”, British Pharmaceutical Conference, Manchester, England, September 24-28, 2005.

“Using PAT to Understand Process and Reduce Time to Market and Speed Drug Development while Avoiding Regulatory Problems,” Bioanalytical Testing World Congress, Philadelphia, PA, and September 19-21, 2006.

“Science-Based Product Management and PAT”, Global Manufacturing Summit, September 7-9, 2005, Atlanta, GA.

“Solid State Strategies for Improving Solubility”, Water-Insoluble Drug Delivery Course, Park Hyatt Hotel, Philadelphia, PA, July 18, 2005.

“Implication of Polymorphism for Formulation Design”, Formulation Development Meeting, Philadelphia, PA, July 26-27, 2006

“Improving Drug Development Via Crystallization And Crystal Growth.” Edinburg, Scotland, Sept 10-12, 2006.

“Physical Stability in the Solid State”, Stephen R. Byrn, AAPS Workshop on Pharmaceutical Stability, September 10-12, Bethesda, MD, 2006.

“Quality by “Design and PAT”, AICHE National Meeting, Salt Lake City Utah, November 5, 2007.

Chairman Polymorphism and Crystallization Scientific Forum, IQPC, December 3-5, Philadelphia, PA. Presented Lead-off Talk entitled: “Designing Optimized Formulations Utilizing Polymorphs/Cocrystals/Amorphous Forms within a Preclinical Timeframe.”

“Leverage Forced Degradation Testing To Improve Stability Prediction and Reduce Time to Market”, Forced Degradation of Small Molecules, February 25-27, 2008

“Strategies for Preparation and Manufacture of Polymer-based Nanoparticulate Formulations”, Bio-Nano Conference, Hyderabad India, March 13-14, 2008.

“Quality by design and Process Analytical Technology for Pharmaceutical Manufacturing in the 21<sup>st</sup> Century”, Bio-Nano Conference, Hyderabad India, March 13-14, 2008.

“Molecules to Medicines: Bringing Drugs to Market Following GMP. Green Chemistry and Production of Essential Medicines in Developing Countries”, March 18-20, 2008, Abuja Nigeria

“A Model for Education and Pharmaceutical Manufacturing in Africa, Green Chemistry and Production of Essential Medicines in Developing Countries”, March 18-20, 2008, Abuja Nigeria

“Understanding Additive Effects on Crystallization, Polymorphic Transformation and Solubility” ACS Award in Separations Science and Technology Symposium, ACS National Meeting, New Orleans, LA, April 7, 2008

“Fast to IND with Quality by Design”, ISPE International Conference, Boca Raton, FL, Oct. 28, 2008.

“Utilizing Amorphous Dispersions to Reduce Time to IND”, AAPS International Meeting, Atlanta, GA, Nov. 23, 2008.

“A QbD Solubility Enhancement Platforms for Fast Drug Development Abstract”, Keynote lecture at the Indo-US Bilateral Workshop on Pharmaceutical Cocrystals and Polymorphs, Mysore, India, February 8 to 11, 2009

“Accelerating Proof of Concept Using Solid State Chemistry”, PGSRM Conference, Purdue University, June 25-27,

“Sustainable Medicines in Africa”, Swintowsky Distinguished Lecture, University of Kentucky, Lexington, KY, Sept. 24, 2009

“Accelerating Proof of Concept”, Swintowsky Distinguished Lecture, University of Kentucky, Lexington, KY, Sept. 25, 2009

“Accelerating Proof of Concept Using Solid State Chemistry,” David Grant Award Lecture, AAPS, Sept 11, 2009, Los Angeles, CA.

“Accelerating Translational/Clinical Research using Solid State Chemistry”, David Grant Symposium, University of Minnesota, June 2, 2010.

“Strategies for Novel Pediatric Formulations,” Peck Symposium, Purdue University, October 14, 2010.

“Solid-state Chemistry of Biopharmaceuticals: Fundamental Issues and Study Approaches”, Arden House AAPS Conference, West Point, NY, March 10, 2011

“Sustainable Medicine Program in Tanzania and East Africa” AAPS Indianapolis-Cincinnati Discussion Group, January 27, 2011

Sustainable Medicines in Africa, AAPS National Meeting, New Orleans, LA, Nov. 15, 2011

Sustainable Medicines in Africa FACCS National Meeting, Reno, NV, Oct. 5, 2011

Design and Characterization of Drug Substance Solid Form for Quality Formulation Development, Strategies for the 21<sup>st</sup> Century, Land of Lakes Conference, Devil’s Lake, Wisconsin, June 11-15, 2012.

Accelerating Proof of Concept Using Solid State Chemistry, Aptuit Conference on Early Drug Development, Florence, Italy, May 15, 2012.

Enhancing Drug Bioavailability and Solubility, Stephen Byrn, Boston Solubility and Bioavailability Conference, January 22, 2013

Sustainable Medicines in Africa, Pittcon, Philadelphia, PA, March 19, 2013

Business and Clinical Rationale for Development of Fixed Dose Combination Products, Land of Lakes Conference on FDC Drugs, Madison, WI, June 3, 2014

Enhancing Drug Bioavailability and Solubility, Stephen Byrn, California Solubility and Bioavailability Conference, June 18, 2013

Framing the Key Properties that Must be Optimized in Drug Molecules in Order to have a Drug Product, AAPS National Meeting, San Antonio, November 12, 2013

Winning the Race: Using the Right Strategies for Phase and Formulation to Rapidly Achieve Clinical Entry, AAPS National Meeting, San Antonio, November 13, 2014

Introducing Levitation Technology for the Production of Amorphous Drugs, Boston Solubility Project, ex Pharma, Boston Mass. Jan. 27-28, 2014.

Structure and Analysis of Amorphous Solids, ICDD Meeting, Hyderabad, India, August, 18, 2017

Regulatory Science of Solid State Chemistry, IUCr Crystallography Meeting, Hyderabad, India, August, 19, 2017.

Pharmaceutical Synchrotron XRPD Workshop, 6-8 May, 2018, Purdue University, Co-organizer. International Synchrotron meeting.

Structure and Analysis of Amorphous Dispersions, Stephen Byrn, Chris Benmore, Gabriel deAraujo, Amrinder Rai, Purdue University, West Lafayette, IN and Argonne National Laboratory, Chicago, IL. Presentation at Pharmaceutical Synchrotron XRPD Workshop, 6-8 May, 2018, Purdue University.

Synchrotron X-Ray Diffraction and Pair Distribution Function Analysis of Drug/Polymer Dispersions: A Comparison of Subtraction Techniques to Isolate Intra-and Intermolecular Interactions, Pamela Smith<sup>a</sup>, Stephen R. Byrn<sup>a</sup>, Gabriel L.B. de Araujo<sup>b</sup>, Chris J. Benmore<sup>c</sup>a) Improved Pharma, b) Department of Pharmacy, University of Sao Paulo, c) X-ray Science Division, Advanced Photon Source, Argonne National Laboratory PPXRD-16 and SS-XRPD-2 at the Swiss National Light Source, Villigen, Switzerland, 9 May 2019 to 12 May 2019.

Co-organized and chaired several sessions of the PPXRD-16 and SS-XRPD-2 at the Swiss National Light Source, Villigen, Switzerland, 9 May 2019 to 12 May 2019.

Continuity of Solids between Amorphous and Crystalline States, Stephen Byrn and Gabriel De Araujo, Purdue University, Chris Benmore, Argonne Laboratories, American Crystallographic Association, National Meeting, American Crystallographic Association Meeting, Cincinnati, Ohio, July 2019.

### **Principal Investigator on Grants:**

"Conformational Isomerism in the Solid State and in Solution," Stephen R. Byrn, Am. Chem. Soc. Starter Grant #2687-G1, \$7,500, 7-1-72 to 6-30-76.

"The Structures of Ion Transporting Antibiotics in the Solid State and in Solution," Stephen R. Byrn, Cottrell Research Grant from the Research Corporation, \$5,345, 1-1-73 to 12-31-75.

"The Interaction of Intercalating Agents with Dideoxynucleotides-Daunomycin," Stephen R. Byrn, Purdue Cancer Committee Grant, \$6,000, 1-1-74 to 12-31-75.

"Structural Studies of Physiologically Active Agents," Stephen R. Byrn, NIH Grant #ES00929, \$91,076 Direct Costs, 5-1-74 to 4-30-77.

"Solid State Reactions in Medicinal Chemistry," Stephen R. Byrn, NIH Grant #GM21174, \$75,000 Direct Costs, 6-1-74 to 5-31-77.

"Structural Studies of Physiologically Active Agents," Stephen R. Byrn, NIH Grant #ES00929, \$127,500 Direct Costs, 5-1-77 to 4-30-80.

"Conformational of Pyridoxal Schiff's Bases in the Presence and Absence of Enzymes," Stephen R. Byrn and M.D. Tsai, David Ross Grant, \$8,400, 3-1-76 to 2-28-78.

"Solid State Reactions in Medicinal Chemistry," Stephen R. Byrn, NIH Grant #GM21174, \$126,000 Direct Costs, 9-1-78 to 8-31-81.

"Molecular Pharmacology of 9-Aminoacridine Antitumor Agents," Purdue Cancer Committee, \$5,000, 7-1-80 to 12-31-82.

"Mechanism of Degradation of Moxalactam and Related Compounds," Eli Lilly and Company, 1-1-81 to 12-31-81, \$50,000 Total Costs.

"Acridine-DNA Interactions," Part of a Program Project Grant from the National Cancer Institute, W.M. Baird Project Director, ca. \$100,000 Direct Costs for 9-1-81 to 6-30-84.

"Solid State Chemistry of Drugs," Eli Lilly and Company, 1-1-82 to 12-31-82, \$46,000 Direct Costs.

"Mode of Action of Mutagenic Drugs," NIH Grant #GM29175, 3-1-83 to 2-28-86, \$181,000 Direct Costs.

"Solid State Chemistry of Insulin, Nabilone and Cefaclor," Eli Lilly and Company, 1-1-83 to 12-31-83, \$34,000 Direct Costs.

"Solid State Chemistry of Insulin and Ceftazidine," Eli Lilly and Company, 5-1-85 to 4-30-86, \$5,000 Total Costs, (0593-57-13335), D.L. Smith Co-PI.

"Polymorphism and the Bioavailability of Drugs," NIH Grant #GM34520, 12-1-84 to 11-30-85, \$180,000 Direct Costs.

"National Cooperative Drug Discovery Group for the Treatment of AIDS - Synthetic Approach," NIH U01 AI25712, 9-1-87 to 8-31-90, \$1,046,000 Direct Costs for three years.

"Anti-HIV (AIDS) Agents Targeted to the RNA Template," NIH Grant #GM24289, 4-1-88 to 3-31-91, \$228,000 for three years.

"Solid State Chemistry of Drugs," Grant from Merck and Company, 1988-1990, \$50,000.

"Center for AIDS Research," \$3,100,000 direct cost, approximately \$4,600,000 total costs. September 30, 1988 - March 1, 1994.

"Chemical Pharmacology Training Grant," 7-1-90 to 6-30-95, approximately \$900,000 Direct Costs for 5 years.

"Chemical Pharmacology Training Grant," 7-1-95 to 6-30-97, approximately \$1,200,000 Direct Costs for 5 years.

"Effect of Water on the Molecular Mobility of Pharmaceuticals," Purdue-Wisconsin Joint Project, S. R. Byrn and G. Zografi. Supported by Merck, Pfizer, Sandoz, Glaxo, Upjohn, Boehringer, Bristol-Myers Squibb, and Syntex 1991-1997, approximately \$115,000 per year.

"Crystal Growth and Nucleation During Drying," 9-1-95 to 8-31-97, \$50,000. NSF Pharmaceutical Processing Center, Purdue University, West Lafayette, IN

"CAMP - Consortium for the Advancement of Manufacturing in Pharmacy" 12-1-96 to 12-31-97, about \$380,000, Drying end Point Detection and Blending Detection, CAMP, Narabeth, PA

"CAMP - Consortium for the Advancement of Manufacturing in Pharmacy" 1-1-98 to 12-31-98, about \$400,000, Blending Detection, Parametric Release, Crystallization, (PI or Co-PI) CAMP, Narabeth, PA.

"CAMP - Consortium for the Advancement of Manufacturing in Pharmacy" 1-1-99 to 12-31-99, about \$467,000, Blending Detection, Parametric Release, Crystallization, Dye Lasers(PI or Co-PI) CAMP, Narabeth, PA.

NSF "Crystallization During Wet Granulation" ca. \$30,000 7/1/97 – 12-31-01

NSF "Solid State Acid Base Reactions" ca. \$35,000 7/1/97-12/31/00

"CAMP - Consortium for the Advancement of Manufacturing in Pharmacy" Founder of CAMP along with Professor C. Cooney, MIT, G.K. Raju, and W. Leishear. Funding for 1-1-99 to 12-31-07 about \$450,000 per year. Projects include: Blending Detection, PAT, Crystallization.

"Effect of Water on the Stability of Solid Pharmaceuticals," Purdue-Wisconsin Joint Project. Founder along with Professor G. Zografi, University of Wisconsin. Program now includes Professors K. Morris, L. Taylor, R. Pinal, and T. Carvajal at Purdue and Professor N. Rodriguez-Hornedo, Univ. of Michigan. Current supporters are Pfizer, Boehringer, Bristol-Myers Squibb, Roche, Inhale, and Abbott. Funding for 1997-present, approximately \$100,000 per year.

"Concretion," NSF, 1-1-00 to 12-31-02, \$54,000.

"PTCC – Particle Technology and Crystallization Consortium" Founder of PTCC along with Professors A. Myerson, IIT, K. Morris, Purdue and C. Cooney, MIT. Funding for 1-1-03 to 12-31-07 about \$400,000 total costs. Projects include: Crystallization monitoring, crystallization inhibition, PAT, and sensors.

"Discovering Once-a-Day Specialty Pharmaceutical Products" A.E. Mann Institute, Purdue University, 12-1-2008 to 5-31-2009, \$98,150 DC.

“Mapping base technologies for detecting counterfeit medications” Lilly Endowment, Purdue University, \$100,000, Jan. 1, 2008 through Dec. 31, 2010.

“Indiana Clinical Translational Institute,” A. Shekhar, PI, Stephen Byrn, Program Leader Regulatory, 2% Effort, UL1RR025761, KL2RR025760, TL1RR025759, 5/1/08 to 4/30/13. Total Award \$24,765,925.

“Drug Reformulation”, Mann Institute, Purdue University, \$265,000, 11/1/08 to 9/30/10.

“In-vitro, In-vivo Correlations for Dissolution Tests”, FDA, \$62,000, 9/1/09 to 9/30/10

Formulation of SMA Compound, DHHA-SAIC, August 2010 through July 31, 2011, ~ \$180,000.

“Industrial Pharmacy Services Laboratory, IPPH Department, Purdue University, July 2012-present, about \$200,000 per year

“Evaluation of Drug Product Formulations of Abuse Deterrent Drugs”, NIPTE and FDA, HHSF2232013011189P, Sept. 16, 2013 – Sept. 12, 2015. Total Award \$500,000.

“Master’s Scholarships for Students Studying in Kilimanjaro School of Pharmacy for Purdue MS Degree, Merck Foundation, \$600,000. Sept 2014 to June 30, 2016.

“Investigations of Active Coating End Point Determination”, Astra Zeneca, Nov. 1, 2015 through April 30, 2016, \$134,000.

“Evaluation of Drug Product Formulations of Abuse Deterrent Drugs”, NIPTE and FDA, April 1, 2017 – August 31, 2017. Total Award \$100,000.

“Pharmaceutical Quality Scorecard Development,” NIPTE and FDA, 2U01FD004275, December 1, 2017 – November 30, 2018, \$329,635 and Dec. 1, 2018 to March 31, 2020, \$329,635.

“Methods of Evaluating Drug Abuse by Smoking,” National Institute of Pharmaceutical Technology and Education/ FDA, 2U01FD004275, March 1, 2018, \$94,000.

“Highly Bioavailable Compositions of URM-099,” University of Rochester, May 1, 2018, \$40,000.

“New Salts of Bedaquiline”, S.R. Byrn, PI, Bill and Melinda Gates Foundation, June 1, 2020 to July 31, 2021, \$180,000.

“Formulation Studies of Mitragynine”, S. R. Byrn, PI, V. Gurvich and S. Hoag, Co-PI, Sept 30, 2020 to August 31, 2024, \$695,000.

“Chemistry, Manufacturing and Controls and Related Services for Development of Drug Products”, SR. Byrn, V. Gurvich, S. Hoag, NIH & NIDA, 75N95023R00037, July 1, 2024 to June 30, 2029

### **Co-Principal Investigator on Grants:**

"Chemical-Antitumor Activity of Lactones and Epoxides," J.M. Cassady and S.R. Byrn, NIH Grant, #CA \$114,906 Direct Costs, 9-1-75 to 8-31-78.

Member of the Cancer Center of Purdue University. This Cancer Center has received two core grants and a building grant from the National Cancer Institute. 1978 to 1994.

RR025759-61NIH/NCRR (A. Shekhar (PI), 07/01/08 - 06/30/13, Indiana Clinical and Translational Science Institute. Description: Multi-institutional project to support translational research in Indiana. Role: Program Leader, Regulatory Knowledge and Support, Member Pediatric Research Team. 2012 to present.

"Sustainable Medicines in Africa," Bill and Melinda Gates Foundation, July 1, 2018-June 30, 2020, \$650,612.

"Sustainable Medicines for Africa", Merck Foundation, July 1, 2018 through June 30, 2020 – Two fellowship grants for \$94,000, K. Clase, PI.

"NIPTE FDA Certification Program in Pharmaceutical Technology", Sept. 1, 2018 – Oct. 31, 2019, co-PI, \$294,722, K Clase, PI.

"Amorphous Pharmaceutical Product Development using Containerless Methods." Oct 1, 2018-December 31, 2020. Phase 2 SBIR, Materials Development, Inc., Evanston, IL. \$50,000.

"Assessment of Smoking and Vaping risk of opioids and commercial products, and standardization of methods to assess these properties" Sept. 1, 2019 to August 31, 2021, \$226,993, Vadim Gurvich, PI, BAA, Contract No., 5F40119C10112.

"Sustainable Medicines in Africa", S.R. Byrn Co-PI, Bill and Melinda Gates Foundation, August 1, 2018 to July 31, 2024, \$1,700,000.

"Promoting Quality Medicines Plus", Task Orders 1 through 5, Co-PI, Technical Partner USP-USAID project, 1/1/2022 through 9/30/2023, \$400,000.

"Quality Scorecard," FDA, BAA, Sept. 1, 2021 to Sept 30, 2023, \$965,000.

"Sustainable Medicines in Africa", S.R. Byrn Co-PI, Bill and Melinda Gates Foundation, August 1, 2024 to July 31, 2028, approximately \$1,700,000.

### **Consultantships and Companies Founded:**

Numerous consultantships with many pharmaceutical companies (including Novartis, Pfizer, BMS, J&J, Wyeth, Lilly, Roche, Abbott, Watson, and Merck) and many others over the years 1975 to present.

Co-Founder and Study Director, SSCI, a research and information GMP contract research firm in West Lafayette, IN employing about 90 people, 1991-2006. SSCI was sold to Aptuit in 2006. Consultant to Aptuit Nov. 2009-present

Consulting for several legal firms on major solid state chemistry, formulation, polymorphism, and salt litigations including the Zantac cases, the Paxil cases, the Norvasc cases, the Plavix cases, the Prevacid cases, the Elan nanoparticle patents 1990-present.

Co-Founder and Chief Scientific Officer (as a consultant), Improved Pharma, West Lafayette, Indiana, 2006 – present.

Co-Founder and Chief Scientific Officer (as a consultant), Innovative Pharma, West Lafayette, Indiana, 2023 – present.

**Last Update:** August 2024



## Testimony in the Last Four Years

Stephen Byrn

June 2, 2025

The company I provided scientific testimony for is listed first. Testimony in trial is marked with an \*.

- *Federal Machinery v. Immunity Bio., Inc.* No. 1-21-cv-01422-CEF
- *Otsuka Pharm. Co. v. Mylan Laboratories, LTD.,* No. 22-464-JLH
- *Arbutus Bio. Corp and Genevant Sci., v. Moderna Inc.,* C.A. No. 22-252-MSG
- \**In re Opana ER Antitrust Litig.,* No. 14 C 10150 (N.D. Ill.)
- *VIIV Healthcare Co. v. Gilead Scis.,* No. 1:18-cv-00224 (D. Del.)
- \**Silvergate Pharms., Inc. vs Bionpharma, Inc.,* No. 18-cv-01962 (consolidated) (D. Del.)
- *In re Novartis and Par Antitrust Litigation,* No. 1:18-cv-04361-AKH (consolidated) (S.D.N.Y.)
- *Intervet, Inc. v. Mileutis, Ltd.,* No. 3:15-cv-01371-RK-TJB (D.N.J.)
- *Intercept Pharms. v. Apotex, Inc.,* No. 20-cv-1105 (D. Del.)
- Israeli Patent Applications 249308 and 276948 in *Unipharm, Ltd. vs. Sierra Oncology, Inc.,* 2022
- *Neurocrine Biosciences v. Lupin Ltd.,* No. 21-cv-01042 (D. Del.)
- *Novartis Pharm. Corp. v. Lupin Inc.,* No. 21-cv-01105 (D. Del.)