CSI - Ohio
The Common Sense Initiative

Business Impact Analysis

Agency Name: Ohio State Board of Pharmacy

Regulation/Package Title: Pharmacists-Administrative Provisions

Rule Number(s): Amended: 4729-11-03

Date: 3/6/2014

Rule Type:

New	5-Year Review
Amended	Rescinded

The Common Sense Initiative was established by Executive Order 2011-01K and placed within the Office of the Lieutenant Governor. Under the CSI Initiative, agencies should balance the critical objectives of all regulations with the costs of compliance by the regulated parties. Agencies should promote transparency, consistency, predictability, and flexibility in regulatory activities. Agencies should prioritize compliance over punishment, and to that end, should utilize plain language in the development of regulations.

Regulatory Intent

1. Please briefly describe the draft regulation in plain language.

The Ohio State Board of Pharmacy (OSBP), pursuant to section 3719.44 of the Ohio Revised Code, proposes that tramadol be listed as a Schedule IV controlled substance.

Tramadol is an opioid analgesic that produces its primary opioid-like action through an active metabolite, referred to as the "M1" metabolite (O-desmethyltramadol). Since March 1995, tramadol has been available as a non-controlled and centrally acting opioid analgesic under the trade name ULTRAM® approved by the Food and Drug Administration (FDA). Subsequently, the FDA approved generic, combination, and extended release products of tramadol.

Over the past seven years, tramadol prescriptions in Ohio have increased by almost 94 percent. This increase may be explained by an awareness of the addictive nature of controlled substance opioids by the prescriber community resulting in a switch to tramadol, which is currently non-controlled. However, studies show that while tramadol has a currently accepted medical use, it has abuse potential similar to that of Schedule IV controlled substances as well as mimics the effects of controlled substance opioid analgesics. By adding tramadol as a Schedule IV controlled substance, the OSBP seeks to educate prescribers and patients on the potential adverse impacts of this medication and to provide additional legal and regulatory oversight to protect the health and safety of Ohioans.

If adopted, Ohio would join the following states (and the U.S. Military) that have added tramadol as a Schedule IV controlled substance: Arkansas, Illinois, Kentucky, Mississippi, New Mexico, New York, North Dakota, Oklahoma, Tennessee, and Wyoming.

2. Please list the Ohio statute authorizing the Agency to adopt this regulation.

The proposed rule is authorized by section 3719.44 of the Ohio Revised Code. The following sections of the Ohio Revised Code are also considered authorizing statutes for this rule package: 3719.36, 3719.28, 4729.26, 3719.05, 4729.51, 3719.01, 3719.011, 3719.02, 3719.021, 3719.04, 3719.06, 3719.07, 3719.08, 3719.09, 3719.11, 3719.121, 3719.18 and 3719.41.

3. Does the regulation implement a federal requirement? Is the proposed regulation being adopted or amended to enable the state to obtain or maintain approval to administer and enforce a federal law or to participate in a federal program?

The rule does not implement a federal requirement.

4. If the regulation includes provisions not specifically required by the federal government, please explain the rationale for exceeding the federal requirement.

This rule package exceeds federal requirements because the Ohio General Assembly provided the Ohio State Board of Pharmacy under 3719.44 of the Revise Code the authority to add new drugs as scheduled compounds. This authorizing statute is intended for the Board to be able to act quickly to address drugs of increasing misuse and abuse. While the Drug Enforcement Agency is currently considering adding tramadol as a controlled substance, the Board feels that the increase in tramadol prescribing coupled with growing rates of opioid addiction and death warrant this proposed regulation.

5. **What is the public purpose for this regulation (i.e., why does the Agency feel that there needs to be any regulation in this area at all)?**

Adding tramadol as a Schedule IV controlled substance will should increase awareness of the public and prescriber community to the addictive nature of the drug in hopes of reducing opioid addiction and diversion. This increased awareness is important, as data collected by the Board suggests an increased misuse of tramadol based on a perception that tramadol is safer and easier to obtain than controlled substance opioid analgesics. In addition, without this regulation, the OSBP would not be able to ensure the regulatory and legal oversight that research and expert opinion suggest that this addictive drug warrants.

6. **How will the Agency measure the success of this regulation in terms of outputs and/or outcomes?**

The success of the regulations will be measured by having rules written in plain language, licensee compliance with the rules, and minimal questions from licensees and prescribers regarding the provisions of the rule.

Development of the Regulation

7. **Please list the stakeholders included by the Agency in the development or initial review of the draft regulation.**

In addition to research conducted and reviewed by board staff, the Ohio State Board of Pharmacy worked with the following experts to develop this rule:

- **Dr. Jon E Sprague, RPh, PhD**, Head of Pharmaceutical Sciences and Director of Research and Discovery at the Ferris State University College of Pharmacy. He has an extensive publishing history that includes peer-reviewed publications, book reviews, and written abstracts for professional publications and seminars. A majority of the peer-reviewed publications have an emphasis on drugs of abuse. Dr. Sprague is a frequent presenter of continuing education courses, professional presentations for organizations such as the Ohio Pharmacist Association and the Council of Colleges of Pharmacy. He has given scientific presentations, reviewed manuscripts for professional journals, written many grants and obtained funding for numerous research projects. Dr. Sprague has also conducted research using rats to study the abuse potential of tramadol.[1]

[1] Reference: Sprague et al., 2002; Synapse 43:118-121

- **Dr. Steven Matson, MD**, is a Staff Physician in the Section of Adolescent Health at Nationwide Children's Hospital and an Associate Professor of Clinical Pediatrics at The Ohio State University College of Medicine. Since 2009, he has served as the director of the Medication Assisted Treatment for the Opiate Addiction Program at Nationwide Children's Hospital and also as the Medical Director of the Franklin County Juvenile Detention Facility. Dr. Matson is Board Certified in Addiction Medicine and the president of the Ohio Chapter of the American Society of Addiction Medicine.

- **Det. Dennis Luken**, Warren County Drug Task Force.

8. What input was provided by the stakeholders, and how did that input affect the draft regulation being proposed by the Agency?

The Ohio State Board of Pharmacy received sworn affidavits from Dr. Matson and Dr. Sprague in support of the proposal to classify tramadol as a schedule IV substance. In addition, the Board received input from Det. Luken who stated the following in a letter submitted on 2/25/14: *"It* should be noted that a contributing factor associated with tramadol investigations that I have conducted is most people believe tramadol is not addictive. Secondly, is that most physicians do not understand the pharmacology of tramadol and do not understand that tramadol is an addictive pain medication and feel it is safe to prescribe because it is not a controlled substance. Thirdly, there are many illegal internet pharmacy operations and physicians practicing telemedicine and prescribing tramadol because it is not a controlled substance and are fueling *the addiction problems of individuals."*

The Ohio State Board of Pharmacy reviewed the formal proposal and approved the rule for filing on 3/5/14.

9. What scientific data was used to develop the rule or the measurable outcomes of the rule? How does this data support the regulation being proposed?

In evaluating the relative abuse potential of tramadol, the OSBP reviewed and evaluated all of the available data from the following:

- Articles from scientific and medical literature;
- Reports from the Food and Drug Administration (FDA);
- Reports from the Ohio Automated Rx Reporting System (OARRS);

- Reports from the Substance Abuse and Mental Health Services Administration (SAMHSA) [Drug Abuse Warning Network (DAWN) and National Survey on Drug Use and Health (NSDUH)];
- Case reports from the Ohio State Board of Pharmacy;
- Reports from the Drug Enforcement Administration (DEA);
- Case reports from the Warren County Drug Task Force;
- Reports from the Ohio Substance Abuse Monitoring Network (OSAM); and
- Sworn affidavits from expert witnesses.

In making a determination to add an unscheduled compound, the board is required to consider the following 8 criteria:

(1) The actual or relative potential for abuse. An examination of Ohio specific data and reports from the FDA and DEA collectively found the following:

   a. Individuals are taking tramadol in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community.

   b. There is significant diversion of tramadol from legitimate drug channels.

   c. Individuals are taking tramadol on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such substance.

   d. The substance is so related in its action to a substance already listed (propoxyphene) as having a potential for abuse to make it likely that it will have the same potential for abuse as such substance, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.

(2) The scientific evidence of the pharmacological effect of the substance. Studies on animals and humans indicate that tramadol produces reinforcing effects (i.e. inducing patterns of non-medical self-administration). In addition, the drug blocks the reuptake of norepinephrine and serotonin, effects also produced by controlled substance opioids.

(3) The state of current scientific knowledge regarding the substance. According to the FDA, the chemical structures of tramadol share similarities with the chemical structure of the opioid, codeine [C-II, C-III and C-V for products]. This similarity is consistent with the findings of pharmacology studies that demonstrate the opioid activity of tramadol.

(4) The history and current pattern of abuse. Tramadol has been abused since its marketing approval in 1995 by a wide spectrum of individuals of different ages, alone and in

combination with other psychoactive substances. A review of OSAM Reports from the Ohio Department of Mental Health and Addiction Services, found reports of tramadol abuse began surfacing around 2002. Since then, subsequent OSAM reports confirm a pattern of abuse, including diversion of the drug and the willingness of prescribers to provide the medication in lieu of controlled substance opioid analgesics.

(5) The scope, duration, and significance of abuse.

a. According to the FDA, clinical case reports describe abnormal behavior that demonstrates an addiction liability of tramadol: drug craving, increasing the tramadol dose, performing self-injury in order to be prescribed more tramadol, taking high doses despite adverse effects that result, and visiting multiple physicians in order to obtain more prescriptions for tramadol.

b. According to the NSDUH data, the estimated number of individuals who have used tramadol products non-medically at least once in their lifetime increased from 994,000 in 2002 to 2,614,000 in 2011.

c. The Drug Abuse Warning Network (DAWN) also provides the scope, duration and significance of abuse for tramadol. A review of the data found that the estimated annual ED visits from non-medical use of tramadol and its combinations continually increased from 4,849 ED visits in 2004 to 20,000 ED visits in 2011, which is a 312 percent increase.

(6) The risk to the public health. To assess the risk to the public health associated with tramadol, the following of information sources were examined: 1) the September 9, 2009, approved labeling for ULTRAM; 2) reports in the medical literature; 3) DAWN emergency room visits and medical examiner reports; 4) data from the American Association of Poison Control Centers; and 5) an overall assessment of prescription opioid abuse and overdose in the state of Ohio. Collectively the data indicates that tramadol presents risks to the public health and, as such, supports the scheduling of tramadol. The DAWN and AAPCC data suggest a lower schedule for tramadol than Schedule III.

(7) The potential of the substance to produce psychic or physiological dependence liability. The FDA reviewed available information from pre-clinical and clinical studies and found that repeated dosing with tramadol resulted in dependence development, and withdrawal syndromes resulted from termination of tramadol treatment. Additionally, medical literature also documents numerous case reports of physiological and physical dependence to tramadol. The medical literature suggests that tramadol produces a modest level of physical dependence, with the studies suggesting a degree of physical dependence development less than that of Schedule II and III opioids but similar to drugs in Schedule IV.

(8) Whether the substance is an immediate precursor. Both the FDA and DEA conclude that tramadol is not an immediate precursor of any substance already controlled under the Federal Controlled Substances Act.

Note: Additional information and supporting data can be found in the proposal accompanying this BIA.

10. What alternative regulations (or specific provisions within the regulation) did the Agency consider, and why did it determine that these alternatives were not appropriate? If none, why didn't the Agency consider regulatory alternatives?

As the regulations are essential to the protecting the public's safety by ensuring that pharmacies, pharmacists and prescribers adhere to uniform regulations when prescribing or dispensing tramadol, the Ohio State Board of Pharmacy did not consider any regulatory alternatives.

11. Did the Agency specifically consider a performance-based regulation? Please explain. Performance-*based regulations define the required outcome, but don't dictate the process* the regulated stakeholders must use to achieve compliance.

The agency did not consider a performance-based regulation for this rule package. The Board determined that it is not feasible to ensure that all of the controls and regulations pertaining to tramadol as a Schedule IV controlled substance can be implemented without explicitly specifying it in rule.

12. What measures did the Agency take to ensure that this regulation does not duplicate an existing Ohio regulation?

The Board of Pharmacy's Director of Legal Affairs reviewed the Ohio Administrative Code to ensure that these regulations do not duplicate an existing Ohio regulation.

13. Please describe the Agency's plan for implementation of the regulation, including any measures to ensure that the regulation is applied consistently and predictably for the regulated community.

The rule will be posted on the Pharmacy Board's web site, information concerning the rule will be included in materials e-mailed to licensees, and notices will be sent to associations, individuals and groups. Pharmacy Board staff are also available via phone or email to answer

questions regarding implementation of the rule. In addition, the Board's compliance agents are trained to educate licensees on current and/or new regulations during on-site inspections.

Pharmacy Board staff receive regular updates on rules via a quarterly internal newsletter, biannual staff meetings featuring a regulatory update, mandatory all-day law reviews for new employees, monthly email updates from the legislative affairs liaison and feedback from the Board's legal director for every citation submitted.

Adverse Impact to Business

14. Provide a summary of the estimated cost of compliance with the rule. Specifically, please do the following:

a. Identify the scope of the impacted business community;

The rules primarily impact health care providers, hospitals, pharmacies, veterinarians and any other entity that legally prescribers, possesses, sells or dispenses tramadol in the state of Ohio.

b. Identify the nature of the adverse impact (e.g., license fees, fines, employer time for compliance); and

Violation of the rules may result in administrative licensure discipline for the dispenser and/or the location licensed as a terminal distributor of dangerous drugs (TDDD) or wholesale distributor of dangerous drugs (WDDD). Discipline might include reprimand, imposition of a fine, and suspension of the license and/or revocation of the license.

If adopted, pharmacies and prescribers would need to be aware that prescriptions for tramadol would need to follow Ohio laws and regulations for controlled substance prescriptions, which include:

- Prescriptions issued for tramadol must include the Drug Enforcement Administration (DEA) registration number of the issuing practitioner.
- Prescribers need a valid controlled substance registration from the DEA to prescribe.
- Prescriptions cannot be filled or refilled more than six months after the date on which such prescription was issued. Prescriptions cannot be refilled more than five times. A prescription may be transferred only one time, with that transfer being from the pharmacy where the prescription was originally filled. It shall not be further transferred by, or to, any other pharmacy.

- Board of Pharmacy licensees (TDDD) and (WDDD) that sell, store or dispense tramadol and do not have a license with a controlled substance category will have to apply for new licensure.

c. Quantify the expected adverse impact from the regulation.

- Prescriptions issued for tramadol must include the Drug Enforcement Administration (DEA) registration number of the issuing practitioner. This will result in a minimal increase in prescriber time to add the DEA registration number.
- Prescribers need a valid controlled substance registration from the DEA to prescribe. Those prescribers who do not have a DEA license and who prescribe tramadol will be required to pay $731 every three years to obtain a DEA registration number.[2]
- Prescriptions cannot be filled or refilled more than six months after the date on which such prescription was issued. Prescriptions cannot be refilled more than five times. A prescription may be transferred only one time, with that transfer being from the pharmacy where the prescription was originally filled. It shall not be further transferred by, or to, any other pharmacy. This will mainly impact the patient and may result in additional costs required to see their physician if they have run out of their medication. However, if being treated for chronic pain, patients should receive regular assessments to determine the best course of care.
- Board of Pharmacy licensees (TDDD) and (WDDD) that sell, store or dispense tramadol and do not have a license with a controlled substance category, will have to apply for a new license. The cost of updating a TDDD license from a non-controlled to a controlled license is $150.00 compared to the $112.50 paid for a non-controlled TDDD. The cost of updating a WDDD license would be $787.50 compared to the $750.00 paid for a non-controlled WDDD. A review of licensing data determined that only 1 terminal distributor and 2 wholesalers have licenses that require reapplication for a controlled license. However, the WDDD renewal date is in June when the rule would take effect and therefore the two WDDD licensees will only incur the added cost of $37.50 when they reapply for their license. The average application time for a WDDD and TDDD is approximately 1 hour.

[2] https://www.deadiversion.usdoj.gov/webforms/jsp/regapps/common/newAppLogin.jsp

15. Why did the Agency determine that the regulatory intent justifies the adverse impact to the regulated business community?

According to the Ohio Department of Health, nearly 5 Ohioans die every day from unintentional drug overdoses, with prescription opioids, including tramadol, associated with more fatal overdoses than illegal drugs including cocaine, heroin and hallucinogens combined. In 2011, nearly half (44.7 percent) of fatal unintentional overdoses involved prescription opioids in Ohio in 2011, an equal percentage to 2010.

Data collected by the Board suggests an increased misuse of tramadol based on a perception that tramadol is safer and easier to obtain than controlled substance opioid analgesics. Widespread diversion of tramadol will only continue to feed the addiction and overdose death crisis that is impacting the state. In fact, fatal drug overdose costs Ohioans $1.9 billion on average each year in medical and work loss costs; while non-fatal, hospital-admitted drug poisonings cost an additional $40 million. The total cost equals an average of $5.4 million each day in medical and work loss costs in Ohio.

By adding tramadol as a Schedule IV controlled substance, the OSBP seeks to educate prescribers and patients on the potential adverse impacts of this medication and to provide additional legal and regulatory oversight to protect the health and safety of Ohioans and prevent further abuse of opioid pain relievers.

Regulatory Flexibility

16. Does the regulation provide any exemptions or alternative means of compliance for small businesses? Please explain.

This rule does not provide any exemptions or alternative means of compliance for small businesses. The law does not differentiate on the size of the business and therefore, applies to all licensees who prescribe, dispense and store controlled substances.

17. How will the agency apply Ohio Revised Code section 119.14 (waiver of fines and penalties for paperwork violations and first-time offenders) into implementation of the regulation?

The Ohio State Board of Pharmacy does not fine licensees or impose penalties for first-time paperwork violations. However, any failure of a standard of care is not considered a paperwork error but a quality assurance issue by the licensee that is necessary for the protection of the public.

18. What resources are available to assist small businesses with compliance of the regulation?

Board staff members are available by telephone and e-mail to answer questions. Board staff members also provide presentations to groups and associations who seek an update on current regulations. Additionally, field staff (i.e. compliance officers) is trained to educate licensees on compliance with all Board of Pharmacy rules and regulations.

4729-11-03 Schedules II, III, IV and V (Proposed Rule)

(A) The State Board of Pharmacy hereby schedules the following compounds as Schedule IV controlled substances:

(1) 2-(dimethylaminomethyl)-1-(3-methoxyphenyl)cyclohexanol hydrochloride, its salts, isomers (including the optical and geometric isomers), salts of isomers, and all isomeric configurations of possible forms including tramadol.