

# Distribution and marketing of drugs in the United States: overview

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A Q&A guide to distribution and marketing of drugs law in the United States.

The Q&A gives a high level overview of distribution and marketing of drugs law, including pre-conditions for distribution; licensing; wholesale distribution; marketing to consumers; marketing to professionals and engagement with patient organisations.

To compare answers across multiple jurisdictions, visit the Distribution and Marketing of Drugs [Country Q&A Tool](#).

This Q&A is part of the global guide to [Distribution and Marketing of Drugs](#).

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## Distribution

### Pre-conditions for distribution

1. What are the legal pre-conditions for a drug to be distributed within the jurisdiction?

## Authorisation

Under the Federal Food, Drug & Cosmetic Act (FDC Act), drugs are defined as articles which are:

- Intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals.
- Intended to affect the structure or any function of the body of humans or other animals (other than food).
- Intended for use as a component of any articles specified above.

A drug can also be any article recognised in the United States Pharmacopeia or National Formulary, the official Homeopathic Pharmacopeia of the United States. The FDC Act states that a prescription drug is a drug that, because of its toxicity or other potential harmful effects, or the method of its use, or the collateral measures necessary to its use, is not safe for use except under the supervision of a practitioner licensed by law to administer such a drug, or the drug approval is limited to use under the supervision of a licensed practitioner. The FDC Act requires approval by the Food and Drug Administration (FDA) for a drug's intended use before introducing a new prescription drug into interstate commerce.

The FDA approves prescription drugs through one of the following routes:

- The full new drug application (NDA) under section 505(b)(1) of the FDC Act. The NDA must include all necessary information to establish the safety and effectiveness of a drug, and all such information must have been generated by or on behalf of the sponsor.
- An NDA where at least some information relied on by the sponsor to establish the safety and effectiveness of the drug is derived from studies not conducted by the sponsor and to which the sponsor has no legal right of reference, known as a 505(b)(2) application.
- The abbreviated new drug application (ANDA) under section 505(j) of the FDC Act (that is, the approval for "generic drugs").

An over-the-counter (OTC) drug may come to market without requiring pre-market review if the product meets the conditions outlined in a monograph.

## Exceptions

The FDA has exceptions to certain drug approval requirements that are intended to speed the requisite approval, including expedited review and accelerated approval. Examples include Subpart E (biological products), Subpart H (new drugs), Fast Track, Priority Review and Breakthrough Therapy Designation. FDA also has a well-established compassionate use programme (see [Question 2](#)).

2. Do any types of named patient and/or compassionate use programmes operate? If so, what are the requirements for pre-launch access?

The Food and Drug Administration's (FDA) Expanded Access (sometimes called “compassionate use”) programme includes:

- Expanded access for individual patients, including use of an unapproved, investigational product in emergencies.
- Expanded access for intermediate-size patient populations (smaller than those typical of a treatment for an Investigational New Drug (IND) (*see Question 3*) or treatment protocol).
- Expanded access treatment for an IND or treatment protocol.

For all three types of expanded access, the programme must meet the following general criteria:

- The patient or patients to be treated have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition.
- The potential patient benefit justifies the potential risks of the treatment use and those potential risks are not unreasonable in the context of the disease or condition to be treated.
- Providing the investigational drug for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use.

Each subcategory has additional requirements.

## Licensing

3. What is the procedural structure regarding licensing a drug for distribution?

The Food and Drug Administration (FDA) is responsible for drug approval (*see Question 1*). As part of the full new drug application (NDA), the applicant (also known as the sponsor) must provide detailed information concerning investigations undertaken to demonstrate the safety and effectiveness of a new drug (or for a new intended use of an approved drug), including pre-clinical and clinical studies. Before initiating investigational studies in human

research subjects, a sponsor must submit an Investigational New Drug (IND) application, which allows a company to investigate an unapproved drug (or unapproved use of an approved drug) in humans. Sponsors can initiate the clinical investigation(s) proposed in the IND if the FDA does not comment within 30 days after it is submitted. FDA can order the halt or discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA regulatory requirements or presents an unacceptable risk to the clinical trial patients.

Clinical trials to support NDAs for marketing approval are typically conducted in three phases:

- **Phase 1.** This phase involves the first use of the drug in humans, in single- and multiple-dose studies conducted with healthy volunteers or, in some cases, patients with the condition intended to be treated by the new drug. The purpose of phase 1 is to examine the safety of a new drug and obtain information on dosages to take into phase 2.
- **Phase 2.** This usually involves clinical trials in a limited patient population to obtain preliminary information regarding the effectiveness of the drug for a particular indication, optimise the dose, and identify adverse effects and safety risks.
- **Phase 3.** These clinical trials seek to establish the clinical efficacy and safety profile of a new drug in a larger number of patients, typically at geographically dispersed clinical trial sites, to generate sufficient information to evaluate the overall benefit-risk profile of the drug and to provide adequate information for the labelling of the drug. The FDA typically requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the safety and efficacy of a new drug.

After completion of the required clinical testing, an NDA is prepared and submitted to FDA. The NDA must include the following types of information:

- A summary that includes a general understanding of the application, and the drug type and rationale.
- Chemistry manufacturing and controls information including information on the drug substance and drug product.
- Non-clinical studies that include pharmacology/toxicology data and a statement of compliance with Good Laboratory Practices.
- Pharmacokinetics and bioavailability in humans.
- A description of the statistical analysis.
- Required paediatric information (or a request for a deferral or waiver of the same, in certain circumstances).
- Clinical data from the phase 1 – 3 studies (*see above*).
- Case report forms.
- Patent information and certifications.

The FDA has 60 days from its receipt of an NDA to determine whether the agency will accept the application for filing based on the agency's threshold determination that the application is sufficiently complete to permit a substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Most NDAs for standard review drug products are reviewed within ten to 12 months; most applications for priority review drugs are reviewed in six to eight months. The FDA can extend

these reviews by three months. Priority review can be applied to drugs that the FDA determines offer major advances in treatment, or provide a treatment where no adequate therapy exists.

The FDA may seek independent advice from outside experts on issues related to human drugs through an advisory committee (a therapeutically-aligned panel that includes clinicians and other experts). The FDA is not bound by the recommendations of an advisory committee, but the agency usually follows such recommendations. Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with good clinical practices and will inspect the facility or the facilities at which the drug is manufactured to ensure satisfactory compliance with current good manufacturing practices (GMPs), a quality system regulating manufacturing.

An NDA submitted under the 505(b)(2) route requires most of the same information as an NDA but also relies on published non-clinical and/or clinical investigations and/or FDA's previous safety and effectiveness findings. The sponsor of a 505(b)(2) application must establish a scientific or clinical "bridge" to the information on which the sponsor relies in its NDA, which generally includes comparative bioavailability or bioequivalence studies, similar to those conducted during phase 1 investigations of new drugs.

Sponsors submit an ANDA to obtain FDA approval to market a "generic" drug—that is, a drug shown to be comparable to a previously-approved innovator drug in dosage form, dose strength, route of administration, manufacturing quality and performance characteristics, and intended use. Sponsors generally are not required to conduct preclinical or clinical studies to establish safety and effectiveness of an ANDA. Rather, sponsors must demonstrate that their generic product is bioequivalent (i.e., performs in the same manner as the innovator drug, based on pharmacokinetic/pharmacodynamic studies).

4. Is there a simplified licence proceeding, or relaxed licensing conditions, for drugs which have already been licensed for distribution in another jurisdiction?

There are no such simplified proceedings for drugs that have already been licensed for distribution in another jurisdiction. Nor is there a simplified procedure for parallel imports. However, under FDA's Personal Importation Policy, a US citizen may want to be treated, or a foreign citizen may want to continue treatment in the US, with a drug that is not FDA approved for use nor available domestically in the US. FDA may exercise enforcement discretion to allow, on a case-by-case basis, the personal importation of an unapproved drug that meets all of the following requirements. It must:

- Be used to treat a serious medical condition.
- Not pose a serious health risk.
- Not be marketed or commercially available in the US.
- Have begun as part of a treatment plan outside the US.

In addition, the drug must not be the subject of an FDA Import Alert, under which FDA would detain the product without physical examination at the border. This Policy cannot be used to import less expensive versions of drugs approved in the US though FDA is currently in the process of developing a policy for such purposes.

5. Is virtual drug distribution possible from your jurisdiction?

There is no such pathway within the United States. For products not manufactured in the United States and not distributed in the United States, there is no need for any authorisation. The strict regulatory and legal framework in the United States surrounding the distribution of drugs would make the attempt to obtain authorisation when the product will not be manufactured or distributed in the United States impractical.

6. What is the procedure to appeal (legal remedy) a licensing decision?

The FDA must find that the NDA contains data that provides substantial evidence that the drug is safe and effective for its intended use before it approves the application. If the FDA decides not to approve the drug, it will issue a complete response letter that outlines the deficiencies in the submission, including possibly substantial additional testing or information needed for the FDA to reconsider an amended application. Sponsors may appeal FDA's decisions using one of several mechanisms, including FDA's Formal Dispute Resolution process.

7. What are the costs of obtaining licensing?

The costs of obtaining approval of a full new drug application (NDA) are substantial and include the costs of:

- Pre-clinical and clinical testing.
- Preparing and submitting the NDA.
- Responding to any FDA questions during the review of the NDA.
- Preparing for an advisory committee meeting if the FDA decides to convene such a meeting.
- Preparing for any FDA pre-approval inspections.

Submission of most NDAs is additionally subject to a substantial application user fee, which is in excess of USD2.9 million (where clinical data is also submitted) or USD1.4 million (without clinical data) for fiscal year 2020. The manufacturer and/or sponsor under an approved new drug application are also subject to annual program fees,

currently exceeding USD325,000 per prescription drug product. Prescription drug product is defined as a drug that is:

- With a specific strength or potency in final dosage form
- Subject to an approved NDA or BLA.
- Dispensed only with a prescription
- Listed in FDA's publication, *Approved Drug Products with Therapeutic Equivalence Evaluations* (the Orange Book).

The FDA cannot assess more than five prescription drug program fees for a fiscal year for prescription drug products identified in a single approved application. Therefore, an application that identifies seven dose strengths will be assessed at approximately USD1.625 million in annual program fees for the financial year 2020. These fees are typically increased annually.

## Distribution to consumers

8. What are the different categories of drugs for distribution?

There are two general categories of drug products that can be provided to consumers:

- Prescription drugs, which include controlled and non-controlled substances.
- Over-the-counter or non-prescription drugs (OTC). OTC drugs are generally defined as drugs that are safe and effective for use by the general public without the need for supervision by a healthcare practitioner and therefore without a prescription.

Controlled substances are regulated under both federal and state law and are generally considered to be drugs with an abuse potential. The federal Controlled Substances Act (CSA) classifies drugs into five schedules (I-V), depending on the abuse potential and potential for psychological or physical dependence. Drugs included in:

- Schedule I have a high potential for abuse with no accepted medical use in the US.
- Schedule II have a high potential for abuse, but there is a medically accepted use in the US
- Schedules III-V have a lower potential for abuse (though still may be addictive), and they are used for medically accepted purposes in the US.

State agencies follow the same scheme, but there are some differences in scheduling depending on the state.

9. Who is authorised to distribute prescription drugs and over-the-counter drugs to consumers?

## Prescription drugs

Prescription drugs may only be dispensed pursuant to a valid prescription or order issued by an authorised practitioner. The preparation, packaging, labelling, record keeping, and transfer of a prescription drug to a patient or intermediary responsible for providing the drug to the patient is considered drug dispensing, which is generally part of the practice of pharmacy. The practice of pharmacy is primarily regulated by the states through boards of pharmacy rather than the federal government. States generally limit the practice of pharmacy to licensed pharmacists and pharmacies. Therefore, licensed pharmacists (including those authorised to work under the supervision of a pharmacist) and pharmacies can provide prescription drugs directly to consumers. In most states, healthcare practitioners (such as physicians) licensed to prescribe or administer prescription drugs can also dispense to patients under certain conditions. In addition, any healthcare practitioner, pharmacy, or other entity (such as a hospital) that dispenses controlled substances is required to obtain a registration from the United States Drug Enforcement Administration (DEA) and the appropriate state regulatory authority. Some states have restrictions or requirements on the dispensing of controlled substances in addition to DEA's restrictions and requirements.

## Over-the-counter drugs

Generally, there are no licensing or registration requirements to distribute or sell over-the-counter (OTC) drugs to consumers in the United States. However, some states require retail outlets providing OTC drugs to consumers to obtain a retail drug dispensing licence. In addition, some OTC drugs have dispensing restrictions because of their potential for misuse or abuse. OTC products containing ephedrine, pseudoephedrine, or phenylpropanolamine are subject to state and federal restrictions (for example, federal daily sales limits of 3.6g per purchaser and 30-day purchase limits of 9g as described in the Combat Methamphetamine Epidemic Act of 2005).

10. What drugs can an attending physician distribute and under what circumstances?

The dispensing of drug products to patients is primarily regulated by the states rather than the Food and Drug Administration (FDA) (*see Question 9*). The vast majority of states allow physicians to dispense and/or administer prescription and over-the-counter (OTC) drugs, as well as controlled substances, to their patients as long as they are properly licensed to do so.



11. Who is authorised to prescribe prescription drugs to consumers?

In general, state-licensed healthcare practitioners are authorised to prescribe drugs to patients. Medical practice and prescribing authority is generally subject to state authority. Therefore, the states determine which practitioners can prescribe drugs. Every state permits licensed physicians to prescribe drugs, but state law can vary widely with respect to the prescribing authority of other healthcare practitioners. Generally, in addition to licensed physicians, licensed physician assistants, nurse practitioners, and advanced registered nurse practitioners can prescribe drugs to patients. It should be noted that any healthcare practitioner that is entitled to prescribe controlled substances under state law must also have a valid federal Drug Enforcement Administration (DEA) registration to prescribe the drugs. Federal and state law forbids a licensed practitioner from prescribing a controlled substance to a patient without a legitimate medical purpose and outside of the usual course of professional practice.

12. Is direct mailing/distance selling of drugs permitted in your jurisdiction?

## Conditions

The selling and dispensing of drugs via the mail and/or the internet is generally permitted in the US. However, for prescription drugs and controlled substances, there must be a valid prescription issued based on an established doctor-patient relationship. Some states have passed telemedicine laws to facilitate long distance prescribing and treatment. As discussed in *Question 9*, states regulate the practice of pharmacy, and the vast majority of states allow out-of-state pharmacies to dispense drugs to their residents through the mail and the internet as long as they are properly licensed. Every state requires pharmacies located within the state to be licensed, and the vast majority of states require out-of-state pharmacies dispensing drugs to consumers in their state to be licensed as well. As such, in order to dispense drugs to customers located outside the state where the pharmacy is based, a pharmacy must be licensed in both its home state as well as the state into which it is dispensing drugs. For example, a pharmacy located in Maryland can dispense drugs to patients in California as long as it holds a pharmacy licence from both the Maryland and California boards of pharmacy. It should be noted that a pharmacy dispensing controlled substances to customers located in another state must also be registered with the Drug Enforcement Administration (DEA) (only one registration is required) as well as applicable state authorities. Internet pharmacies must also meet federal requirements, especially for controlled substances.

## Cross-border sales

Generally, pharmacies are prohibited from dispensing prescription drugs to patients in foreign countries. Additionally, patients located in the US are generally prohibited from obtaining prescriptions from foreign countries.

13. What regulatory authority is responsible for supervising distribution activities?

The government agencies primarily responsible for regulating the dispensing of drugs to patients are the state boards of pharmacy or similar state authorities. Other state agencies can also be involved to the extent that other healthcare practitioners (such as physicians and nurses) dispense drugs. The Drug Enforcement Administration (DEA) regulates the dispensing of controlled substances at the federal level, and some states also have controlled substance regulatory authorities separate from their boards of pharmacy that are responsible for regulating the dispensing of controlled substances in that state.

14. What is the procedure to appeal (legal remedy) a distribution decision?

Most state boards of pharmacy provide for administrative hearings to challenge an adverse decision by a state agency. Dispensing entities can generally seek administrative and/or judicial appeals of adverse actions. Entities aggrieved by adverse administrative decisions by the Drug Enforcement Administration (DEA) can challenge that action in an administrative hearing or seek judicial review of such decisions.

15. What are the legal consequences of non-compliance with consumer distribution laws?

Penalties for violating state laws related to drug dispensing vary depending on the state, but they may include a suspension, revocation, or denial of the pharmacy/professional healthcare licence, administrative fines, civil penalties, injunctions, or criminal penalties. If the Drug Enforcement Administration (DEA) determines that a pharmacy or healthcare practitioner is not operating in compliance with the Controlled Substances Act (CSA) or implementing regulations, it can seek to suspend, revoke, or deny a registration, and registrants can request an administrative hearing. The DEA can also impose civil monetary penalties, seek an injunction, or pursue criminal charges if applicable.

## **Wholesale distribution**

16. What is the legal regime regarding wholesale distribution of drugs?

**Wholesale distribution of drugs is regulated by both federal and state authorities. All states require a licence to engage in wholesale distribution under the established federal requirements.**

## **Federal prescription drug wholesale distribution requirements**

The Drug Supply Chain Security Act of 2013 (DSCSA) amended the Federal Food, Drug, & Cosmetic Act (FDC Act) and governs the wholesale distribution of prescription drug products.

The DSCSA defines “wholesale distribution” as the "distribution of a drug...to a person other than a consumer or patient, or receipt of a drug...by a person other than the consumer or patient." A wholesale distributor is "a person (other than a manufacturer, a manufacturer's co-licensed partner, a third-party logistics provider, or repackager) engaged in wholesale distribution". The DSCSA pre-empts states from licensing third-party logistics providers (3PLs) as wholesale distributors, and pre-empts any state requirements that differ from the federal statute.

The DSCSA prohibits any person from engaging in wholesale distribution without:

- A licence in the state from which the prescription drugs are distributed (or from FDA if the state does not require a licence).
- A licence from any state in which the prescription drugs are distributed if the state requires a licence.

As applied to wholesale distributors, the DSCSA has several key provisions:

- It limits wholesale distributors of prescription drugs to transactions only between authorised trading partners that are appropriately licenced under federal and state law.
- It creates new drug tracing requirements (also referred to as "track-and-trace") under which a wholesale distributor can only legally receive and transfer ownership of prescription drugs when the product is accompanied by certain product tracing information, including the product's transaction history and transaction information, as well as a transaction statement. This product tracing provision pre-empts all state pedigree requirements.
- Wholesale distributors must report their licensing status and contact information to the FDA on an annual basis.
- Wholesale distributors must put in place a system to:
  - verify the legitimacy of all prescription drug products that they receive;
  - deal with suspect and illegitimate product; and
  - properly notify the FDA and appropriate trading partners concerning illegitimate products.
- Finally, the DSCSA charges FDA with instituting by regulation new minimum standards for the licensing of prescription drugs by wholesale distributors to replace the current set of minimum standards introduced under the Prescription Drug Marketing Act of 1987 (PDMA). FDA has yet to promulgate such regulations, despite a statutory duty to do so within two years of enactment of the DSCSA. The FDA's prior regulations

under the PDMA set out minimum standards that states must comply with during the licensing process, as well as minimum qualifications wholesale distributors must meet in order to receive a state licence. *See* 21 C.F.R. Part 203.

## Federal controlled substances wholesale distribution requirements

The distribution of prescription drugs that are classified as controlled substances under the Controlled Substances Act (CSA) and its implementing regulations are regulated by the Drug Enforcement Administration (DEA). Wholesale distributors of controlled substances must comply with registration, record keeping, reporting, and security requirements that vary depending on drug schedules, as discussed below.

**Registration.** Each facility that distributes or otherwise handles controlled substances must obtain a registration from the DEA specific to each activity, drug schedule, and geographic location. The facility is only authorised to handle a drug in the schedules identified on its application for registration, which may be modified to add additional schedules. Additionally, a DEA manufacturing registration is required if the facility repackages or re-labels controlled substances.

**Records.** There are significant record-keeping requirements involved with the distribution of controlled substances. A registered facility must maintain a record of the quantity, location, and identification of the customer of all controlled substance distributions. Wholesale distributors must also maintain complete and accurate records of every controlled substance received, manufactured, and distributed or disposed of, as well as of certain List I chemicals. Each registered facility must maintain records for schedule I-II drugs separately from schedule III-V drugs.

**Inventories.** Every wholesale distributor must take a physical inventory of all controlled substances before engaging in distribution. Wholesale distributors must also take an inventory of all controlled substances every two years and maintain separate inventories of schedule I-II drugs from schedule III-V drugs.

**Reports.** A wholesale distributor must notify the DEA of any theft or significant loss upon discovery. Registrants are responsible for reporting in-transit losses. Additionally, distributors must report "suspicious orders" of controlled substances, which include orders of unusual size, orders that deviate from the normal patterns, or orders of unusual frequency. They must also notify the DEA regarding the intended destruction of controlled substances (for example, damaged goods, returns). Distributors also must report to DEA through its Automation of Reports and Consolidated Orders System (ARCOS) all transactions concerning schedules I and II materials; Schedule III narcotic and gamma-hydroxybutyric acid (GHB) materials. Since the SUPPORT Act was passed in 2018, distributors also must review anonymised ARCOS data made available by DEA to assist in the identification and reporting of suspicious orders.

**Security.** Wholesale distributors of schedule I and II controlled substances must store them in a safe, steel cabinet, or vault, depending on the amount. Wholesale distributors of schedule III, IV, and V controlled substances must store such drugs in a safe, steel cabinet, vault, cage, or other secure enclosure as defined in the DEA regulations. In addition to physical security, the DEA requires electronic security for all storage areas. Other required security can include:

- Secure fencing around receiving, order picking and packaging areas;
- Key, pass code, or combination lock controls.
- On-site guard force.

- Local police protection.
- Employee screening and restriction.

## State wholesale drug distribution requirements

Although the DSCSA will establish minimum requirements for wholesale distributors of prescription drugs, most states have established their own requirements and licensing for wholesale distribution.

Many states have essentially adopted the federal requirements set out in the PDMA for distributors regarding personnel, security, storage, and record keeping, but most states also license wholesale distribution facilities located within and outside of the state if products are distributed into the state. The process and timeframe for obtaining state wholesale distributor licenses varies significantly from state to state. While federal requirements only apply to the wholesale distribution of prescription drugs, some states enforce licensing requirements for the distribution of over-the-counter (OTC) drugs as well.

In addition to requiring wholesale distributors of prescription drugs to be licensed, several states also require distributors of controlled substances to obtain an additional registration. In those states, wholesale distributors of controlled substances (which are, by definition, also prescription drugs) must obtain a distributor licence as well as a state-controlled substance registration. State-controlled substance registrations are typically not difficult to obtain, provided that the wholesale distributor has a drug distributor licence in that state and a DEA registration. Most states have adopted DEA's requirements regarding record keeping, inventories, security, and required reporting for controlled substances distributors, but some states have developed additional requirements.

17. What regulatory authority is responsible for supervising wholesale distribution activities?

**Federal agencies.** The Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) are the federal agencies generally responsible for regulating the wholesale distribution of prescription drugs, including controlled substances. See [Question 16](#).

**State agencies.** Each state is responsible for licensing and monitoring wholesale drug distributors operating in that state. See [Question 16](#).

The state agency responsible for regulating wholesale distributors is usually the board of pharmacy, but that may vary depending on the state.

In some states, the same agency regulates distributors of both prescription drugs and controlled substances while those responsibilities are divided among different agencies in other states.

18. What are the legal consequences of non-compliance with wholesale distribution laws?

Under the Drug Supply Chain Security Act of 2013 (DSCSA), no entity can operate as a drug wholesaler in the United States unless it is licensed by the appropriate state(s).

Therefore, operating as a prescription drug wholesaler without the proper state licence can result in imprisonment of up to 10 years, a fine of up to USD250,000, or both. Other violations of requirements discussed in *Question 16* can result in up to a one-year prison sentence, a USD1,000 fine, or both. If a wholesaler violates a requirement with the intent to defraud or mislead, the potential penalty increases to a prison sentence of up to three years, a fine of up to USD10,000, or both. The Food and Drug Administration (FDA) can also seek an injunction against the wholesaler to prevent the activity at issue. A wholesaler can appeal adverse penalties through the courts.

The Drug Enforcement Administration (DEA) is the federal agency that registers wholesale distributors of controlled substances, and no entity can operate as a wholesaler of controlled substances in the United States without a DEA registration. If the DEA determines that a wholesaler is not operating in compliance with the Controlled Substances Act (CSA) or related regulations, it can seek to suspend, revoke, or deny a registration. A registrant can contest such action through an administrative hearing. The DEA, through the Department of Justice, can also impose civil monetary penalties, seek an injunction, or pursue criminal charges (if applicable) in federal courts. Wholesalers can seek judicial review of any adverse decisions.

Penalties for violating state laws related to drug wholesale distribution vary depending on the state, but they can include a suspension, revocation, or denial of the wholesale licence, administrative fines, civil penalties, injunctions, or criminal penalties. The ability to appeal an adverse decision varies by state as well, but wholesalers can generally seek administrative and/or judicial appeal of adverse decisions.

## Marketing

### Promotion

19. What is the general legal regime for the marketing of drugs?

The FDA has authority over and regulates the labelling, advertising, and promotion of prescription drugs. The FDA has asserted its jurisdiction over drug marketing in three main ways.

- First, the FDC Act lists a number of "prohibited acts", for which penalties can be assessed. Introducing a drug in interstate commerce that is "misbranded" is a prohibited act. A drug is misbranded if, among other things, its labelling is false and misleading in any particular way. Labelling consists of "written, printed, or graphic matter" on or "accompanying" a drug. The material does not physically need to accompany the

drug or device to be labelling. Labelling includes quotations by physicians or other third parties about drug products if made on behalf of the drug company.

- Second, through the new drug approval process, the FDA regulates a drug's intended use. Intended use means the objective intent of the persons legally responsible for the labelling of drugs, which can be demonstrated by labelling claims, advertising materials, or oral or written statements by such persons or their representatives. Oral statements can include:
  - speeches by company officials;
  - statements by sales representatives;
  - presentations or discussions at trade shows; and
  - speeches at certain Continuing Medical Education (CME) or other third party programmes.
- Where the intended use of a prescription drug differs from the intended use approved by FDA, as listed in the product's approved labelling, FDA has asserted that the product is a "new drug" for which FDA approval is required. Placing a new drug in interstate commerce without FDA approval is a violation of the FDC Act.
- Third, any drug is misbranded according to the FDC Act if its labelling does not bear adequate directions for use. For prescription drugs, this means a drug must have labelling that contains adequate information so that licensed healthcare professionals can use the drug safely and for its intended use, including all conditions for which the manufacturer advertises or represents it can be used. Such labelling must be authorised under an approved NDA (or supplement to an approved NDA).

The most important labelling approved by FDA at the time a drug is approved to be marketed in the US is its full prescribing information (PI). The sponsor can promote information that relates to, and is consistent with, the FDA-approved PI, which must include the indication and can include information about the drug's mechanism of action, clinical results, pharmacology, special populations, dosing, and safety information.

In general, marketing materials disseminated by the sponsor must present information regarding both risks and benefits of the product with "fair balance". All printed promotional labelling must be accompanied by the approved PI for the drug. Drug advertisements must contain a brief summary of the drug's risk information. A "brief summary" is a summary of the drug's side effects, warnings, precautions, contraindications, cautions, special considerations, important notes, and effectiveness. The FDC Act states that advertisements include those published in journals, magazines, other periodicals, and newspapers, and broadcast through media such as radio, television, and telephone communications systems. This list is illustrative and not exhaustive.

In addition to criminal or civil penalties under the FDC Act for the unlawful dissemination of information about prescription drugs, other penalties can be imposed for improper payments made in connection with the promotion of drugs. The US Department of Health and Human Services (HHS) Office of Inspector General (OIG) and the US Department of Justice (DOJ) direct the investigation and prosecution of federal healthcare fraud and abuse laws, most notably the federal anti-kickback statute (AKS) and False Claims Act (FCA). Under the AKS, it is unlawful for a pharmaceutical manufacturer to offer any item of value to anyone if one purpose of the offer is to induce the person to purchase or order a product or arrange for or recommend the purchase or order of a product if the product is reimbursable under a federal health care program.

Many states have similar anti-kickback statutes.

The FCA prohibits knowingly presenting, or causing to be presented, a false claim for payment or using, or causing to be used, a false record or statement to get a false claim paid.

The FCA includes a "*qui tam*" provision that allows a whistle blower, known as a relator, to sue on behalf of him or herself and the government. A claim submitted for items or services, the provision of which resulted from a violation of the AKS, is false under the FCA. Many states also have false claims laws.

In addition, the Federal Physician Payment Sunshine provisions of the Affordable Care Act require disclosure of certain payments made by pharmaceutical manufacturers to physicians and teaching hospitals to the federal government. The Centers for Medicare & Medicaid Services (CMS), a sister agency of FDA within HHS, implements these provisions and finalised regulations implementing that requirement. Failure to submit the required information can result in civil monetary penalties. A number of states also require pharmaceutical manufacturers to report payments made to healthcare professionals.

20. Are there other codes of conduct for the marketing of drugs (for example, by professional or industrial organisations)?

The Pharmaceutical Research and Manufacturers of America (PhRMA), the industry group that represents brand-name drug manufacturers, has published a Code on Interactions with Healthcare Providers (HCPs).

The Code includes the following limitations:

- No entertainment or recreational events for HCPs.
- Modest meals involving HCP can be offered as part of an educational programme or detail and can be held only in HCP's office or hospital by sales representatives.
- Consulting agreements must be bona fide.
- Consultant meetings/advisory boards cannot be held at resort locations.
- A drug manufacturer can occasionally give items of less than USD100 for education of HCP or patients.
- No practice-related items such as pens or flash drives.
- No gifts for personal benefit of HCP (floral arrangements, artwork, CDs, golf balls, tickets to sporting events).

Although the PhRMA Code is technically a voluntary code, OIG has identified the Code as a minimum standard. Furthermore, a handful of states require that drug manufacturers adopt a compliance code that is at least as stringent as the PhRMA Code. In addition, certain states have directly adopted as law some of the provisions in the Code, for instance gift prohibitions. Moreover, other states have adopted provisions more conservative than the Code. For example, Massachusetts and Vermont have enacted laws that discourage certain types of remuneration paid to HCPs, including free meals under certain circumstances.



## Marketing to consumers

21. What is the legal regime for marketing to consumers?

The legal regime with respect to promoting and to consumers is generally the same as described in *Question 19*. Certain controlled substances, those drugs maintained on Schedule I by the DEA, cannot be advertised to consumers. All direct-to-consumer advertising materials must be in consumer-friendly language. In addition, as described in *Question 19*, there are specific requirements pertaining to broadcast advertisements.

22. What kinds of marketing activities are permitted in relation to consumers and the products which may be advertised to them?

The kinds of marketing activities permitted with regard to consumers and the products which might be advertised to them are generally the same as those for professionals (such as print materials disseminated directly by the manufacturer, published materials and audio or video broadcast advertisements) (*see Question 27*).

23. Is it permitted to provide consumers with free samples? Are there particular restrictions on special offers (for example, "buy-one-get-one-free")?

Drug manufacturers can provide free samples of prescription drugs to physicians, in accordance with FDA regulations, who then can provide those samples to their patients free of charge. The Prescription Drug Marketing Act of 1987 (PDMA) imposes certain record keeping and reporting requirements on the distribution of samples. Certain states have also imposed drug sample reporting requirements.

With certain exceptions, the AKS prevents the provision of items of value (including drugs) to patients whose treatments are covered by federal healthcare programs. Also, such samples cannot be billed to the federal health care programmes (*see Question 19*). Drug manufacturers can establish patient assistance programmes if the programmes abide by certain terms. Manufacturers can also provide discounts and coupons for prescription drugs under certain circumstances.

Discounts for prescription drugs reimbursed under federal health programmes are permitted under a "safe harbour" to the AKS if the following conditions are met:

- Reporting obligations for the buyer, seller and offeror.
- The buyer's requirements depend on the type of provider.
- The seller must fully report a discount on the invoice, coupon, or statement to the buyer, and inform the buyer of its obligation to report the discount.
- Maintain a paper trail.
- Documentation that will permit accurate reporting to federal programmes.

24. Are there particular rules of practice on the use of the internet/social media regarding drugs and their advertising?

There are no specific rules/codes of practice on the use of the internet/social media in respect of drugs and advertising. The Food and Drug Administration (FDA) considers product information posted on the internet to be labelling or advertising and restrictions apply, such as no off-label promotion and including fair balance.

In June 2014, the FDA published two draft guidance notes related to social media. It published guidance on how drug manufacturers can achieve fair balance on the internet or social media platforms with character space limitations. It also published guidance on correcting independent third-party information about drugs.

25. What regulatory authority is responsible for supervising marketing activities to consumers?

The Food and Drug Administration (FDA) regulates the labelling and the advertising of prescription drugs. For over-the-counter drugs, the FDA has jurisdiction over labelling, but the Federal Trade Commission has jurisdiction over advertising. The Office of Inspector General has jurisdiction over violations under the anti-kickback act, and the state attorneys general, acting in concert with the Department of Justice, can bring litigation under the False Claims Act (FCA) or related state laws.

26. What are the legal consequences of non-compliance with consumer marketing laws?

The Food and Drug Administration (FDA) can issue untitled or warning letters on its own initiative. The Department of Justice (DOJ) brings actions such as seizure or injunction on behalf of the FDA.

The performance of a prohibited act under the Federal Food, Drug & Cosmetic Act (FDC Act) can result in untitled or warning letters, civil fines, seizure, injunction and jail time.

Penalties under the anti-kickback act include jail time, criminal monetary penalties and exclusion from participation in all health care programs. The False Claims Act (FCA) allows for the recovery of approximately USD11,000 to USD22,000 per claim plus three times the amount in damages.

## Marketing to professionals

27. What kinds of marketing activities are permitted in relation to professionals?

Drug manufacturers can promote their prescription drugs to professionals in accordance with FDA regulations and, in general, for intended uses consistent with FDA-approved drug package inserts (PI). Advertising to professionals can occur in multiple venues including educational conferences, journal advertisements, trade conferences and webinars and so on.

28. Are there any restrictions on marketing to professionals?

## Marketing activities

The dissemination of journal reprints has been a controversial topic in the United States that has not been entirely resolved. In *Washington Legal Foundation v Friedman* (13 F. Supp. 2d 51 (D.D.C. 1998)), a federal district court judge ruled that the Food and Drug Administration (FDA) could not prohibit the dissemination of truthful and non-misleading reprints of peer-reviewed articles, even if the articles describe off-label uses of the drugs, without violating the First Amendment of the US Constitution. The Court of Appeals vacated the decision without reaching the constitutional issue, leading to uncertainty. The FDA published revised draft guidance on good reprint practices in February 2014.

In addition, in the more recent cases of *United States v Caronia* (703 F.3d 149 (2d 2012)), and *Amarin Pharma, Inc. v. U.S. Food & Drug Administration* (No. 15-CIV-3588 (S.D.N.Y. Aug. 7, 2015)), some federal courts in one federal jurisdiction have held that the dissemination of truthful and non-misleading information is protected by the First Amendment.

Provision of gifts to physicians have been allegations in False Claims Act (FCA) or anti-kickback actions. In addition, as discussed in [Question 20](#), the Pharmaceutical Research and Manufacturers of America (PhRMA) Code prohibits provision to Healthcare Professionals (HCPs) of all non-educational items, and even for educational items, there is a limit of less than USD100. In addition, certain states either have a code similar to the PhRMA Code or have adopted certain of the prohibitions directly into their laws (*see Question 20*). Also, the Sunshine provisions of the Affordable Care Act require disclosure of certain promotional activities to the federal government.

There are restrictions on providing other items of value to healthcare professionals (*see Question 20*). In certain instances, the Department of Justice (DOJ) and state attorneys general have cited detailing practices as evidence of off-label promotion (for example, if the sales representatives are detailing physician practices that specialise in medical areas not related to the indication included in the package insert (PI)).

## Provision of hospitality

The PhRMA code establishes several restrictions such as not allowing entertainment and limiting meals ([Question 20](#)). As previously discussed, several states either require adoption by companies of a code that is very similar to the PhRMA code or have incorporated into law restrictions on the provision of hospitality. Also note that meals must be disclosed pursuant to the Sunshine provisions of the Affordable Care Act.

29. What information is it legally required to include in advertising to professionals?

Information that is legally required includes a "brief summary" and "fair balance". For the concepts of the brief summary and fair balance for prescription drugs, see [Question 19](#) and [Question 24](#). The package insert (PI) must be included (*see Question 19*).

30. Are there rules on comparisons with other products that are particularly applicable to drugs?

A drug manufacturer must possess substantial evidence to make claims that its product is better or superior to another drug. Substantial evidence for comparative claims generally consists of two adequate well-controlled head-to-head comparative trials.

31. What other items, funding or services are permitted to be provided to professionals?

The provision of any item of value to a healthcare professional raises potential risk under the AKS. The PhRMA Code provides guidelines on the type of funding and other items of value that are ethically permissible, which have been referenced by the OIG in its guidance to pharmaceutical manufacturers. While adherence to the PhRMA Code provisions does not completely protect a manufacturer from civil or criminal sanctions under the AKS, the OIG has stated that compliance with the Code substantially reduces the risk of liability under the AKS for conduct undertaken by manufacturers and also shows a good faith effort to comply with applicable federal law.

Under the PhRMA Code guidelines:

- Items (even those with nominal value, such as pens or mugs) that have no educational value should not be provided by manufacturers to healthcare professionals.
- Educational items whose value does not exceed USD100 and only have value in the context of a healthcare provider's professional practice can be provided by a manufacturer.
- Modest meals can be provided in conjunction with information presentations by manufacturers as long as such meals are not provided with an entertainment or recreational event.
- Manufacturers must generally not provide any entertainment or recreational events for healthcare providers, regardless of the event's value, the relationship between the manufacturer and healthcare provider, or the context in which the event takes place.
- Manufacturers must not provide any subsidy for a healthcare provider to attend a Continuing Medical Education (CME) event or medical conference, but can provide financial support to an accredited CME provider or conference organiser to reduce the overall cost of attendance.
- Bona fide consulting agreements that serve a legitimate business need and provide fair market value payment for services rendered are appropriate.
- Manufacturers must require healthcare providers who serve on committees that make formulary decisions or clinical practice guidelines to disclose their financial relationships with the manufacturer.

It is permitted to provide professionals with free samples if the conditions of the Prescription Drug Marketing Act of 1987 (PDMA) are followed and the professional does not bill federal healthcare programmes for the samples. See Question 23.

32. What regulatory authority is responsible for supervising marketing activities regarding professionals?

See [Question 25](#).

33. What are the legal consequences in case of non-compliance with professional marketing laws?

See [Question 26](#).

## Engagement with patient organisations

34. What kinds of activities are permitted in relation to engagement with patient organisations? What are the restrictions that are imposed on relationship with patient organisations?

Activities undertaken by patient organisations in the course of an engagement with a drug manufacturer are generally subject to the legal regime set out in [Question 19](#). For engagements relating to an investigational new drug that is not yet FDA-approved, special attention should be given to two areas:

- Pre-approval promotion.
- Issues related to clinical trials.

Drug manufacturers and patient organisations acting in concert with or on behalf of drug manufacturers are subject to FDA regulations that prohibit the promotion of an investigational new drug by making claims of safety or effectiveness for the intended use(s) for which it is being investigated. Patient organisations must also ensure that any communications with its patient members or constituents regarding clinical investigations (such as clinical trial recruitment) are consistent with the investigational materials approved by the Institutional Review Board/Ethics Committee that is overseeing the investigation. This is because such communications may constitute the beginning of the informed consent process for the investigation.

## Recent developments and outlook

35. Are there notable recent developments or regulatory projects in the field of distribution and marketing of drugs?

See [Question 16](#) regarding state prescription drug requirements.

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#### Publications

- *Tobacco Products (Chap. 14) and Promotion and Marketing of Prescription Drugs, Biologics Devices (Chap. 18), in FDA Deskbook: A Compliance and Enforcement Guide (2019) (co-author).*
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- *Telemedicine: Understanding the FDA's role in recent regulatory and enforcement actions*, Compliance Today Magazine (2019) (co-author).
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### Publications

- *Drug Compounding (Chap. 7), Animal Products (Chap. 15), FDA Inspections (Chap. 21) in FDA Deskbook: A Compliance and Enforcement Guide (2019) (co-author).*
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