

Current and Emerging Domestic Regulations That Affect Supply Chain Operations

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Compliance Trends



DEA, FDA, US Attorneys, and State agencies are increasing scrutiny in all areas, particularly in Manufacturing, Distribution and Pharmacy related to the diversion and abuse of controlled drugs, listed chemicals and prescription drugs

- Companies are not meeting the regulatory requirements
- Inconsistent implementation and lack of understanding of regulatory requirements
- Increase in inspections by DEA, FDA, states



- **Multi-Million dollar fines and penalties being levied**
- **Several large recent cases**
 - Pharmacy
 - Manufacturer
 - Distributor

Penalties / Actions



- **2008 – \$57,000,000 in civil fines / SOM**
- **2008 / 2009 – Numerous registrations suspensions, show cause, subpoenas, revocations and/or fines**
- **2009**
 - Various registrants (Controlled and List I) – 16
 - Pharmacy
 - Distributor
 - Manufacturer
 - Importer
 - Exporter
- **100 Distributors – Cold Chain Reviews / FDA**
- **State requirements**
- **List I**
 - Security
 - Know your customer



- **The FDA and States, like the DEA, are looking to impact and reduce the diversion and abuse of controlled substances. Whether intentional or unintentional, the FDA / REMS, the DEA / Suspicious Order Monitoring and State requirements, together, will impact the distribution, prescribing and dispensing of controlled and non-controlled substances**

The Role of the Drug Enforcement Administration

SUSPICIOUS ORDER MONITORING

(SOM)





- **A number of companies have had actions taken against them by DEA for having non-complaint SOM programs**

- **SOM, as well as appropriate due diligence and “know your customer” efforts, are key to DEA’s efforts to curb diversion of controlled drugs and listed chemicals**

- **DEA Actions:**
 - Immediate Suspension of DEA Registrations
 - Show Cause actions to deny the DEA Registration
 - Loss of DEA Registration
 - Large Civil Fines - Approx. 52 Million / 2008
 - Subpoenas / Criminal prosecution



Controlled Substances – Requirement

21CFR 1301.74 (b)

The registrant shall design and operate a system to disclose to the registrant suspicious orders of controlled substances. The registrant shall inform the Field Division Office of the Administration in his area of suspicious orders when discovered by the registrant. Suspicious orders include orders of unusual size, orders deviating substantially from a normal pattern, and orders of unusual frequency

Applies to manufacturers, distributors and pharmacies that distribute controlled substances

- Further clarification in September 06, February 07, and December 2007 DEA letters



Listed Chemicals – Requirements under 21 CFR 1309.71

- (a) All applicants and registrants must provide effective controls and procedures to guard against theft and diversion of List I chemicals...
- (b) *In evaluating the effectiveness of security controls and procedures, the Administrator shall consider the following factors:*
 - ...
 - (8) The adequacy of the registrant's or applicant's systems for monitoring the receipt, distribution, and disposition of List I chemicals in its operations.
- In addition, DEA's Chemical Handler's Manual devotes several pages to know-your-customer and proof of identity/due diligence issues.

December 27, 2007 DEA letter



- **DEA has not sanctioned an approach or system**
 - “DEA does not approve or otherwise endorse any specific system for reporting suspicious orders. Past communications with DEA, whether implicit or explicit, that could be construed as approval of a particular system for reporting suspicious orders, should no longer be taken to mean that DEA approves a specific system”
- **Registrant must inform DEA when suspicious orders are discovered by the registrant.**
 - Filing a report of completed transactions (e.g. “excessive purchase report” or “high unit purchases”) does not meet the regulatory requirement
- **Must review suspicious orders before completing sale and shipping.**
 - “Registrants must conduct an independent analysis of suspicious orders prior to completing a sale to determine whether the controlled substances are likely to be diverted from legitimate channels”
 - “Reporting an order as suspicious will not absolve the registrant of responsibility if the registrant knew, or should have known, that the controlled substances were being diverted”

December 27, 2007 DEA letter (cont.)



- **Regulation states that suspicious orders include:**
 - Orders of unusual size
 - Orders deviating substantially from a normal pattern
 - Orders of an unusual frequency
- **Criteria are not meant to be all inclusive**
- **Examples mentioned in the letter:**
 - If an order deviates substantially from a normal pattern, then the size of order does not matter. Report as suspicious
 - Registrant should not wait for a “normal pattern” to develop
 - Size of an order alone is enough to trigger need to report (regardless of order pattern)
- **Determination of order suspicion depends not only on specific customer ordering pattern, but also on patterns of:**
 - Registrant’s customer base
 - Relevant segment of the regulated industry



- **Rigid formulas to define suspicious orders “may be failing to detect suspicious orders”**
 - “For example, a system that identifies orders as suspicious only if the total amount of a controlled substance ordered during one month exceeds the amount ordered the previous month by a certain percentage or more is insufficient.”
 - Per DEA, this fails to identify orders as suspicious that have been unusually large from the beginning or that are solely for highly abused controlled substances.
 - Recent DEA actions indicate that this also applies to registrants with SOM systems that only look for orders that exceed an average “monthly purchase volume” or threshold (even if techniques like X standard deviations above the mean are utilized).



■ Reporting suspicious orders to DEA:

- Must be clear that order is being categorized as suspicious.
 - Daily, weekly, or monthly “excessive purchase” reports do not comply even if they are called “suspicious order reports”

■ Must evaluate potentially suspicious orders prior to filling the order.

- Order must be confirmed as going into legitimate medical, scientific, or industrial channels.
- Otherwise...”may be failing to maintain effective controls against diversion...and may result in revocation of the registrant’s DEA Certificate of Registration.”

SOM Recommendations



- **Develop a “total statistical SOM solution” to review each of your customer’s orders product by product, comparing orders with historical ordering patterns for that customer and product**
- **Determine the legitimacy of EVERY order BEFORE IT IS SHIPPED**
- **Include all controlled substances (Schedule II, III, IV, and V) and listed chemicals**



- **Overall Objective: A total SOM program**
 - Update order management system and implement a statistically based model to identify suspicious orders
 - Complete a formal computer system validation to confirm the accuracy and suitability of the system
 - Institute best practices for investigation and disposition of accounts flagged as potentially suspicious
 - Verification of new accounts which could include on-site
 - Potentially suspicious accounts are investigated, which could include on-site so informed decisions can be made on continuing service to the account
 - Documentation of reviews
 - Reporting suspicious orders

Risk Evaluation and Mitigation Strategy (REMS) for Controlled Substances





- **Food and Drug Administration Amendments Act of 2007 (FDAAA)**
 - Authorizes FDA to require applicants submitting a marketing application for an Rx drug or biological product to submit and implement a REMS if the FDA determines that a REMS is required to ensure that the benefits outweigh the risks of the product
 - A strategy to manage a known or potential serious risk associated with a drug or biological product
- **Restricted distribution**
 - Training and certification for prescribers
 - Training and certification for dispensers
 - Registration of patients

REMS – Distribution and Use Restrictions



■ **Could Include:**

- Patient medication guide
- Patient package insert
- Communication plan
- Timetable for assessment

■ **Elements**

- Health care providers who prescribe have training or experience or are specially certified
- Pharmacies, practitioners, or health care settings that dispense are specially certified
- The drug is dispensed to patients only in certain health care settings, such as hospitals
- The drug is dispensed to patients with evidence or other documentation of safe use conditions, such as laboratory test results
- Each patient using the drug is subject to certain monitoring
- Each patient using the drug is enrolled in a registry

REMS – Distribution and Use Restrictions



- **Failure to submit a proposed REMS within 180 days may subject the sponsor to an enforcement action, including civil money penalties**
 - NMT \$250,000 per violation; or
 - \$1,000,000 for all violations adjudicated
 - Violation continues after written notification
 - \$250,000 for the 1st 30 day period or any portion;
 - Not to exceed \$1,000,000 for any 30 day period; and
 - Not to exceed \$10,000,000 for all violations adjudicated in a single proceeding

REMS – Distribution and Use Restrictions



- **The need to assess if there is prescribing changes to less effective or less safe medication**
- **The potential to impact medication for legitimate medical purposes**
- **Health care professionals will require better education on detection and management of substance use, regulatory requirements, diversion prevention and abuse**
- **The “Impact on Distribution”, prescribing and dispensing**
- **Acceptance by the health care providers**

Actual REMS Requirements for a Product



REMS – Actual REMS Requirements for a Product



- **“New safety Information”**
- **Based upon the safety, and in accordance with 505-1 of the FDCA, FDA has determined that a REMS is required to ensure that the benefits of the product outweigh the risks**
- **REMS must include the following:**
 - Medication Guide
 - Elements to Assure Safe Use – FDA determined that elements to assure safe use are necessary to mitigate serious risks listed in the label of the product
 - Prescribed by prescribers who are specially certified under 505 - 1(f)(3)(A)



- **Prescribed by prescribers who are specially certified (continued)**
 - Prescribers are trained about:
 - Patient selection
 - Product dosing and administration
 - Use and abuse
 - The risks of the drug
 - How to enroll patients into the REMS program
 - Prescribers have obtained certification by attesting to the following:
 - Trained and understand the risks and benefits
 - Understand abuse issues
 - Understand use
 - Will prescribe after ensuring documentation of safe use
 - Will enroll patients into REMS program
 - Sponsor will maintain a list of prescribers
 - Prescribers will be retrained and recertified periodically at a specified interval



■ **REMS must include the following: (continued)**

- A plan to ensure that the product is only dispensed by pharmacies, practitioners, or healthcare settings who are specially certified under 505 -1(f)(3)(B) by requiring that:
 - Dispensed through certified pharmacies , practitioners, or healthcare settings
 - To obtain certification a pharmacy, practitioner, or healthcare setting must agree to:
 - Train their staff
 - Ensure documentation of safe use
 - Sponsor maintains list of the pharmacies , practitioners, or healthcare settings who have obtained certification and make available
 - Pharmacies , practitioners, or healthcare settings will be retrained and recertified periodically at a specified interval



■ **REMS must include the following: (continued)**

- A plan to ensure the drug is dispensed to patients with documentation of the following safe use conditions under 505 - 1(f)(3)(D)
 - A prescriber must document that he or she:
 - Has enrolled each patient by obtaining at the time of 1st prescribing and on specified periodic frequency thereafter a signed physician-patient agreement form that documents safe use conditions
 - Provides a copy of the signed physician-patient agreement to the sponsor
 - Sponsor maintains a list of the patients and verifies patient enrollment to those needing to verify that a patient has been or has not yet been enrolled
 - Sponsor provides a unique patient identifier when each patient is enrolled
 - Patient is always tracked using the unique identifier so that the sponsor can monitor the product prescribing for each patient



■ **REMS must include the following: (continued)**

- A plan to ensure the drug is dispensed to patients with documentation of the following safe use conditions under 505-1(f)(3)(D) (continued)
 - Pharmacies, practitioners, or health care settings who dispense the drug must document that the drug has been dispensed under the following conditions:
 - The pharmacy, practitioner, or healthcare setting has dispensed the product only to enrolled patients, based on a valid prescription from a certified prescriber (enrolled patients and certified prescribers to be determined from a list maintained by the sponsor)
 - The pharmacy, practitioner, or healthcare setting has ensured that patients who are receiving the higher strengths are tolerant
 - The pharmacy, practitioner, or healthcare setting has counseled patients on appropriate product use
 - The pharmacy, practitioner, or healthcare setting has provided each patient a Medication Guide with each prescription and instructed the patient to read the Guide



■ **REMS must include the following: (continued)**

- An implementation system (IS) to monitor and evaluate the implementation of the elements to assure safe use that require that the product be dispensed to patients with documentation of safe-use conditions. Include an intervention plan to address any findings of non-compliance with elements to assure safe use and to address any findings that suggest an increase risk
- The IS must include the following:
 - A database of all enrolled entities including prescribers, pharmacies, practitioners, healthcare settings and patients
 - A plan to monitor distribution and prescription data to ensure that only certified pharmacies, practitioners, healthcare settings and patients are distributing and dispensing the product and that only certified prescribers are prescribing the product
 - A plan to monitor and conduct audits of certified pharmacies, practitioners and healthcare settings to ensure these entities are only dispensing the product after documenting safe use conditions



- **REMS must include the following: (continued)**
 - The proposed REMS should include a timetable for assessment that shall be no less frequent than every six months for the first two years, and annually thereafter once the REMS is initially approved. FDA also recommended that the company specify the interval that each assessment will cover and the planned date of submission to the FDA of the assessment
 - Each assessment must assess the extent to which the elements to assure safe use of the REMS are meeting the goals of the REMS and whether the goals or elements should be modified



- **FDA suggested that the proposed REMS submission include two parts: a “Proposed REMS” and a REMS Supporting Document.”**
 - FDA included a template
 - Require the including of info that is specific to the proposed REMS
 - Include all proposed materials
 - Append to the proposed REMS
 - Once FDA finds the content acceptable, FDA will include this document as an attachment to the approval letter that includes REMS.
 - Once approved, will create enforceable obligations

State Regulatory Impact



Why Validate (Verify) Practitioners



- **Drug distributors that make shipments to practitioners are coming under increased scrutiny from the State's Department of Health and FDA/PDMA requirements to ensure that shipments of prescription drugs are being made to valid practitioners**
- **These regulations require that the distributor has appropriate processes and procedures that assures themselves that the recipient is either a duly licensed doctor of medicine, dentistry, or veterinary medicine or holds a registered pharmacy permit from the board by contacting the office of the board**
- **Fines & Penalties: increasing number of distributors being fined for non compliance**

Regulations:

- **State Regulatory Requirements**
- **NABP Model Rule (VAWD)**
- **Prescription Drug Marketing Act (PDMA)**



■ Alabama 34-23-32 – Division 1 – General Provisions – Registration Verification

“All holders of a permit shall, before shipping any drug bearing the legend, “caution, federal law prohibits dispensing without prescription” or similar wording causing these drugs to be known as legend drugs to new customers, assure themselves that the recipient is either a duly licensed doctor of medicine, dentistry, or veterinary medicine or holds a registered pharmacy permit from the board by contacting the office of the board. No holder of a permit shall ship any legend drug to any person or firm after receiving written notice from the Board that the person or firm no longer holds a registered pharmacy permit. Any person violating this section shall be guilty of a misdemeanor (Acts 1966, Ex. Sess., No. 205, p. 231, SS 24; Acts 1985, No. 85-702, p. 1151, SS 1, Acts 1991, No. 91-475, pg. 860, SS 1; Acts 2004-450, p. 801, SS1.)”



■ Colorado Rules and Regulations – 3 CCR 719-1 Pharmacy Rules and Regulations – Registration Verification - 15.09.19 Distribution

- A manufacturer or wholesaler as defined in regulation 15.01.00 shall furnish prescription drugs only to a person or entity licensed by the appropriate regulatory board. Before furnishing prescription drugs to a person not known to the wholesaler, the wholesaler shall affirmatively verify that the person or entity is legally authorized to receive the prescription drugs by contacting the appropriate regulatory board
- Prescription drugs furnished by a manufacturer or a wholesaler shall be delivered only to the premises listed on the license. ...



■ Louisiana Wholesale Drug Distributor Statutes - 311.

Drug or Device Distribution Recordkeeping (Registration Verification)

- Wholesale drug or device distributors physically located and conducting operations in Louisiana shall verify prior to purchasing or receiving product that their suppliers of drugs or devices are licensed by the Board to ship or sell in or into Louisiana; and are responsible for notifying the Board of any unlicensed wholesalers

Examples of State Requirements for Practitioner Validation



- **Oregon Board of Pharmacy the wholesale distributor – Pursuant to OAR 855-065-0013,**
 - “before furnishing a drug to any person not known to the wholesale distributor who is required to be registered with the Oregon Board of Pharmacy the wholesale distributor must verify that the person is registered with the Board and legally authorized to receive the drug” and “before purchasing a drug from any person not known to the wholesaler distributor who is required to be registered with the Oregon Board of Pharmacy the wholesale distributor must verify that the person is registered with the Board and legally authorized to sell the drug”



■ Illinois Senate Bill 0509 Enacted

- “A manufacturer or wholesale distributor licensed under this Act may furnish prescription drugs only to a person licensed by the appropriate state licensing authorities. Before Furnishing prescription drugs to a person not known to the manufacturer or wholesale distributor, the manufacturer or wholesale distributor must affirmatively verify that the person is legally authorized to receive the prescription drugs by contacting the appropriate state licensing authorities”.

State Requirements



■ Colorado

- Monetary penalty from companies receiving product from non licensed companies

■ Louisiana

- Company receiving product must maintain copy of state license of supplier

■ Georgia

- Requires SOM report

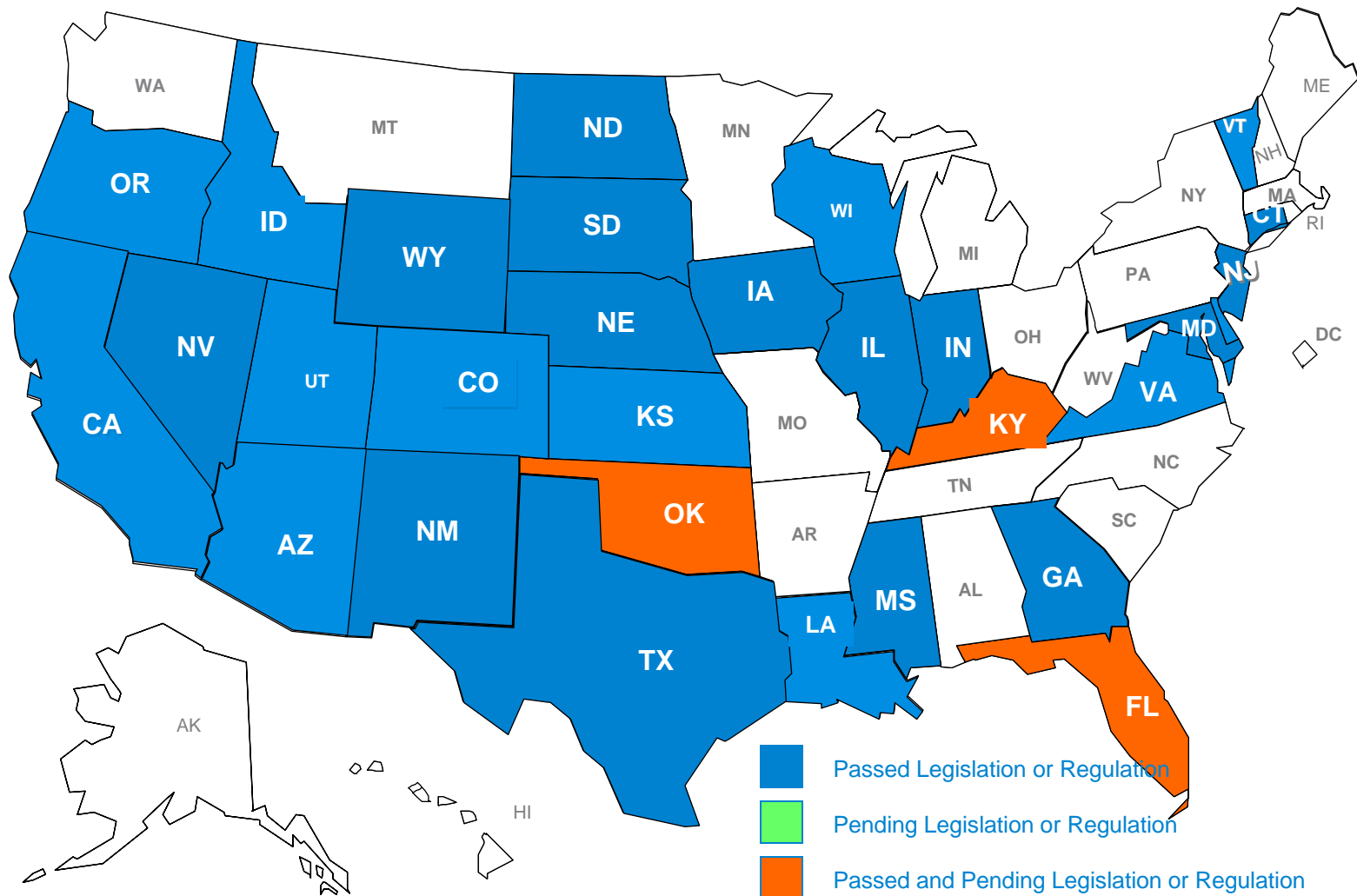
■ Minnesota

- Gift reporting law provides a limitation as well as a disclosure. Law prohibits manufacturers, wholesale drug distributors and their agents from offering a gift of any value to a practitioner.
 - Annual report
 - Establishes categories

Drug Pedigree States with Enacted and/or Pending Laws



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Thank You

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