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Mississippi Pharmacists' Knowledge and Attitudes about Pharmacy Compounding Safety and Regulation

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By

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DEDICATION

My thesis is dedicated to my parents, Bill and Jeanne Allen. From my first day in a classroom as a young child, they have encouraged me to put forth my best effort and grasp every opportunity to expand my educational knowledge. In addition to their endless support of my past, present, and future academic endeavors, I thank them for their support and guidance of my spiritual and emotional maturity as well.

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ABSTRACT

Mississippi Pharmacists' Knowledge and Attitudes about Pharmacy Compounding Safety and Regulation

Introduction: Pharmacy compounding, which is defined by The Food and Drug Administration (FDA) as a "practice in which a licensed pharmacist combines, mixes, or alters ingredients in response to a prescription to create a medication tailored to the medical needs of an individual patient,"[1] has gained recent attention at both national and state levels. Outbreaks of adverse events associated with pharmacy compounding have led to many proposed and enacted changes in how to appropriately and best regulate traditional compounding pharmacies and those that act as manufacturers. Given such recent controversies and potential confusion as to exactly how compounding is regulated, the purpose of this study is to measure pharmacists' knowledge and attitudes regarding the regulation of pharmaceutical compounding. **Methods:** A cross-sectional, descriptive design was used by surveying 2,499 Mississippi-licensed pharmacists via email and Qualtrics Survey Software. **Results:** 199 useable responses were gathered from practicing Mississippi pharmacists. Respondents' appeared somewhat knowledgeable about compounding regulation and were generally positive about the practice of compounding. Significant differences in knowledge found at the .05 level of significance based on place of employment and number of compounds prepared. Significant differences in attitude were found at the 0.05 level of significance based on number of compounds prepared. **Discussion:** Respondents' appeared somewhat knowledgeable

about compounding regulation and were generally positive about the practice of compounding. The results of this study were not surprising, and suggest that a pharmacist's practice location and number of compounds made in their facility can be related to their knowledge of compounding, and that the number of compounds their facility makes can be related to their attitude.

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LIST OF ABBREVIATIONS

FDA	Food and Drug Administration
IRB	Institutional Review Board
NECC	New England Compounding Center
PCCA	Professional Compounding Centers of America

INTRODUCTION

Purpose

The Food and Drug Administration (FDA) defines pharmacy compounding as a "practice in which a licensed pharmacist combines, mixes, or alters ingredients in response to a prescription to create a medication tailored to the medical needs of an individual patient."[1] While the practice of pharmacy compounding itself has been in effect for thousands of years, recent decades have witnessed the rise of specific "compounding pharmacies." Today the term compounding pharmacy typically refers to any physical pharmacy that is permitted to combine or "compound" specific chemical ingredients to produce a specific type of medicine. These medications are produced for individual patients based on prescriptions written and ordered by a physician or another legally authorized prescriber.[2]

In the 1940s it was assumed that nearly fifty percent of prescriptions were compounded, but as the demand for prescription drugs dramatically increased, manufacturing companies like Pfizer and Merck arose. Today compounding pharmacists only compound approximately three percent of the 4 billion prescriptions that are filled each year. Although this seems like an insignificant number, the demand for compounded medicines continues to rise because manufactures find it difficult to meet the specific needs of individual patients. Physicians are also beginning to prescribe an added number of compounded prescriptions.[3]

As compounding pharmacy developed into its own pharmacy specialty, the distinction between traditional compounding and drug manufacturers began to blur. Traditional compounding falls under the regulations of state boards of pharmacy and is used to create specified medications for patients when manufactured drugs are not an appropriate option of treatment. [4] Drug manufacturers fall under the regulation of the FDA, which holds the manufacturing companies responsible for the Current Good Manufacturing Practice Regulations to ensure that drug products are safe before they are packaged and shipped across state lines.[5] Issues have arisen within recent years, as some compounding pharmacies have begun to take on roles more traditionally associated with drug manufacturing companies.

Given recent controversies and potential confusion over exactly how compounding is regulated, the purpose of this study is to measure pharmacists' perceptions of the regulation of pharmaceutical compounding. The specific objectives of this study are to:

1. Describe the practice characteristics of responding pharmacists;
2. Measure pharmacists' perceived knowledge about pharmacy compounding;
3. Measure pharmacists' attitudes about pharmacy compounding safety; and
4. Compare pharmacists' knowledge and attitudes about compounding based on their practice characteristics (practice type, preparation of compounded medications, and pharmacy association affiliation).

Background

Studying pharmacists' current perspectives on the demand for stricter regulation of pharmacy compounding first requires sufficient background knowledge of the basic compounding timeline. Understanding the history of outbreaks associated with compounding pharmacy and how such outbreaks were and continue to be addressed with various governmental changes and regulations sets the stage for the most recent proposed regulations and government intervention. Issues with outbreaks may be traced back to even the mid-1930s up until 2013. Within the past two decades alone, 200 adverse events related to compounding have taken place. Such events have involved 71 compounded products, and some of them with "devastating repercussions", according to the FDA.[9]

One of the first major outbreaks associated with compounding drugs that led to serious changes with regard to changes in drug laws and regulations occurred in 1937 and was known as the Sulfanilamide Disaster. Sulfanilamide was long a drug used to treat streptococcal infections and had been proven effective when taken in powder or tablet forms. However, in June 1937, a salesman for the S.E. Massengill Co., located in Bristol TN, indicated the rising demand for sulfanilamide to be made in liquid form. In response to such demands, the primary chemist for the company conducted experiments to find that Sulfanilamide would dissolve in diethylene glycol. The company then proceeded to compound a quantity of elixir, package, and ship 633 of the products across the country. Within a month of receiving shipments, physicians began reporting deaths, associated with the compounded medicine, to the American Medical Association. Diethylene glycol was discovered to be toxic- leading to kidney damage or failure and ultimately death. At the time it was compounded, the newly synthesized drug was not tested for toxicity

because in 1937 drug laws did not prohibit the sale of "dangerous, untested, or poisonous drugs," and no law required that safety studies be done on new drugs. The company was able to recover most of the toxic product, but the amount of product that was consumed led to the deaths of more than 100 persons in 15 states. The disaster quickly led to the passage of the 1938 Food, Drug, and Cosmetic Act, which increased FDA authority to regulate drugs, and created a new system of drug control. [10]

While the outbreak associated with the S.E. Massengill Co. that occurred in 1937 may be attributed to the lack of existence of many strict federal and FDA regulations associated with drug manufacturing and transporting, controversy has continued to surround pharmaceutical compounding as a whole in the years following. Such controversy has continued to affect compounding firms across the nation and led to constant changes in how effectively regulate drug manufacturers and even small compounding pharmacies.

Dozens of incidents related to pharmaceutical compounding have occurred even since 2000. One primary incident occurred in 2006, when the FDA was forced to issue a warning to a few different pharmacies that were noted as having produced and distributed over thousands of doses of inhalation medications that were compounded and not approved by the FDA. Such inhalation medications were compounded and given to patients in order to treat various respiratory diseases including asthma, bronchitis, cystic fibrosis, and emphysema. Meeting minutes from a 2007 meeting of the Ohio State Board of Pharmacy indicate that one of the pharmacies received negative consequences for such actions. Calculations were done to determine that between July 2005 and November 2005, the said pharmacy compounded and filled 119 prescriptions for an estimated 7530

doses of inhalation medications. Two of the five mixed medications were identical in nature to FDA-approved medications. However three of the compounds were unapproved. Seven drug substances were used to create the combinations, and five were cited as FDA-approved inhalation medications, but two of the substances were not approved by the FDA. Further analysis of the minutes showed that after quality tests were conducted on some of the compounded medications, the "potency of the tested drugs ranged from approximately 27% to 85% of the amounts of active ingredients listed on the products' labels." In addition, a significant amount of the medications were not tested for sterility, fungi, or endotoxins prior to being dispensed. This resulted in fungal contamination in 1380 doses that were ultimately prescribed to twenty-three patients. Upon discovery, the patients were then told to dispose of the compounded prescriptions.[11]

During the fall of 2012, the New England Compounding Center (NECC) became a compounding pharmacy under intense scrutiny. The compounding center, located in Framingham, MA, was accused of "unsafe manufacturing practices." Such practices ultimately led to the death of more than sixty individuals and over seven hundred injuries through steroid injections that were tainted with a fungus that led to a rare and deadly form of meningitis in many individuals. Such steroid injections were packaged and shipped across state lines with NECC exhibiting manufacturing characteristics. [6] Similar, yet smaller scaled instances, have occurred prior to and after the NECC meningitis outbreak- leading many to seek stricter regulations for compounding pharmacies.

The instances previously mentioned have led to many proposed and enacted changes in how to appropriately and best regulate traditional compounding pharmacies and those that act as manufacturers. In 2013 alone, twenty five bills or resolutions related

to compounding pharmacies were filed across sixteen different states. Seven of the bills that were proposed have been adopted as law. [2] Proposals have also been made at the national level as well. In May 2013, The Pharmaceutical Compounding Quality and Accountability Act was introduced in the Senate. The goal of the proposed act is to make a clear distinction between traditional compounding and compounding manufacturers. Under the act, traditional compounding continues to be regulated primarily by state pharmacy boards, while compounding manufacturers, that make sterile products "without, or in advance of, a prescription and sell those products across state lines" would be regulated by the U.S. Food and Drug Administration (FDA). [7]

METHODS

Design

The study objectives were met by employing a descriptive, cross-sectional design. Responses were gathered using a self-administered survey that was distributed electronically through Qualtrics Survey Software.

Sample

The study sample consisted of Mississippi-licensed pharmacists who had valid email accounts, acquired from the state board of pharmacy on October 7, 2013. The study sample was not limited to Mississippi-licensed pharmacists practicing in certain fields but rather included pharmacists practicing in all fields of the profession. Mississippi-licensed pharmacists who were not actively practicing at the time of the survey were excluded from completing the survey upon answering that they were not actively practicing. A total of 2,499 emails were sent to Mississippi-licensed pharmacists.

Data Collection

Prior to sending the survey to Mississippi-licensed pharmacists, an Abbreviated IRB Application was submitted to the University of Mississippi IRB for approval to begin data collection. The University of Mississippi IRB approved the application as Exempt under 45 CFR 46.101(b)(#2). The study to be completed by the pharmacists was conducted by first using an online survey generated by the Qualtrics Survey Software. The survey generated may be found in Appendix A. The link to complete the survey was sent to the sample described above in an email that explained both the survey and the

purpose of the study. Following the initial sending of the survey, a week later another email was sent to those in the sample that had not yet completed the survey. The follow-up email also contained the link to the survey and a reminder of the purpose of the study. The body of the initial and follow-up emails may be found in Appendices B and C.

The survey began by first asking whether or not the participant was currently practicing pharmacy. If the participant answered "no" the individual was excluded from completing the remainder of the survey. If the participant answered "yes" the individual continued answering a few more basic, demographic questions about employment. These questions included identifying the type of pharmacy practice as primary place of employment, how many hours per week spent at this primary place of employment, and how many years practicing pharmacy.

Following the basic, demographic questions were more questions primarily pertaining to pharmacy compounding practices, prefaced by a definition of pharmacy compounding, as relevant to this study. These questions included identifying the amount of compounded medications made per week at primary place of employment, number of continuing education courses, seminars, or training sessions related to prescription compounding attended, all categories for which compounded prescriptions have been made (i.e. pain management, podiatry, hormone replacement therapy, etc.), and all professional pharmacy organizations to which the respondent is a member.

The next section of the survey measured respondents' reported level of knowledge regarding pharmacy compounding and its current significance. Respondents' reported level of knowledge (where 1 = not at all knowledgeable and 5 = extremely knowledgeable) was measured using statements related to compounding laws and

regulations, new legislative acts related to pharmacy compounding, compounding techniques, adverse events related to pharmacy compounding, and federal and state involvement in pharmacy compounding practices.

The remainder of the survey was intended to measure participants' level of agreement (where 1 = strongly disagree and 5 = strongly agree) with statements regarding both (1) appropriate management of pharmacy compounding and safety regulations and (2) the importance of the practice of pharmacy compounding and need for compounded medications. Following these questions was a place for participants to include any comments about the practice of compounding or the regulation of compounding.

Analysis

Various aspects were examined including the response rate, the study objectives, and qualitative data. The response rate of practicing Mississippi pharmacists was calculated and evaluated. Objective 1 (sample description) was analyzed using means, frequencies, and percentages. Frequencies were used to analyze the type of primary employment, number of pharmacy professional organizations, and number of compounded medications. Means were used to analyze hours per week spent at primary employment and number of years practicing pharmacy. Objectives 2 (knowledge) and 3 (attitude) were also analyzed using descriptive statistics and means, including Cronbach's alpha. Cronbach's alpha is a coefficient of internal consistency. The value may be between 0 and 1, with higher values associated with increasing intercorrelation among test items.

Objective 4 (comparisons) was first analyzed using size distinct one-way ANOVA tests. Three one-way ANOVAS were conducted comparing knowledge with

place of primary employment, number of compounded medications, and number of pharmacy association affiliations respectively. The other three one-way ANOVAS were conducted comparing attitude with place of primary employment, number of compounded medications, and number of pharmacy association affiliations, respectively. The one-way ANOVA tests that revealed differences at the .05 level of significance were further analyzed by post hoc multiple comparison tests via Tukey HSD tests.

RESULTS

Response Rate

The response rate of Mississippi-licensed pharmacists was calculated. A total of 2,499 emails containing the link to the survey was sent to Mississippi-licensed pharmacists. Of the 2,499 total emails, 266 responses were obtained. Of the 266 responses, 67 responses were removed from data analysis for reasons including the responder was not currently practicing, the survey was not fully completed, etc. The total was then calculated to be 199 responses that were fully completed by currently practicing Mississippi pharmacists. The final response rate was calculated to be 8.0%.

Objective 1 (Sample Description): Results

The first objective was to describe the practice characteristics of responding pharmacists. The respondent reported working in a variety of primary places of employment. The majority at 24.1% reported working in "other" places of primary employment. The next highest percentage were found to be working in traditional chain stores, hospital inpatient, and single store independent at 19.1%, 17.6%, 16.1%, respectively. Respondents reported working an average of 38.63 hours per week at said place of primary employment. In addition, respondents reporting having practiced pharmacy for an average of 20.14 years. Additional characteristics related to basic employment demographics may be found in Table 1.

Respondents were also asked to report, from a given list, the professional pharmacy organizations with which they are affiliated. This information was used to

determine the number amount of professional pharmacy organizations with which each respondent identified. The majority of respondents, at 33%, identified with one professional pharmacy organization. The next highest percentage were found to be affiliated with 0 organizations and 2 organizations at 28.9% and 18.8%, respectively. Additional characteristics related to the reported number of organizations may be found in Table 2.

Respondents reported the number of medications that their primary place of employment compounds per week. This self-reported data that was collected was then organized into groups of intervals. The four sets of intervals were organized to be 0, 1-9, 10-99, and $\geq$100. The majority of respondents, at 32.3%, identified with compounding 1-9 medications per week. The next highest percentages were found to compound 0 and 10-99 medications per week at 25.5% and 22.9%, respectively. Additional characteristics related to the reported number of medications compounded per week may be found in Table 3.

Table 1: Demographic Data – Employment Characteristics from Pharmacist Sample for Objective 1

Type of Pharmacy Primary Employment	**Number of Respondents (%)**
Single Store Independent	32 (16.1)
Multiple Store Independent	21 (10.6)
Traditional Chain Store	38 (19.1)
Supermarket with a pharmacy	11 (5.5)
Mass Merchandiser with a pharmacy	10 (5.0)
Hospital Inpatient	35 (17.6)
Hospital Outpatient	4 (2.0)
Other	48 (24.1)
*Total Number Respondents = 199	
Hours Per Week at Primary Employment	**Number of Hours**
Minimum Number of Hours Reported	4
Maximum Number of Hours Reported	65
Mean	38.63
Std. Deviation	9.059
*Total Number Respondents = 197	
Total Years Actively Practicing Pharmacy	**Number of Years**
Minimum Number of Years Reported	0
Maximum Number of Years Reported	48
Mean	20.14
Std. Deviation	13.419
*Total Number Respondents = 193	

Table 2: Demographic Data – Pharmacy Association Affiliations for Objective 1

Number of Pharmacy Assoc. Affiliations	Number of Respondents (%)
0	57 (28.9)
1	65 (33.0)
2	37 (18.8)
3	20 (10.2)
4	11 (5.6)
5	7 (3.6)
*Total Number Respondents = 197	

Table 3: Demographic Data – Amount of Compounded Medications for Objective 1

Number of Compounded Medications Per Week	Number of Respondents (%)
0	49 (25.5)
1 – 9	62 (32.3)
10 – 99	44 (22.9)
≥ 100	37 (19.3)
*Total Number Respondents = 192	

Objective 2 (Knowledge): Results

Descriptive statistics, including means and Cronbach's alpha was used to analyze and measure pharmacists' self-reported, perceived knowledge about pharmacy compounding. Table 4 contains the overall per-item mean for all knowledge statements in the survey as well as the individual mean reported for each knowledge statement.

Overall, responders reported the highest knowledge of basic medication compounding techniques (mean = 3.85) and recently reported adverse events from pharmacy compounding (mean = 3.46), respectively. Responders also reported the lowest knowledge of the Drug Quality and Security Act (mean = 2.76) and federal penalties for violations related to compounding (mean = 2.88), respectively.

Table 4: Knowledge Data for Objective 2

Items	Number of Items	Cronbach's Alpha	Means ± SD	Per-Item Mean
Knowledge	**8**	**0.941**	**25.41 ± 8.035**	**3.177**
Pharmacy compounding laws and regulations				3.29
The Drug Quality and Security Act				2.76
Basic medication compounding techniques				3.85
Recently reported adverse events from pharmacy compounding				3.46
Mississippi Pharmacy Practice Regulations concerning compounding				3.19
The FDAs level of oversight over Compounding				3.14
Federal penalties for violations related to compounding				2.88
State penalties for violations related to compounding				2.83

Objective 3 (Attitude): Results

Descriptive statistics, including means and Cronbach's alpha was used to analyze and measure pharmacists' self-reported, attitudes about pharmacy compounding. Table 5 contains the overall per-item mean for all attitude statements in the survey as well as the individual mean reported for each attitude statement.

Overall, responders reported the highest agreement for compounding meets unmet needs of patients (mean = 4.38) and compounded medications are beneficial to patients (mean = 4.37), respectively. Responders also reported the lowest agreement for the line between compounding and manufacturing has become blurred (mean = 3.17) and compounded pharmacies should be more strictly regulated (mean = 3.26), respectively.

Table 5: Attitude Data for Objective 3

Items	Number of Items	Cronbach's Alpha	Means ± SD	Per-Item Mean
Attitudes	**9**	**.678**	**34.71 ± 4.921**	**3.856**
Compounded medications are generally safe for patients				4.04
Compounded pharmacies should be more strictly regulated				3.26
Compounding pharmacies should be inspected more often than other pharmacies				3.29
Compounding should undergo regular quality testing				4.01
The line between compounding and manufacturing has become blurred				3.17
Compounded medications are beneficial to patients				4.37
Compounded medications are beneficial to society				4.21
Compounding meets unmet needs of patients				4.38
The benefits of compounding outweigh its risks				3.97

Objective 4 (Comparisons): Results

Six separate one-way ANOVA tests were conducted to evaluate objective 4. Three one-way ANOVAS were conducted comparing knowledge with place of primary employment, number of compounded medications, and number of pharmacy association affiliations. The results of these one-way ANOVAS are in Tables 6, 7, and 8, respectively. Three one-way ANOVAS were conducted comparing attitude with place of primary employment, number of compounded medications, and number of pharmacy association affiliations. The results of these one-way ANOVAS are in Tables 9, 10, and 11, respectively.

Of the six one-way ANOVA tests that were conducted, three revealed significant differences at the 0.05 level of significance. For knowledge, primary place of employment and number of compounds prepared on a weekly basis made appeared to make a difference. For attitude, number of compounds made appeared to make a difference. The one-way ANOVA tests that did not reveal a significant difference at the .05 level of significance was testing for differences in knowledge by the number of associations a pharmacist belonged to, testing for differences in attitude based on the primary place of employment, and testing for differences in attitude based on the number of associations a pharmacist belonged to.

Further post hoc tests were conducted from the one-way ANOVA tests that revealed significant differences at the 0.05 level of significance. Tukey HSD Test with knowledge as the dependent variable revealed significant differences between single store independent and traditional chain drug store, supermarket with a pharmacy, and mass merchandiser with a pharmacy respectively. The results are located in Table 12. Tukey

HSD Test with knowledge as the dependent variable also revealed significant differences between $\geq$ 100 compounded medications and 0, 1-9, and 10-99 compounded medications respectively. The results are located in Table 13. Tukey HSD Test with attitude as the dependent variable revealed significant differences between $\geq$ 100 compounded medications and 0 compounded medications. The results are located in Table 14.

Table 6: One Way ANOVA - Knowledge by Primary Place of Employment for Objective 4

Item	Categories	Mean	Standard Deviation	F	P-value
Type of Pharmacy	Single Store Independent	3.68	0.93	3.289	0.003
	Multiple Store Independent	3.42	1.19		
	Traditional Chain Drug Store	2.86	1.15		
	Supermarket with Pharmacy	2.61	0.85		
	Mass Merchandiser with a Pharmacy	2.56	0.87		
	Hospital Inpatient	3.10	0.66		
	Hospital Outpatient	3.25	0.93		
	Other (please indicate)	3.29	0.94		

Table 7: One Way ANOVA - Knowledge by Number of Compounded Medications for Objective 4

Item	Categories	Mean	Standard Deviation	F	P-value
Number of Compounded Medications (weekly)	0	2.83	1.00	13.299	<0.000
	1-9	2.91	0.99		
	10-99	3.28	0.82		
	≥ 100	3.95	0.73		

Table 8: One Way ANOVA – Knowledge by Number of Professional Organizations for Objective 4

Item	Categories	Mean	Standard Deviation	F	P-value
Number of Professional Pharmacy Organizations	0	3.01	1.08	0.543	0.743
	1	2.98	1.02		
	2	3.33	0.71		
	3	3.27	1.17		
	4	3.50	0.95		
	5	3.20	0.96		

Table 9: One Way ANOVA – Attitude by Primary Place of Employment for Objective 4

Item	Categories	Mean	Standard Deviation	F	P-value
Type of Pharmacy	Single Store Independent	3.92	0.51	1.319	0.243
	Multiple Store Independent	3.69	0.78		
	Traditional Chain Drug Store	3.89	0.60		
	Supermarket with pharmacy	3.69	0.35		
	Mass merchandiser with a pharmacy	3.62	0.39		
	Hospital Inpatient	4.03	0.42		
	Hospital Outpatient	3.81	0.46		
	Other (please indicate)	3.83	0.54		

Table 10: One Way ANOVA - Attitude by Number of Compounded Medications for Objective 4

Item	Categories	Mean	Standard Deviation	F	P-value
Number of Compounded Medications (weekly)	0	3.76	0.62	2.874	0.033
	1-9	3.80	0.50		
	10-99	3.85	0.61		
	≥ 100	4.09	0.40		

Table 11: One Way ANOVA – Attitude by Number of Professional Organizations for Objective 4

Item	Categories	Mean	Standard Deviation	F	P-value
Number of Professional Pharmacy Organizations	0	3.96	0.46	1.596	0.170
	1	3.81	0.75		
	2	4.18	0.23		
	3	3.77	0.41		
	4	4.16	0.35		
	5	4.10	0.39		

Table 12: Tukey HSD – Multiple Comparisons Primary Place of Employment
Dependent Variable Knowledge

Population 1	Population 2	Mean Difference	Std. Error	P-value
Single store independent	Traditional chain drug store	0.83	0.23	0.011
	Supermarket with a pharmacy	2.07	0.34	0.037
	Mass merchandiser	1.12	0.35	0.033

Table 13: Tukey HSD – Multiple Comparisons Number of Compounded Medications
Dependent Variable Knowledge

Population 1	Population 2	Mean Difference	Std. Error	P-value
≥ 100	0	1.11	0.20	0.000
	1-9	1.04	0.19	0.000
	10-99	0.67	0.20	0.006

Table 14: Tukey HSD – Multiple Comparisons Number of Compounded Medications
Dependent Variable Attitude

Population 1	Population 2	Mean Difference	Std. Error	P-value
≥ 100	0	0.33	0.12	0.030

DISCUSSION

Discussion of Objective 1 Findings

The purpose of objective 1 was to gather and analyze basic demographic information including primary place of employment, number of pharmacy association affiliations, and number of compounded medications per week, from responding Mississippi pharmacists. The majority of responders considered other type of employment as their primary place of employment at 24.1% followed by traditional chain store at 19.1%, hospital inpatient at 17.6%, and single store independent at 16.1%. The large percentage of those identifying with other may be explained by the fact that many identified other responses may be able to fall under one of the other broad types of primary employment places listed. Traditional chain stores occupy a large portion of the Mississippi pharmacy workforce and those identifying with hospital inpatient and single store independent have contributed to selection bias, as it is possible they compound more medications.

The majority of responders identified as being associated with only one professional pharmacy organization (33.0%) or not being associated with any (28.9%). The frequencies and percentages of the number of respondents associating with a specific number of compounded medications per week were more evenly dispersed. The majority of responders identified as compounding at least 1-9 medications at their primary place of employment (32.3%) with a still decent number compounding at least 100 of more per week at 19.3%. These frequencies may be due to selection bias of responders. Those that

spend more time compounding and take an interest in it would be more likely to open and complete the survey, as it affects their daily employment practices.

Discussion of Objective 2 Findings

The purpose of objective 2 was to gather and analyze descriptive statistics related to responders self-reported, perceived knowledge of eight statements related to pharmacy compounding regulations and safety practices. The statements varied from broad to specific knowledge indicators. Responders were asked to select an answer on a 1-5 scale, with 1 being not at all knowledgeable and 5 being extremely knowledgeable. Overall, data revealed a knowledge, per-item mean of 3.177 as seen in Table 4.

The data in Table 4 revealed somewhat of a knowledge trend. Responders seemed to report knowing the most about basic medication compounding techniques (mean = 3.85), recently reported adverse events from pharmacy compounding (mean = 3.46), and pharmacy compounding laws and regulations (mean = 3.29). The aforementioned are fairly general, especially the first statement. This may be due to the fact that the majority of registered pharmacists have at least a basic knowledge of compounding from their higher education and the fact that any licensed pharmacist may practice compounding. No further licensure or certification is required. Many are also aware of recently reported adverse events due to the widespread news media that has surrounded events related to compounding pharmacy. Responders seemed to report knowing the least about The Drug Quality and Security Act (mean = 2.76), state penalties for violations related to compounding (mean = 2.88), and federal penalties for violations related to compounding (mean = 2.88). The aforementioned three statements are more specific and would likely

require a deeper involvement in the practice and interest of pharmacy compounding. It would also require staying current on regulations and laws passed related to compounding, as the Drug Quality and Security Act was only passed in late 2013.

Discussion of Objective 3 Findings

The purpose of objective 3 was to gather and analyze descriptive statistics related to responders self-reported, attitude of nine statements related to pharmacy compounding needs and safety qualities. The statements varied from the importance of pharmacy compounding to the need for pharmacy compounding regulation attitude indicators. Responders were asked to select an answer on a 1-5 scale, with 1 being strongly disagree and 5 being strongly agree. Overall, data revealed an attitude per-item mean of 3.856 as seen in Table 5.

The data in Table 5 revealed somewhat of an attitude trend. Responders seemed to report the strongest in agreement about compounding meets unmet needs of patient (mean = 4.38), compounded medications are beneficial to patients (mean = 4.37), and compounded medications are beneficial to society (mean = 4.21). The aforementioned are fairly general, broad statements about the importance and benefits that compounded medications provide to patients. Responders seemed to report the least agreement about the line between compounding and manufacturing has become blurred (mean = 3.17), compounded pharmacies should be more strictly regulated (mean = 3.26), and compounding pharmacies should be inspected more often than other pharmacies (mean = 3.29). The aforementioned statements have the commonality of altering how pharmacy compounding is regulated. The lower mean values for these three may be explained by

the fact that the 74.5% of respondents reported compounding at least 1 medication per week, with 19.3% of responders compounding over 100 medications a week, likely contributing to a large portion of their weekly duties at their primary place of employment.

Discussion of Objective 4 Findings

The purpose of objective 4 was to use the data and information that was gathered from respondents to compare knowledge and attitudes about compounding based on their practice characteristics, specifically practice type, preparation of compounded medications, and pharmacy association affiliation.

The one-way ANOVA comparing primary place of employment with knowledge revealed significant differences at the .05 level of significance with a p value of 0.003. A post hoc Tukey HSD test further revealed that the significant differences were between single store independent and traditional chain drug store, supermarket with a pharmacy, and mass merchandiser with p values of 0.011, 0.037, and 0.033 respectively. The common theme is that significant differences existed between the self-reported knowledge of pharmacists working in single store independent and those working in various chains. These differences may be explained by the fact that pharmacists in single store independent compound more medications and not only have an interest in staying current on pharmacy compounding but also have a need to remain informed for compounding duties associated with their practices.

The one-way ANOVA comparing number of compounded medications with knowledge revealed significant differences at the .05 level of significance with a p value

of 0.000. A post hoc Tukey HSD test further revealed that the significant differences were between ≥ 100 compounded medications and 0, 1-9, 10-99 with p values of 0.000, 0.000, and 0.006 respectively. The common theme is that significant differences existed between those compounding ≥ 100 medications per week and responders compounding any other amount. These differences may be explained, similar to those in single store independent, by the fact that pharmacists compounding ≥ 100 medications per week are involved in practices that have a heavy emphasis on pharmacy compounding and not only have an interest in staying current on pharmacy compounding but also have a need to remain informed in order to adequately complete compounding duties associated with their practices.

The one-way ANOVA comparing number of compounded medications with attitude revealed significant differences at the .05 level of significance with a p value of 0.030. A post hoc Tukey HSD test further revealed that the significant difference was between ≥ 100 compounded medications and 0 with a p value of 0.030. While knowledge revealed differences among all categories of number of compounded medications, attitude just revealed differences among the two extremes. This may be explained by the fact that those that compound a large amount of compounded medications per week feel more strongly about the importance of compounded medications and appropriate regulations than those that are not involved in compounding in their practice at all.

Discussion of Pharmacists' Qualitative Comments

The last question of the survey that was distributed asked for responders to record any additional comments regarding pharmacy compounding. The data, tests, and analysis

of the study seem to support the idea that knowledge and attitude regarding the importance, safety, and regulation of pharmacy compounding are impacted by factors like primary place of employment and level of involvement in compounding medications, the comment section of the data reveal that within the data there was still a wide spectrum of opinions regarding the subject.

Comments ranged from expressing support for little to no governmental regulation of compounding to support for some form of a middle ground to support for more, tighter regulations at the federal level.

Limitations

A major limitation of this research study was the response rate of Mississippi-licensed pharmacists that chose to complete the survey. Due to the limitations of the response rate, the responses represented in this study may not be broadened to reflect the opinions of all Mississippi-licensed pharmacists. Another significant limitation of the study was the measurement of self-reported knowledge by the participants. This method of measuring knowledge was subjective and was difficult to accurately and objectively measure participants' knowledge regarding compounding regulatory procedures.

Formed Hypothesis

This was an exploratory study intended to better understand pharmacists' knowledge and attitudes about compounding in light of very recent regulatory changes in compounding. Conducting exploratory research was necessary in order to describe a phenomenon that has not been previously described in the literature. The hypothesis

provided below have been developed as a result of this study and are intended to direct future research in the area.

1) Pharmacists who work for independents will be more knowledgeable about compounding than pharmacists who work for other types of retail pharmacies.
2) The number of compounded medications a pharmacist makes is directly proportional to their knowledge about pharmacy compounding.
3) The number of compounded medications a pharmacist makes is directly proportional to their attitude about pharmacy compounding.

Areas of Future Research

It appears that this study is the first that has been conducted in Mississippi regarding pharmacists' knowledge and attitudes regarding the practice of pharmacy compounding safety and regulation. The discussion of compounding regulation and safety control is an ongoing issue at both the federal and state levels and new laws and policies are continuing to be proposed in light of the matter. This area of research can continued to be explored as new proposals are constantly on the horizon. Another interesting area of study would be to survey typical adult individuals in Mississippi to assess their knowledge and perspectives on the issues of pharmacy compounding. It may also be interesting to conduct a follow up survey with Mississippi-licensed pharmacists should further, intense regulations be proposed at either the federal and/or state levels.

Another area of future study may be a different perspective of the impact of pharmacy organizations on reported knowledge and attitudes about pharmacy compounding safety and regulations. Although it appeared that the number of

professional pharmacy organizations did not significantly affect reported attitude and knowledge, members of specific organizations may show trends in opinions.

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APPENDICES

A. Pharmacist Survey

B. Pharmacist Invitation Letter

C. Pharmacist Reminder Letter

APPENDIX A: Pharmacist Survey

Dear Pharmacist:

Thank you for participating in our survey!

This survey is being conducted by Kimberly Allen who is a pharmacy student and honors college student at the University of Mississippi, under the direction of Dr. Erin Holmes, with the University of Mississippi Department of Pharmacy Administration. In this survey we are interested in garnering your perspectives about pharmacy compounding, especially with regard to how it is regulated.

It should take you approximately 5 minutes to take this survey. Your patience in answering the questions honestly and carefully is valued. To move through the survey, please click the >> at the bottom of the screen. Statement of Consent I have read the above information.

By continuing to the next screen, I consent to participate in the study.

Q1 Are you currently practicing pharmacy?

- ❍ Yes
- ❍ Yes, but currently on leave (medical, maternity, family, etc.)
- ❍ No

Q2 Which of the following best describes the type of pharmacy practice that is your PRIMARY place of employment

- ❍ Single store independent
- ❍ Multiple store independent
- ❍ Traditional chain drug store (For example: Eckerd, CVS, Walgreens, Rite-Aid, Fred's, etc.)
- ❍ Supermarket with a pharmacy (For example: Kroger, etc.)
- ❍ Mass merchandiser with a pharmacy (For example: Costco, Target, Wal-Mart, K-Mart, etc.)
- ❍ Hospital Inpatient
- ❍ Hospital Outpatient
- ❍ Other (please indicate) _____

Q3 For how many hours per week do you work in this PRIMARY place of employment, on average?

_____

Q4 For how many years have you been actively practicing pharmacy?

_____

Q5 How many compounded medications does your pharmacy make per week, on average? For the purpose of this study, pharmacy compounding is defined as a practice in which a licensed pharmacist combines, mixes, or alters ingredients in response to a prescription to create a medication tailored to the medical needs of an individual patient.

_____

Q6 How many continuing education courses, seminars, or training sessions related to prescription compounding have you attended in the past year? For the purpose of this study, pharmacy compounding is defined as a practice in which a licensed pharmacist combines, mixes, or alters ingredients in response to a prescription to create a medication tailored to the medical needs of an individual patient.

_____

Q7 Please check each category for which you have compounded prescriptions (Please check all that apply).For the purpose of this study, pharmacy compounding is defined as a practice in which a licensed pharmacist combines, mixes, or alters ingredients in response to a prescription to create a medication tailored to the medical needs of an individual patient.

- ❑ Pain management (1)
- ❑ Podiatry (2)
- ❑ Hormone replacement therapy (3)
- ❑ Surgical (4)
- ❑ Dermatology (5)
- ❑ Steroid therapy (6)
- ❑ Dental prescriptions (7)
- ❑ Rheumatology (8)
- ❑ Veterinary (9)
- ❑ Parenterals (10)
- ❑ Oncology (11)
- ❑ Ophthalmic (12)
- ❑ Inhalation/respiratory (13)
- ❑ Neuropathy (14)
- ❑ Other (15) _____

Q8 Please indicate to which of the following professional pharmacy organizations you belong (Please check all that apply).

- ❑ AACP (American Association of Colleges of Pharmacy) (1)
- ❑ ACA (American College of Apothecaries) (2)
- ❑ ACCP (American College of Clinical Pharmacy) (3)
- ❑ APhA (American Pharmacists Association) (4)
- ❑ ASHP (American Society of Health System Pharmacists (5)
- ❑ IACP (International Academy of Compounding Pharmacists) (6)
- ❑ MIPA (Mississippi Independent Pharmacists Association) (7)
- ❑ MPhA (Mississippi Pharmacists Association) (8)
- ❑ MSHP (Mississippi Society of Health System Pharmacists) (9)
- ❑ MSPS (Magnolia State Pharmaceutical Society) (10)
- ❑ NCPA (National Community Pharmacists Association) (11)
- ❑ NPhA (National Pharmaceutical Association) (12)
- ❑ PCCA (Professional Compounding Centers of America) (13)
- ❑ Other (14) _____

Q9 Please indicate the extent to which you consider yourself knowledgeable about each of the following topics by selecting the number where 1 = Not at All Knowledgeable and 5 = Extremely Knowledgeable. For the purpose of this study, pharmacy compounding is defined as a practice in which a licensed pharmacist combines, mixes, or alters ingredients in response to a prescription to create a medication tailored to the medical needs of an individual patient.

	Not at All Knowledgeable 1 (1)	2 (2)	3 (3)	4 (4)	Extremely Knowledgeable 5 (5)
Pharmacy compounding laws and regulations (1)	❍	❍	❍	❍	❍
The Drug Quality and Security Act (2)	❍	❍	❍	❍	❍
Basic medication compounding techniques (3)	❍	❍	❍	❍	❍
Recently reported adverse events from pharmacy compounding (4)	❍	❍	❍	❍	❍
Mississippi Pharmacy Practice Regulations concerning compounding (5)	❍	❍	❍	❍	❍
The FDAs level of oversight over compounding (6)	❍	❍	❍	❍	❍
Federal penalties for violations related to compounding (7)	❍	❍	❍	❍	❍
State penalties for violations related to compounding (8)	❍	❍	❍	❍	❍

Q10 Please indicate the extent to which you agree or disagree with each of the following statements where 1 = Strongly Disagree and 5 = Strongly Agree. For the purpose of this study, pharmacy compounding is defined as a practice in which a licensed pharmacist combines, mixes, or alters ingredients in response to a prescription to create a medication tailored to the medical needs of an individual patient.

	Strongly Disagree 1 (1)	2 (2)	3 (3)	4 (4)	Strongly Agree 5 (5)
Compounded medications are generally safe for patients (1)	❍	❍	❍	❍	❍
Compounded pharmacies should be more strictly regulated (2)	❍	❍	❍	❍	❍
Compounding pharmacies should be inspected more often than other pharmacies (3)	❍	❍	❍	❍	❍
Compounding should undergo regular quality testing (4)	❍	❍	❍	❍	❍
The line between compounding and manufacturing has become blurred (5)	❍	❍	❍	❍	❍

Q11 Please indicate the extent to which you agree or disagree with each of the following statements where 1 = Strongly Disagree and 5 = Strongly Agree. For the purpose of this study, pharmacy compounding is defined as a practice in which a licensed pharmacist combines, mixes, or alters ingredients in response to a prescription to create a medication tailored to the medical needs of an individual patient.

	Strongly Disagree 1 (1)	2 (2)	3 (3)	4 (4)	Strongly Agree 5 (5)
Compounded medications are beneficial to patients (1)	❍	❍	❍	❍	❍
Compounded medications are beneficial to society (2)	❍	❍	❍	❍	❍
Compounding meets unmet needs of patients (3)	❍	❍	❍	❍	❍
The benefits of compounding outweigh its risks (4)	❍	❍	❍	❍	❍

Q12 Please feel free to include any comments about compounding or the regulation of compounding.

Appendix B: Pharmacist Email

Dear Mississippi Pharmacist:

The practice of pharmacy compounding has received a lot of recent attention in the media. Much of this attention has dealt with the development of blurred lines between the actions of compounding pharmacies and those of drug manufacturers. Instances in recent years that have involved compounding pharmacies have led to many proposed and enacted changes in how to appropriately and best regulate traditional compounding pharmacies and those that act as manufacturers. Such incidents have stemmed much discussion and debate as to the best way to regulate pharmacy compounding.

As a first year pharmacy student at the University of Mississippi, I am interested in understanding your perceptions of the safety and regulatory requirements of pharmacy compounding, regardless of whether you regularly make pharmacy compounds or not. This project is being conducted as part of my honor's thesis requirement.

This study has been reviewed by The University of Mississippi's Institutional Review Board (IRB). The IRB has determined that this study fulfills the human research subject protections obligations required by state and federal law and University policies. If you have any questions, concerns or reports regarding your rights as a participant of research, please contact the IRB at (662) 915-7482. For specific questions about this research project, please call Erin Holmes at 662-915-5914.

We have provided the direct link to our survey below. It should take no more than 5 minutes to complete. In the event that you are unable to complete the instrument in one sitting, you may return to the incomplete instrument using the link provided below, which allows you to return to the last prompt attempted. Each and every survey completed and returned helps to ensure we get an accurate assessment of pharmacists' knowledge and opinions.

Your participation and support in this study is greatly appreciated.

[SurveyLink]

Sincerely,

Kimberly Allen
PY1 Pharmacy Student
University of Mississippi School of Pharmacy
Erin Holmes, PharmD, PhD
Assistant Professor of Pharmacy Administration
University of Mississippi School of Pharmacy

Appendix C: Pharmacist Reminder Email

Dear Mississippi Pharmacist:

About a week ago you should have received a questionnaire by email that asks about the regulation of pharmacy compounding. If you have already completed it, please disregard this letter-we thank you for your response. If you haven't, we hope you will consider completing it because each and every survey completed helps to ensure we get an accurate assessment of pharmacists' opinions. The survey (link provided below) should take no more than 5 minutes to complete.

As a current pharmacy student at the University of Mississippi, I am interested in understanding the Mississippi pharmacist community's perspective on the regulatory changes associated with pharmacy compounding. This project is being conducted as part of my honor's thesis requirement.

This study has been reviewed by The University of Mississippi's Institutional Review Board (IRB). The IRB has determined that this study fulfills the human research subject protections obligations required by state and federal law and University policies. If you have any questions, concerns or reports regarding your rights as a participant of research, please contact the IRB at (662) 915-7482.

We have provided the direct link to our survey below. In the event that you are unable to complete the instrument in one sitting, you may return to the incomplete instrument using the link provided below, which allows you to return to the last prompt attempted. Each and every survey completed and returned helps to ensure we get an accurate assessment of pharmacists' opinions.

[SurveyLink]

Sincerely,

Kimberly Allen
PY1 Pharmacy Student
University of Mississippi School of Pharmacy

Erin R. Holmes, PharmD, PhD
Assistant Professor of Pharmacy Administration
University of Mississippi School of Pharmacy