



DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1301

[Docket No. DEA-394F]

RIN 1117-AB38

Removal of Exemption from Registration for Persons Authorized Under U.S. Nuclear Regulatory Commission or Agreement State Medical Use Licenses or Permits and Administering the Drug Product DaTscan

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final rule.

SUMMARY: On November 25, 2014, the Drug Enforcement Administration published the interim final rule titled “Exemption from Registration for Persons Authorized Under U.S. Nuclear Regulatory Commission or Agreement State Medical Use Licenses or Permits and Administering the Drug Product DaTscan.” The Drug Enforcement Administration is hereby removing this interim final rule as it is no longer needed, as a result of the removal of [¹²³I]ioflupane from the schedules of controlled substances effective September 11, 2015.

DATES: *Effective Date:* [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

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SUPPLEMENTARY INFORMATION:

Legal Authority

The Drug Enforcement Administration (DEA) implements and enforces Titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. 21 U.S.C. 801–971. Titles II and III are referred to as the “Controlled Substances Act” and the “Controlled Substances Import and Export Act,” respectively, and are collectively referred to as the “Controlled Substances Act” or the “CSA” for the purpose of this action. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, each controlled substance is classified into one of five schedules based upon its potential for abuse, its currently accepted medical use in treatment in the United States, and the degree of dependence the substance may cause. 21 U.S.C. 812. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and pursuant to 21 U.S.C. 812 (a) and (b), the current list of all scheduled substances is published at 21 CFR part 1308.

Pursuant to 21 U.S.C. 822(a)(1), every person who manufactures or distributes any controlled substance or list I chemical, or who proposes to engage in the manufacture or

distribution of any controlled substance or list I chemical, shall obtain annually a registration issued by the Attorney General in accordance with the rules and regulations promulgated by the Attorney General. Further, pursuant to 21 U.S.C. 822(a)(2), every person who dispenses, or who proposes to dispense, any controlled substance, shall obtain from the Attorney General a registration issued in accordance with the rules and regulations promulgated by the Attorney General.

The Attorney General however may, by regulation, waive the requirement for registration of certain manufacturers, distributors, or dispensers if the Attorney General finds it consistent with the public health and safety pursuant to 21 U.S.C. 822(d). The Attorney General delegated this authority to the Administrator of the DEA, 28 CFR 0.100(b), who in turn re delegated that authority to the Deputy Assistant Administrator of the DEA Office of Diversion Control (“Deputy Assistant Administrator”). 28 CFR part 0, subpart R, App. section 7.

Background

On November 25, 2014, the DEA published an interim final rule (IFR) exempting from registration persons authorized under Nuclear Regulatory Commission (NRC) or Agreement State Medical Use Licenses or permits and administering the drug product DaTscan directly to patients for diagnostic purposes. 79 FR 70085. The IFR was intended to alleviate the regulatory burdens on those administering the drug product DaTscan, to allow more patients to receive important diagnostic testing. Additionally, because persons who administer DaTscan are subject to strict NRC/Agreement State requirements, the DEA determined in the IFR that the waiver from registration of persons who administer DaTscan was consistent with the public health and safety. The IFR

provided an opportunity for interested persons to submit written comments on the rulemaking on or before January 26, 2015.

However, effective September 11, 2015, the DEA removed [¹²³I]ioflupane from the schedules of controlled substances. 80 FR 54715. [¹²³I]ioflupane is the active pharmaceutical ingredient in DaTscan. Accordingly, a registration exemption is no longer necessary for persons who administer the drug product DaTscan. As the DEA explained in the final rule removing [¹²³I]ioflupane from the schedules of controlled substances, all of the administrative, civil, and criminal sanctions applicable to controlled substances no longer apply to those persons who handle [¹²³I]ioflupane, or any drug products that contain [¹²³I]ioflupane, on or after September 11, 2015.

Because the decontrol of [¹²³I]ioflupane supersedes the registration exemption provided in the IFR, the DEA hereby finalizes the rulemaking procedure that was initiated with the November 25, 2014, IFR (79 FR 70085) by publishing this final rule removing that regulation. Below the DEA has provided a discussion of comments received in response to the IFR. 79 FR 70085.

Comments Received

The DEA received six comments on the IFR. Two comments were from GE Healthcare, the manufacturer of the drug product DaTscan, one comment was from a professor of pharmaceutical sciences, two comments were from nuclear medicine industry groups, and one comment was from a Parkinson's Disease advocacy group.

Decontrol of DaTscan:

Five commenters requested that the DEA follow the November 2, 2010, recommendation by the U.S. Department of Health and Human Services (HHS) to

decontrol the drug product DaTscan. One commenter stated that the DEA is bound by the HHS' recommendation. Additionally, five of these commenters cited the lack of abuse of the drug product DaTscan as a reason why it should be decontrolled.

Response: There is no doubt that, as a derivative of cocaine, ioflupane is a schedule II controlled substance. Congress specified that “cocaine, its salts, optical and geometric isomers, and salts of isomers; ecgonine, its derivatives, their salts, isomers, and salts of isomers; or *any compound, mixture, or preparation which contains any quantity of any of the substances* referred to in this paragraph” are schedule II controlled substances. 21 U.S.C. 812(c), Schedule II, (a)(4) (emphasis added). A radioactive form of ioflupane is contained within the drug product DaTscan; accordingly DaTscan was controlled as a schedule II substance at the time of the IFR. The fact that there is a low likelihood of diversion of the drug product DaTscan at the dispensing level supported the registration exemption provided by the IFR at that time.

As stated in the IFR, the DEA was continuing to review the control status of [¹²³I]ioflupane pursuant to 21 U.S.C. 811. The IFR was separate and apart from the control process, and did not resolve the control status of [¹²³I]ioflupane. The purpose of the IFR was to encourage use and expand access of this drug product as a diagnostic tool until the control status of DaTscanTM was resolved. Subsequently, effective September 11, 2015, the DEA removed [¹²³I]ioflupane from the schedules of controlled substances. The factors in support of removing [¹²³I]ioflupane from the schedules of controlled substances are summarized in the notice of proposed rulemaking and the final rule, (80 FR 13455 and 80 FR 54715, respectively). The DEA explained in the final rule that as a result of removing [¹²³I]ioflupane from the schedules of controlled substances, all of the

administrative, civil, and criminal sanctions applicable to controlled substances no longer apply to those persons who handle [¹²³I]ioflupane.

Expedited Rulemaking under the Administrative Procedure Act:

One commenter expressed concern that the DEA did not undertake notice and comment procedures before promulgating the IFR. The same commenter stated that the IFR did not meet the legal requirements for expedited rulemaking nor for the issuance of a rule with an immediate effective date, asserting that the IFR did not meet the requirements of the good cause exception to make a rule immediately effective.

Response: A rule is exempt from certain provisions of the Administrative Procedure Act (APA), including notice of proposed rulemaking and the pre-promulgation opportunity for public comment, if the agency for good cause determines that those procedures are unnecessary, impracticable, or contrary to the public interest. 5 U.S.C. 553(b)(3)(B). The IFR was intended to enable more persons to administer DaTscan, thereby helping to increase patient access to its diagnostic benefits. The DEA for good cause found that it was unnecessary and contrary to the public interest to seek public comment prior to promulgating the IFR because, without prompt exemption from registration, some members of the health care community would not have been able to utilize this diagnostic tool. It was reasonable to expect that alleviating the registration burden would stimulate use, thereby expanding access. In addition, this exemption was intended to reduce costs for imaging centers because they would not have had to pay DEA registration fees (unless they also handle other pharmaceutical controlled substances).

The IFR alleviated certain registration, security, recordkeeping, reporting, and

labeling requirements for persons authorized under the NRC, or Agreement State medical use licenses or permits, who administer the drug product DaTscan to a patient for diagnostic purposes. The APA requires the publication of a substantive rule to be made not less than 30 days before its effective date. 5 U.S.C. 553(d). However, the APA allows an exception for “a substantive rule which grants or recognizes an exemption or relieves a restriction.” 5 U.S.C. 553(d)(1). The DEA found that the IFR met this criterion.

Although a notice of proposed rulemaking was not published with regard to the drug product DaTscan, the DEA published an IFR with request for comment on November 25, 2014. The comment period for the IFR closed on January 26, 2015, and in that 60-day time frame, the DEA received six comments on the rulemaking, and has considered those comments herein.

Exemption from Registration for Radiopharmacies:

One commenter stated that the registration exemption should be expanded to include nuclear pharmacies (also known as radiopharmacies) that distribute DaTscan, because it would increase patient access to DaTscan.

Response: At the time of the IFR, radiopharmacies that transferred DaTscan to imaging centers and hospitals were required to be registered as distributors because they transferred the now decontrolled substance to other registrants for subsequent administration pursuant to the authority of a DEA Form 222 or digitally signed electronic order rather than pursuant to the authority of a prescription or other lawful order. The commenter does not state how such an exemption would increase patient access, and the radiopharmacy (i.e., the registered distributor of DaTscan) commented that the barrier to

patient access is the registration requirement at the imaging centers, rather than at the distributor or manufacturer levels. Therefore, it was appropriate that the IFR did not include radiopharmacies within the scope of the registration exemption.

Inconsistency between Federal and State Law:

Three commenters asserted concern that the IFR could not directly exempt anyone from state requirements since most states would not automatically incorporate federal exemptions into their corresponding regulatory systems. The commenters expressed further concern that each state would require an independent rulemaking process to implement the registration exemption.

Response: Before promulgation of the IFR, only imaging centers that operated in accordance with NRC or Agreement State regulations and that were DEA registrants were able to administer the drug product DaTscan. The IFR alleviated the requirement to register with the DEA, as well as the associated security, recordkeeping, and reporting requirements for persons authorized under the NRC or Agreement State medical use licenses or permits who administer the drug product DaTscan to a patient for diagnostic purposes.

With respect to the relationship between Federal and State law in the area of controlled substances, the IFR did not alter State law. The CSA shall not be “construed as indicating an intent on the part of the Congress to occupy the field in which that provision operates, including criminal penalties, to the exclusion of any State law on the same subject matter which would otherwise be within the authority of the State, unless that is a positive conflict between that provision . . . and that State law so that the two cannot consistently stand together.” 21 U.S.C. 903. Accordingly, any applicable State law that

is more stringent than Federal law applies.

This lack of uniformity between Federal and State law with respect to the treatment of controlled substances is not uncommon, and it is encountered by registrants and non-registrants that lawfully handle controlled substances. For example, some states control substances that are not Federally controlled or control substances more stringently than the Federal controls (e.g., carisoprodol, tramadol, pseudoephedrine products). Still other states prohibit activities that are allowed under the CSA (e.g., collection and disposal of controlled substances by certain entities). These issues with respect to lack of uniformity between Federal and State law may also be present with respect to the recent removal of [¹²³I]ioflupane from the schedules of controlled substances.

In addition, the exemption provided by the IFR was very similar to the DEA-authorized exemption for certain chemical preparations pursuant to 21 CFR 1308.23. In accordance with 21 CFR 1308.23 and 1308.24, certain preparations or mixtures containing one or more controlled substances can be exempt from regulations pertaining to registration, security, labeling, records, and reports. In 2014, the DEA exempted almost 1,500 preparations from certain regulatory requirements, a number that has increased considerably since 2011 when the DEA exempted 390 chemical preparations. It is the DEA's understanding that there has been no confusion with respect to State laws which apply to these chemical preparations. As the registration exemption in the IFR was similar to the exemptions provided for certain chemical preparations, the DEA believed at the time of the IFR that it was unlikely that the IFR would create complications with State laws.

Disposal:

Three commenters discussed the issue of disposal of the drug product DaTscan. One commenter expressed concern that hospitals and other practitioners currently registered with the DEA and administering the drug product DaTscan are required to change their existing disposal practices with respect to DaTscan as a result of the IFR. The commenter noted that the IFR language can be read to impose new requirements for those handling the drug product DaTscan. The commenter also stated that it was not practice for the current distributor to take back unused portions of DaTscan from those administering the drug product, and that the current distributor is not licensed as a reverse distributor. The commenter also stated that the DEA did not specify the volume of the drug product DaTscan which would constitute “unused” product, and inquired about the use of DEA Forms 41 and 222.

Another commenter expressed concern that requiring exempt entities (e.g., imaging centers) to return the unused DaTscan to the distributor will increase costs to exempt entities.

Response: Under the IFR, hospitals, imaging centers, and other practitioners that were already registered with the DEA were not required to follow the procedures in the IFR if they chose to handle DaTscan as a DEA registrant. Only those entities that chose to benefit from the exemption had to adhere to the requirements of the IFR. Therefore, those entities already registered with the DEA that did not wish to be exempt from registration when handling DaTscan, were permitted to continue to handle the drug product DaTscan, including disposal, in accordance with applicable law.

At the time of the IFR, the DEA understood that it was common practice for radiopharmacies to take back unused radioactive material in vials and dosage unit

syringes, as well as empty vials and empty dosage unit syringes from the medical use licensee, as long as they were originally provided by the radiopharmacy. Further, the DEA understood that as long as the radiopharmacy is authorized under its NRC or Agreement State license for this return, and does not receive anything that it did not send to the medical use licensee, the radiopharmacy is not considered a waste broker in accordance with NRC or Agreement State regulations. The DEA appreciates the commenter's clarification of the business practices relating to the drug product DaTscan.

As discussed, effective September 11, 2015, the DEA removed [¹²³I]ioflupane from the schedules of controlled substances. The DEA explained in the final rule removing [¹²³I]ioflupane from the schedules of controlled substances, none of the requirements applicable to controlled substances will apply on or after that date to those persons who handle [¹²³I]ioflupane, such as the drug product DaTscan, including use of the DEA Form 41 and 222. 80 FR 54715.

Compliance with Executive Order 12866:

One commenter expressed concern that the DEA determined that the IFR was a non-significant regulatory action and had, therefore, circumvented interagency review. The commenter stated that the IFR represents a drastic and notable departure from established practice in the healthcare industry. The commenter was also concerned that the interaction with existing laws and regulations promulgated by other federal agencies should have resulted in interagency review, and the process undertaken by the DEA for the IFR will have a precedential effect on future DEA rulemakings.

Response: To be a significant regulatory action in accordance with Executive Order

12866 (EO 12866) the action must meet one of the four factors set forth in EO 12866.¹ The DEA determined that the IFR did not meet any of the four factors. In addition, the Office of Management and Budget concurred with the assessment that the IFR was not significant under EO 12866, sec. 6.

Labeling Requirements:

One commenter stated that the DEA is unable to waive the CSA’s requirement (21 U.S.C. 825) that controlled substances be labeled as such, and that the DEA is unable to waive labeling requirements enforced by the Food and Drug Administration (FDA).

Response: Initially the DEA included the waiver for labeling so that those exempted by this waiver would not be confused by the “C-II” labeling on the DaTscan packaging. The comments, however indicated that not requiring “C-II” labeling would cause more confusion than requiring it. However, due to the recent removal of [¹²³I]ioflupane from the schedules of controlled substances, the “C-II” label is no longer required on DaTscan packaging.

Regulatory Analyses

Executive Orders 12866 and 13563

This final rule has been drafted and reviewed in accordance with Executive Order

¹ As provided in Executive Order Section 12866, Regulatory Planning and Review, sec. 3(f): “Significant regulatory action” means any regulatory action that is likely to result in a rule that may: (1) Have an annual effect on the economy of \$100 million or more or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities; (2) Create a serious inconsistency or otherwise interfere with an action taken or planned by another agency; (3) Materially alter the budgetary impact of entitlements, grants, user fees, or loan programs or the rights and obligations of recipients thereof; or (4) Raise novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in this Executive order.

12866, “Regulatory Planning and Review” section 1(b), Principles of Regulation, and in accordance with Executive Order 13563, “Improving Regulation and Regulatory Review” section 1(b) General Principles of Regulation.

The Department of Justice has determined that this rule is not a “significant regulatory action” under Executive Order 12866, section 3(f), Regulatory Planning and Review, and accordingly this rule has not been reviewed by the Office of Management and Budget.

Executive Order 12988

This regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 Civil Justice Reform to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132

This rulemaking does not have federalism implications warranting the application of Executive Order 13132. The proposed rule does not have substantial direct effects on the States, on the relationship between the national government and the States, or the distribution of power and responsibilities among the various levels of government.

Executive Order 13175

This rule does not have tribal implications warranting the application of Executive Order 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes.

Regulatory Flexibility Act

The Regulatory Flexibility Act (RFA) (5 U.S.C. 601–612) applies to rules that are subject to notice and comment under section 553(b) of the APA. As explained above and in the interim final rule, the DEA determined that there was good cause to exempt the IFR from notice and comment. Consequently, the RFA does not apply to this final rule.

Paperwork Reduction Act of 1995

This rule does not involve a collection of information within the meaning of the Paperwork Reduction Act of 1995, 44 U.S.C. 3501-3521.

Unfunded Mandates Reform Act of 1995

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995 (2 U.S.C. 1501 *et seq.*), the DEA has determined and certifies pursuant to UMRA that this action would not result in any Federal mandate that may result “in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100 million or more (adjusted for inflation) in any one year * * *.” Therefore, neither a Small Government Agency Plan nor any other action is required under the provisions of UMRA of 1995.

Congressional Review Act

This rule is not a major rule as defined by the Congressional Review Act (CRA) (5 U.S.C. 804). This rule will not result in an annual effect on the economy of \$100,000,000 or more, a major increase in costs or prices, or have significant adverse effects on competition, employment, investment, productivity, innovation, or the ability of U.S.-based companies to compete with foreign-based companies in domestic and export markets. However, pursuant to the CRA, the DEA has submitted a copy of this final rule to both Houses of Congress and to the Comptroller General.

Administrative Procedure Act

The APA requires the publication of a substantive rule to be made not less than 30 days before its effective date. 5 U.S.C. 553(d). However, one exception is “as otherwise provided by the agency for good cause found and published with the rule.” Because the DEA removed [¹²³I]ioflupane from the schedules of controlled substances as of September 11, 2015, [80 FR 22919], there is no longer any need for a registration exemption for persons administering DaTscan, and the DEA is hereby removing the IFR through this final rule. The broader decontrol action has superseded it. Therefore, it is unnecessary to delay the effective date of this final rule by 30 days, and this rule shall take effect immediately upon publication.

List of Subjects in 21 CFR Part 1301

Administrative practice and procedure, Drug traffic control, Controlled substances, Drug abuse, Reporting and recordkeeping requirements.

Accordingly, 21 CFR part 1301 is amended as follows:

PART 1301--- REGISTRATION OF MANUFACTURERS, DISTRIBUTORS, AND DISPENSERS OF CONTROLLED SUBSTANCES

1. The authority citation for 21 CFR part 1301 continues to read as follows:

Authority: 21 U.S.C. 821, 822, 823, 824, 831, 871(b), 875, 877, 886a, 951, 952, 953, 956, 957, 958, 965.

§ 1301.29 [Removed and Reserved]

2. Remove and reserve § 1301.29.

Dated: February 23, 2016

Louis J. Milione,

Deputy Assistant Administrator

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