Legislative & Regulatory Update

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Current Climate and Perceptions

- DEA regulated 480,000 registrants when it was established in 1973; today DEA regulates more than 1.65 million registrants.
- The Office of Diversion Control Restructured in 2008:
  - Renewed focus on regulatory oversight of registrants with aggressive enforcement.
  - More frequent and increased depth of cyclic inspections.
  - Substantial expansion of Tactical Diversion Squads from 37 in 2011 to 76.
  - National conferences: pharmacy diversion awareness; distributor; manufacturer/importer/exporter.
  - DEA sponsored drug take-back programs (12th to be held October 22nd).
  - DEA supports and encourages use of state PDMPs (now in 48 states).

Current Climate and Perceptions

- Recent Leadership Changes
  - Chuck Rosenberg appointed Acting Administrator on May 13, 2015.
  - Louis Milione replaced Joe Rannazzisi as Deputy Assistant Administrator, Office of Diversion Control, on October 1, 2015.
  - Change in approach?

Current Climate and Perceptions

- Renewed Partnership with Industry
  - DEA Acting Administrator and Chief of the Office of Diversion Control hosted pharmaceutical industry leaders on February 29, 2016.
  - The purpose of the meeting was to discuss ways to minimize diversion of controlled substances while ensuring legitimate patient access.
  - DEA recognizes role of pharmaceutical industry to prevent drug misuse and abuse and announced plans to work with industry.
  - This appears to represent a change in DEA's perception of the regulated industry as the agency reached out to partner and collaborate in addressing the prescription drug abuse epidemic.

Scheduling Actions

- Eluxadoline
  - New entity with CNS opioid properties approved for irritable bowel syndrome.
  - HHS/DEA 8 factor analyses found abuse potential similar to schedule IV drugs butorphanol and pentazocine.
  - Final rule placed into schedule IV.
- Kratom
  - Citing imminent hazard to public safety, published notice of intent to temporarily place into schedule I on August 31st.
  - An opium substitute from SE Asia available over the Internet and in smoke shops.
  - Withdrawal of notice of intent to temporarily place in schedule I on October 13th.
  - DEA requested expedited medical and scientific evaluation from HHS and solicited comments to permanently schedule.

Marijuana

- Generally
  - A growing number of states now authorize use of marijuana or limited use of low-THC oil (e.g., cannabidiol) for medical purposes.
  - Several jurisdictions (CT, DC, IA, OR) have rescheduled marijuana for medical use.
  - And several states and DC have authorized marijuana for recreational use.
  - Federally, marijuana remains a schedule I controlled substance that may not be sold, prescribed or otherwise lawfully distributed under federal law and regulations.

Marijuana

- Generally
  - DOJ has stated it will not preempt state law in states that have legalized marijuana for medical or recreational use.
  - DOJ and DEA are unlikely to take action against a marijuana-related business operating in compliance with state law if its activity does not implicate certain enforcement priorities that were spelled out in an August 28, 2013 memo issued by Deputy Attorney General James Cole.

Marijuana

- Generally
  - The federal enforcement priorities include:
    - Preventing distribution of marijuana to minors;
    - Preventing revenue from sale of marijuana to criminal enterprises, gangs and cartels;
    - Preventing diversion of marijuana from states where it is legal under state law in some form to other states;
    - Preventing state-authorized marijuana activity from being used as a cover or pretext for trafficking other illegal drugs or other illegal activity and
    - Preventing violence and use of firearms in marijuana cultivation and distribution.

Marijuana

- Rescheduling
  - There were several significant developments this year relating to marijuana, cannabidiol ("CBD") and industrial hemp.
  - DEA denied 2 petitions, one from the governors of RI and WA, to initiate proceedings to reschedule marijuana.
  - The petitions asserted that marijuana has accepted medical use in the U.S., is safe for use under medical supervision and has a low potential for abuse.
  - DEA found that rescheduling turned on whether marijuana has a currently accepted medical use for treatment in the U.S.
  - DEA requested a scientific and medical recommendation from HHS as required by the CSA, which is binding on DEA.

Marijuana

- Rescheduling
  - HHS analyzed marijuana under the “eight factor analysis” which includes:
  - 1. Drug’s actual or relative potential for abuse;
  - 2. Drug’s scientific evidence of its pharmacologic effect, if known;
  - 3. State of current scientific knowledge regarding the drug;
  - 4. Drug’s history and current pattern of abuse;
  - 5. Drug’s scope, duration, and significance of abuse;
  - 6. Risk, if any, to public health;
  - 7. Drug’s psychic or physiological dependence liability and
  - 8. Whether drug is an immediate precursor of a controlled substance.

Marijuana

- Rescheduling
  - Upon considering the 8 factors, HHS concluded that marijuana meets the scheduling criteria for remaining in schedule I.
  - Most importantly, HHS found marijuana does not have a currently accepted medical use in the U.S.
  - Without a finding from HHS that marijuana has an accepted medical use, DEA has to deny any petition to reschedule marijuana.
  - To reschedule marijuana, HHS must find and DEA must support, that the drug has an accepted medical use in the U.S.

Marijuana

- Rescheduling
  - Takeaways from the denials are that future petitions should limit rescheduling to a particular strain from which standardized doses can be processed for a specific medical disorder.
  - The strain should be subject to safety and efficacy studies for use in specific, recognized conditions.
  - Petitioners should elicit expert opinions about the medical utility of the strain for treating a specific disorder.
  - Petitioners should provide data sufficiently addressing the chemistry, toxicology and effectiveness of the strain.

Marijuana

- Cultivation for Research
  - Concurrent with the petition denials, DEA abrogated its long-held policy limiting marijuana cultivation for research to a single grower.
  - For 50 years DEA granted 1 manufacturer registration for marijuana, thus restricting marijuana production for research to a single grower, the University of Mississippi, under contract with the National Institute on Drug Abuse ("NIDA").
  - DEA limited marijuana cultivation to a single grower based on its belief that fewer registrants decreased the likelihood of diversion and it could meet the limited demand for research-grade marijuana.

Marijuana

- Cultivation for Research
  - DEA stated that along with NIDA and FDA, it "fully supports expanding research into the potential utility of marijuana and its chemical constituents."
  - DEA recognized the recent interest in research of certain cannabinoids, including CBD, and based on discussions with NIDA and FDA, concluded that it had to increase the number of authorized marijuana growers to satisfy current researcher demand.
  - DEA's new approach fosters private sector commercial endeavors for product development rather than limitation to federally-funded and academic research.

Marijuana

- Industrial Hemp
  - In the third marijuana-related development, also published in the Federal Register on August 12th, the USDA, in consultation with DEA and FDA, issued a Statement of Principles on participation in industrial hemp pilot programs in compliance with the Agricultural Act of 2014.
  - Industrial hemp is the *Cannabis sativa L.* plant with delta-9 THC concentration of not more than 0.3% on a dry weight basis.
  - Products containing any THC, including hemp, are federally-controlled schedule I substances.
  - Industrial hemp can be used for paper, rope, clothing, textiles, shampoo, soap, body lotion and animal feed products.

Marijuana

- Industrial Hemp
  - DEA has exempted certain products containing THC from control if
  - 1. They are made from certain parts of the Cannabis plant (including mature stalks, fiber from the stalks, oil or cake from the seeds, and sterilized seeds incapable of germination) and
  - 2. They are not intended for human consumption.
  - In addition, over 30 states have established industrial hemp research or pilot programs authorizing hemp industry studies or commercial industrial hemp programs.

Marijuana

- Industrial Hemp
  - The Agricultural Act of 2014 limits cultivation of industrial hemp to agricultural pilot programs for research where production is legal under state law.
  - The Statement of Principles restricts industrial hemp cultivation to state departments of agriculture and persons authorized to conduct research under a pilot program and universities.
  - The Statement of Principles restricts sale of industrial hemp products within states or among states with pilot programs; they cannot be sold “for general commercial activity” or in states that prohibit their sale.

Marijuana

- Cannabidiol Research
  - DEA also eased some regulatory requirements for FDA-approved clinical trials with CBD.
  - CBD, an extract of the marijuana plant, contains less than 1% THC and appears to have a very low potential for abuse.
  - Researchers submit a protocol with their DEA application indicating the quantity of CBD they will use in their research, and had to submit a written request to modify their registration if they required additional CBD.
  - DEA and FDA had to approve the modification request.
  - DEA now allows researchers granted a waiver to modify their protocol, continue their research and obtain additional needed CBD.

Marijuana

- Conclusion
  - When considering the marijuana, CBD and hemp decisions altogether, it appears the federal government is trying to find a way to maintain authority in the face of a growing majority of less restrictive state laws.
  - These measures may minimize some aspect of the federal/state conflict in the short term, especially in encouraging research.
  - But there will be no reconciliation of federal and state law until the ultimate question is resolved: whether marijuana has a legitimate medical use in the U.S. and can be rescheduled federally out of schedule I.

Regulation of Registrants

- Suspicious Order Update
  - Last year Ruth Carter, Chief of DEA's Office of Liaison and Policy, told this group that DEA was considering issuing further clarification of suspicious order requirements, including regulations specifying the format for reporting and how registrants must maintain those reports.
  - The CSA requires distributors (and all registrants) to maintain effective controls to guard against diversion of controlled substances into other than legitimate medical, scientific, or industrial channels.
  - Distributors and manufacturers must also design and operate a system to disclose suspicious orders of controlled substances to registrants and to "inform" the local DEA Field Division about suspicious orders upon discovery.

Regulation of Registrants

- Suspicious Order Update
  - But the $64,000 question was and continues to be “what constitutes a suspicious order?”
  - Clarification of what DEA requires and expects for suspicious order reporting is long overdue and would be welcome by registrants.
  - In the meantime, DEA continues to take enforcement action in the form of suspending registrations and collecting civil penalties against distributors it believes have failed to comply with their suspicious order responsibilities.

Regulation of Registrants

- Opioid Aggregate Production Quotas ("APQ")
  - DEA reduced the aggregate quantity of schedule II opiate and opioid medication, including oxycodone, hydrocodone, fentanyl, hydromorphone and morphine, that can be manufactured in 2017 by at least 25%.
  - DEA reduced some medications, including hydrocodone, by 33%.
  - DEA establishes the APQ for schedule I and II substances, from which it allocates individual procurement and manufacturing quotas to manufacturers.
  - Much of the reduction is due to elimination of a 25% buffer added to the APQ annually beginning in 2013 to protect against shortages.
  - DEA asserted that demand for the opioid medications has decreased as evidenced by sales data provided by IMS.

Regulation of Registrants

- Comprehensive Addiction and Recovery Act ("CARA")
  - Signed into law July 22, 2016.
  - Addresses prescription drug abuse and pain management.
  - Requires HHS to convene a Pain Management Best Practices Inter-Agency Task Force to update best practices for pain management, prescribing pain drugs and review alternatives to opioids.
    - Task Force to include HHS, DOD, VA, ONDCP, practitioners, pharmacists and other experts.
  - Addresses opioid abuse at VA facilities by improving Opioid Therapy Risk Report tool and improving education and training.
  - Authorizes HHS to establish a grant program to support prescribing of opioid overdose reversal drugs such as naloxone.

Regulation of Registrants

- Comprehensive Addiction and Recovery Act ("CARA")
  - Removes financial disincentive that discourages drug manufacturers from developing abuse-deterrent formulations of pain medications.
  - Amends CSA to allow a pharmacist to partially fill a schedule II prescription if requested by a prescriber or patient.
    - The objective was to attempt to limit the quantity of pain medication received by the patient to no more than is medically necessary.
    - The remainder must be filled within 30 days of the original prescription.
    - Pharmacists will have to be more diligent in monitoring dispensing, especially if the partial filling is directed by the practitioner rather than the patient.
    - The pharmacist may have to consult with the practitioner should the patient request to fill the remainder of the prescription.

Regulation of Registrants

- Comprehensive Addiction and Recovery Act ("CARA")
  - Authorizes nurse practitioners and physician's assistants to administer, prescribe and dispense narcotics in office-based treatment programs.
    - This practice was previously limited to physicians.
  - Also authorizes HHS to increase patient limit for office-based treatment from 30 patients to 100.
  - Contains provisions to expand the reporting requirements and access to state PDMPs by practitioners and law enforcement.
    - This will increase access by practitioners to assist in treating patients and expand use of PDMPs as a tool for law enforcement to investigate practitioners, pharmacies and patients.

Regulation of Registrants

- CDC Opioid Prescribing Guidelines
  - The CDC weighed in on the appropriate treatment of chronic pain with guidelines for prescribing opioids.
  - The guidelines are voluntary, but they will be influential on opioid therapy for chronic pain.
  - The guidelines are intended for primary care clinicians (family physicians and internists) and provide recommendations for prescribing opioid pain medication for chronic pain (pain lasting longer than 3 months or past time of normal tissue healing) in outpatient settings.
  - The guidelines apply to patients 18 years and older with chronic pain unrelated to cancer, outside of palliative and end-of-life care.

Regulation of Registrants

- CDC Opioid Prescribing Guidelines
  - CDC organized the guidelines into three general areas:
  - 1. When to initiate or continue opioids for chronic pain;
  - 2. Opioid selection, dosage, duration, follow-up, and discontinuation; and
    3. Assessing risk and addressing harms of opioid use.

Regulation of Registrants

- CDC Opioid Prescribing Guidelines
  - When to Initiate or Continue Opioids for Chronic Pain
  - 1. Nonpharmacological and nonopioid pharmacological therapy preferred for chronic pain. Clinicians should consider opioid therapy only if benefits for pain and function outweigh risks. Opioids, if used, should be combined with nonpharmacological and nonopioid pharmacological therapy.
  - 2. Clinicians should establish realistic treatment goals with patients for pain and function, and consider discontinuing if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is meaningful improvement in pain and function.
  - 3. Clinicians should discuss known risks and realistic benefits of opioid therapy with patients and patient responsibilities for therapy.

Regulation of Registrants

- CDC Opioid Prescribing Guidelines
  - Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation
  - 4. Clinicians should prescribe immediate-release opioids instead of extended-release/long acting opioids.
  - 5. Clinicians should prescribe the lowest effective dosage. Clinicians should carefully reassess benefits and risks when considering increasing dosage to ≥ 50 morphine milligram equivalents ("MME")/day, and avoid increasing dosage to ≥ 90 MME/day.

Regulation of Registrants

- CDC Opioid Prescribing Guidelines
  - Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation
  - 6. For acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and prescribe no greater quantity than needed for the expected duration of pain requiring opioids. Three days or less is often sufficient, rarely more than 7 days.
  - 7. Clinicians should evaluate benefits and harm with patients, and evaluate benefits and harm of continued therapy every 3 months or more frequently. If benefits do not outweigh harms of continued therapy, clinicians should optimize other therapies, taper opioids to lower dosages or discontinue.

Regulation of Registrants

- CDC Opioid Prescribing Guidelines
  - Assessing Risk and Addressing Harms of Opioid Use
  - 8. Clinicians should evaluate risk factors for opioid-related harms. They should incorporate strategies to mitigate risk, including offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥ 50 MME/day), or concurrent benzodiazepine use, are present.
  - 9. Clinicians should review patient's history of controlled substance prescriptions through state PDMP data to determine whether patient is receiving opioids that put them at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy, then periodically.

Regulation of Registrants

- CDC Opioid Prescribing Guidelines
  - Assessing Risk and Addressing Harms of Opioid Use
  - 10. Clinicians should use urine testing before starting opioid therapy and consider urine testing at least annually to assess for prescribed medications as well as other controlled prescription and illicit drugs.
  - 11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently when possible.
  - 12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

Regulation of Registrants

- CDC Opioid Prescribing Guidelines
  - There has been increased enforcement against physicians for failing to ensure the prescriptions they issue are for a legitimate medical purpose in the usual course of their professional practice.
  - And there has been action against pharmacists and pharmacies who have failed in their corresponding responsibility to ensure that the prescriptions they dispense are for a legitimate medical purpose.
  - The guidelines are reasonable and commonsensical, constitute good medical practice, and should apply to prescribing any medication, not just opioids or controlled substances.

Regulation of Registrants

- CDC Opioid Prescribing Guidelines
  - Primary clinicians in the field should familiarize themselves with the guidelines and detailed explanation for each.
  - The guidelines help clarify the opioid prescribing standards for physicians, pharmacies and regulators.
  - But there may be occasions when legitimate medical treatment conflicts with strict adherence to the guidelines.
  - There may be instances when opioid therapy is required for more than 7 days or a patient requires more than 50 or 90 MMEs per day.
  - CDC recognizes the recommendations in the guidelines are “voluntary, rather than prescriptive standards” and cautions clinicians to “consider the circumstances and unique needs of each patient when providing care.”

Regulation of Registrants

- SAMHSA's Proposed Buprenorphine Patient Increase
  - SAMHSA published a proposed rule on March 30th that would expand access to buprenorphine medication assisted treatment ("MAT") for patients with opioid abuse disorder.
  - SAMHSA cited evidence that the current maximum 100 patient limit is a barrier for patient access to needed treatment.
  - The rule would expand access to MAT by doubling the maximum number of patients a qualified practitioner could treat for opioid use disorder with buprenorphine to 200.
  - Currently, under the CSA, qualified practitioners can prescribe, administer or dispense buprenorphine for opioid use disorder in an office, community hospital, health department or correctional facility.

Regulation of Registrants

- SAMHSA's Proposed Buprenorphine Patient Increase
  - Practitioners must hold a valid medical license and DEA registration, and have completed required training.
  - Practitioners submit notification of intent to dispense or prescribe buprenorphine to a maximum of 30 patients at a time, which precludes having to obtain separate DEA registration as an NTP.
  - Practitioners can file a second notification after a year to increase the number of patients they can treat to 100 patients at a time.

Regulation of Registrants

- SAMHSA's Proposed Buprenorphine Patient Increase
  - The proposed rule would increase the maximum number of patients to 200 that a practitioner could treat at 1 time if they meet certain criteria.
  - To be eligible, practitioners must have held a waiver to treat 100 patients for at least 1 year and possess a subspecialty board certification in addiction psychiatry or addiction medicine or practice in a qualified practice setting.
  - Practitioners must submit a request to increase their patient limit and SAMHSA will approve or deny requests within 45 days of receipt.
  - Approved practitioners must submit reports, documentation and data demonstrating compliance.

Regulation of Registrants

- SAMHSA's Proposed Buprenorphine Patient Increase
  - SAMHSA can suspend a practitioner's approval to protect the public health and safety, and revoke it if the practitioner made misrepresentations, no longer satisfies requirements or has violated the CSA.
  - The rule's graduated MAT authority for first 30 patients, then 100 and finally 200 over 2 years is reasonable.
  - Doubling the number of patients for practitioners already providing MAT may require their expending only minimal additional resources.
  - Conscientious practitioners may conclude that they cannot responsibly treat more than 30 or 100 patients.

Regulation of Registrants

- SAMHSA's Proposed Buprenorphine Patient Increase
  - Qualified practitioners may perceive the additional reporting requirements as too onerous to offer MAT or increase their patient numbers.
  - Increased scrutiny and enforcement by SAMHSA and DEA may deter some practitioners.
  - To increase treatment availability, SAMHSA should tailor requirements to protect patient health and safeguard against controlled substance diversion, making them as least burdensome as possible.
  - If SAMHSA determines waivers should be renewed every 3 years, it could synchronize renewal with practitioners' DEA registration cycles.
  - And with accessibility to state PDMPs, SAMHSA may be able to monitor MAT activity for practitioners without requiring detailed reports.

Regulation of Registrants

- Proposed Import/Export/Listed Chemical Changes
  - DEA published an NPRM on September 15th that would revise regulations governing controlled substance, listed chemical and tableting and encapsulating machine imports and exports.
  - The comment period closed yesterday.
  - DEA requires importers and exporters to apply for permits (for schedule I or II substances, schedule III-V narcotic substances, and certain schedule III non-narcotic drugs), submit declarations (for schedule III, IV or V non-narcotic substances not requiring a permit) and file reports (for listed chemicals).
  - The NPRM mandates submission of all applications and filings electronically through DEA's Diversion Control secure network application.

Regulation of Registrants

- Proposed Import/Export/Listed Chemical Changes
  - Electronic submission allows DEA to electronically file required information with U.S. Customs and Border Protection, reducing errors and enhancing import and export monitoring and information sharing.
  - Importers and exporters will obtain information about permit approvals and DEA receipt of declarations, notices, returns, and reports through the DEA Diversion Control secure network application.
  - Electronic submission also alerts registrants of missing information or failure to meet validation requirements.
  - The mandatory electronic import/export submissions represent DEA's latest move from a paper-based system for applications, reports and communications to an electronic one.

Regulation of Registrants

- Proposed Import/Export/Listed Chemical Changes
  - The Improving Regulatory Transparency for New Medical Therapies Act, amended the CSA in 2015 to allow additional reexportation of certain controlled substances among members of the European Economic Area ("EEA").
  - The CSA provides that schedule I or II controlled substances and narcotic drugs in schedule III or IV could be exported from the U.S. for subsequent reexport from the recipient country to a second country, but allowed no further reexports.
  - The New Medical Therapies Act removed certain restrictions on reexporting if every subsequent recipient country is an EEA member and meets certain conditions.

Regulation of Registrants

- Proposed Import/Export/Listed Chemical Changes
  - The first, second, and subsequent EEA countries must be parties to the Single Convention on Narcotic Drugs, 1961, and the Convention on Psychotropic Substances, 1971.
  - Each country must have a system of controls that DEA deems adequate.
  - Importers and exporters must be properly licensed and the controlled substances must be exclusively for medical, scientific, or other legitimate uses.
  - DEA will no longer require further manufacturing of bulk substances within the first EEA country for reexport within the EEA.
  - Exporters will no longer be required to provide product and consignee information beyond the first country prior to export from the U.S.

Regulation of Registrants

- Proposed Import/Export/Listed Chemical Changes
  - DEA will continue to require exporters who submit an application for reexport among EEA members to supply information about the consignee in the first country, but will not require information about subsequent consignees, countries, and products prior to export from the U.S. or prior to each reexportation among EEA members.
  - Exporters to the EEA for reexport will have to submit an affidavit that the consignee in the second country and subsequent EEA countries are authorized under their laws to receive the controlled substances, the package labeling conforms with treaty obligations, the drugs are for medical or scientific use, they will not be reexported outside the EEA, and there is actual need for medical or scientific use within the recipient country.

Regulation of Registrants

- Proposed Import/Export/Listed Chemical Changes
  - The NPRM would eliminate requirements that controlled substances be reexported from the first EEA country to the second or subsequent EEA countries within 180 days after exportation from the U.S.
  - Reexports outside the EEA must be completed no later than 180 days after initial export from the U.S.
  - DEA's removal of restrictions on further reexport among EEA members strikes an adequate balance allowing commerce under certain conditions while maintaining controls against diversion of controlled substances internationally and fulfilling U.S. treaty obligations.

Regulation of Registrants

- Proposed Import/Export/Listed Chemical Changes
  - DEA did not loosen reexport restrictions outside the EEA because Congress did not require it to do so and the agency believes the restrictions protect against international diversion and "promote compliance with international treaty obligations."
  - Further loosening of reexport restrictions may be in order if reexports to EEA members proves problem-free.

Regulation of Registrants

- Proposed Import/Export/Listed Chemical Changes
  - The NPRM would also require regulated persons to report any unusual or excessive loss or disappearance of listed chemicals orally to DEA “at the earliest possible moment” and submit a DEA Form 107 electronically within 15 calendar days after becoming aware of the circumstances.
  - Substantively, the NPRM establishes guidelines similar to controlled substance theft and loss criteria for determining whether a listed chemical loss or disappearance is unusual or excessive (thus reportable).

Regulation of Registrants

- Proposed Import/Export/Listed Chemical Changes
  - The listed chemical criteria include:
  - Actual quantity of the listed chemical;
  - The specific listed chemical involved;
  - Whether the loss or disappearance can be associated with access by specific individuals, or can be attributed to unique activities involving the listed chemical; and
  - A pattern of losses or disappearances over a specific time period, whether the losses or disappearances appear to be random, and the result of efforts taken to resolve the losses.

Regulation of Registrants

- Proposed Import/Export/Listed Chemical Changes
  - Chemical handlers, like controlled substance registrants, have struggled with what constitutes a reportable chemical loss.
  - Significant controlled substance losses and thefts must be reported, but DEA would require reports of “any unusual or excessive loss or disappearance” of listed chemicals.
  - What makes a chemical loss “unusual,” thus reportable, from other non-reportable chemical losses?
  - “Significant” (controlled substance losses) does not necessarily equate with “excessive” (chemical losses).
  - All controlled substance thefts are reportable but listed chemical thefts appear to be reportable if they are “unusual or excessive.”

Regulation of Registrants

- Proposed Import/Export/Listed Chemical Changes
  - How listed chemicals must be reported would also be more ambiguous than what is required for controlled substances.
  - Registrants must report controlled substance losses in writing within 1 business day of discovery and follow-up with a DEA-106, while regulated persons would have to first report chemical losses orally “at the earliest practicable opportunity” followed 15 calendar days later by a DEA-Form 107.
  - DEA’s final rule should make listed chemical and controlled substance loss reporting requirements less ambiguous and more uniform.

Regulation of Registrants

- Proposed Import/Export/Listed Chemical Changes
  - DEA is also proposing mandatory electronic submission of required monthly reports of domestic mail-order transactions involving ephedrine, pseudoephedrine, phenylpropanolamine, and GHB.
  - The NPRM is also proposing to standardize domestic, import and export regulated transaction reports involving tableting and encapsulating machines through use of new a DEA Form 452.
  - Regulated persons would have to orally report domestic regulated transactions of a tableting machine or an encapsulating machine when an order is placed rather than at the earliest practicable opportunity after the regulated person becomes aware of the circumstances involved.

Regulation of Registrants

- FDA DSCSA State Licensing Requirements
  - FDA recently indicated that it will issue proposed regulations on December 31st establishing licensing standards for prescription drug wholesale distributors and 3PLs and, in the absence of state licensing requirements, a federal system as mandated by the Drug Supply Chain Security Act ("DSCSA").
  - The FDA regulations, in achieving some degree of licensing uniformity, will preempt states' "inconsistent" and less stringent requirements.
  - Every state requires prescription drug wholesale distributors within their borders to obtain a license issued by their board of pharmacy or other licensing authority.

Regulation of Registrants

- FDA DSCSA State Licensing Requirements
  - Fewer jurisdictions also require non-resident wholesale distributors to obtain licenses to distribute prescription drugs to customers within their borders.
  - The states broadly define what constitutes wholesale distribution and who must obtain licenses.
  - States typically include distributors, manufacturers, brokers, virtual manufacturers, 3PLs and others within their definition of “wholesale distributors” requiring a resident or non-resident license.
  - Different states require licenses for prescription drugs and controlled substances but those who distribute over-the-counter drugs and devices may also have to obtain licenses.

Regulation of Registrants

- FDA DSCSA State Licensing Requirements
  - States required non-resident wholesale distributors to obtain licenses if they physically moved drugs directly into them.
  - States began requiring non-resident distributors to obtain licenses if they:
  - Own or hold title to drug products;
  - Hold the New Drug Application of the drug products;
  - Have their name on the label of drug products;
  - Direct movement of drug products into the state;
  - Invoice customers in the state;
  - Conduct marketing activities in the state;
  - Have customer contacts in the state;
  - Employ sales representatives in the state; or
  - Distribute drug samples in the state.

Regulation of Registrants

- FDA DSCSA State Licensing Requirements
  - States also vary widely on what changes require licensees to obtain a new license or just submit notification to authorities.
  - Changes of ownership, corporate officers, company name and location can require a licensee to obtain a new license or notify the responsible agency.
  - Asset ownership changes require new licenses in many states while fewer states require new licenses for stock ownership transfers.
  - Most states require new licenses for ownership changes of the licensed entity, and fewer require new licenses for ownership changes at the entity's parent or grandparent level.

Regulation of Registrants

- FDA DSCSA State Licensing Requirements
  - States also vary widely on whether new owners must submit applications before or after an ownership change and whether entities can continue to distribute drugs into their state while the application for a new license is pending.
  - Most states allow distributors to continue shipping and selling drugs after an ownership change before they have issued licenses to the new owners, but some states prohibit these activities until they have issued a new license.
  - This poses a problem for distributors because some states can take up to 8 weeks and longer to review applications and issue licenses due to backlogs and criminal background checks.

Regulation of Registrants

- FDA DSCSA State Licensing Requirements
  - The DSCSA imposes uniformity as to what constitutes wholesale distributors and 3PLs.
  - It defines a wholesale distributor as a “person (other than a manufacturer, a manufacturer’s co-licensed partner, a third-party logistics provider, or repackager) engaged in wholesale distribution” which in general is distribution of a drug to, or receipt by, a person other than a consumer or patient.
  - Under the DSCSA, 3PLs provide or coordinate warehousing or other logistics services for products in interstate commerce on behalf of a manufacturer, wholesale distributor, or dispenser, do not take ownership of the product and are not responsible for directing its sale or disposition.

Regulation of Registrants

- FDA DSCSA State Licensing Requirements
  - The DSCSA requires wholesale distributors and 3PLs to hold licenses issued by their home state from which they distribute drugs or with FDA if that state has no license requirement, and with the state into which they distribute drugs.
  - In lieu of holding a license with the state into which they ship drugs, 3PLs can hold a license issued by FDA.
  - The DSCSA prohibits states from regulating 3PLs as wholesale distributors, requiring specific licensure as a 3PL.

Regulation of Registrants

- FDA DSCSA State Licensing Requirements
  - Consistent with this DSCSA requirement, for example, California requires non-resident 3PLs to obtain a 3PL license and will not issue a non-resident 3PL license unless the home state has issued a 3PL license.
  - Few states currently issue 3PL licenses, leaving 3PLs requiring a California non-resident 3PL license unable to obtain that license.
  - The DSCSA preempts state requirements by prohibiting states from establishing or continuing "any standards, requirements, or regulations… inconsistent with, less stringent than, directly related to, or covered by the standards and requirements."

Regulation of Registrants

- FDA DSCSA State Licensing Requirements
  - So, while prohibiting states from establishing or continuing standards less stringent than those of future FDA regulations, states may establish or continue to implement more stringent standards, but the more stringent standards cannot be "inconsistent with" FDA's standards.
  - FDA regulations must clearly define what state standards "inconsistent with" FDA standards means.
  - More stringent though "consistent" state licensing standards could threaten the DSCSA's goal of establishing uniform licensing standards.

Regulation of Registrants

- FDA DSCSA State Licensing Requirements
  - FDA's licensing standards and requirements will no doubt address the need for uniform and unambiguous requirements regardless of where distributors and 3PLs are situated or where they distribute their products.
  - Will FDA adhere closely to the mandated DSCSA licensing standards framework or will it introduce additional requirements?
  - How will different states react to the FDA regulations that establish a floor but not a ceiling for licensing standards and requirements?
  - Will the states impose their own more stringent standards and requirements or will they largely adopt FDA requirements?

Regulation of Registrants

- FDA DSCSA State Licensing Requirements
  - States would do well to recognize the value of uniform licensing and application requirements when FDA publishes its proposed regulations in the context of their own requirements.
  - The states and stakeholders should carefully consider and comment on FDA's proposed regulations upon publication.
  - The FDA regulations should establish licensing and application standards that all states can adopt and adhere to.
  - FDA should establish a universal application states can use that while in-depth, requires the minimum information and documentation necessary to ensure the applicant will comply with federal and state licensing, handling, recordkeeping, reporting and security requirements.

The End

Questions?

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Thank You!

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