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# PRACTICAL LAW

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# United States

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## REGULATORY OVERVIEW

**1. What is the regulatory framework for the authorisation, pricing and reimbursement of drugs, biologicals and devices (as they are termed in your jurisdiction)?**

### Legislation

The US Food and Drug Administration (FDA) (*see box, The regulatory authorities*) enforces many statutes and rules that govern the regulation of pharmaceutical products. The primary legislation governing the FDA is the Federal Food, Drug and Cosmetic Act (FDCA) (*21 USC § 301, et seq.*). A list of laws enforced by the FDA and related statutes is available at *www.fda.gov/RegulatoryInformation/Legislation/default.htm*.

### Regulatory authorities

The FDA is responsible for protecting the public health by assuring the safety, efficacy and security of:

- Human and veterinary drugs.
- Biological products.
- Medical devices.
- Food.
- Cosmetics.
- Dietary supplements.
- Products that emit radiation.

The FDA also regulates tobacco products, advancing public health by helping expedite product innovation, and helps the public get accurate science-based information regarding the products it oversees.

While the FDA does not develop, manufacture or test drugs, it requires evidence of a new drug's safety and efficacy demonstrated through clinical trials of the drug on human volunteers (*see Question 7*) before it will approve a drug for marketing. Drug manufacturers submit reports of these drug studies so that the FDA can:

- Evaluate its data.
- Assess the benefit-to-risk relationship.
- Determine if a drug will be approved.

Within the FDA, the Center for Drug Evaluation and Research (CDER) oversees the research, development, manufacturing and marketing of drugs. Also within the FDA, the Center for Biologics Evaluation and Research (CBER) regulates all biological and related products for human use, which includes blood, vaccines, allergenics, tissues, and cellular and gene therapies (*see box, The regulatory authorities*).

### Biotechnology and combination products

While CBER usually regulates biologics, therapeutic biological products are considered drugs and therefore regulated by CDER.

Combination products include components that would individually be regulated by separate FDA centres with varying regulatory authority (that is, biologics, devices and drugs). The Office of Combination Products (OCP) is responsible for determining which FDA department is responsible for the regulation of various combination products. OCP releases updates that announce the jurisdiction of specific product classes.

## PRICING AND STATE FUNDING

**2. What is the structure of the national healthcare system, and how is it funded?**

There is no current national healthcare system that covers all citizens in the US. Most Americans have medical insurance through private insurance companies, which pays a percentage of healthcare costs. Employers may provide or subsidise the cost of medical insurance premiums. There are two government programmes, Medicare and Medicaid, which cover or assist with medical costs for the elderly, poor and disabled.

Legislation enacted in March 2010 provides for significant reform to the US healthcare system, including reform to healthcare insurance and funding. The legislation includes various provisions to be phased in over the next decade, with a number of key reforms to be implemented by 2014. For example, in 2014, there will be an individual mandate that most citizens must buy health insurance or be required to pay a tax penalty, with certain exceptions for the poor. Additionally, the legislation provides incentives for employers to provide healthcare benefits for their employees (*see Question 35*).

**3. How are the prices of medicinal products regulated?**

Pharmaceutical companies can set their own prices within market demands. Anti-trust regulations overseen by the Federal Trade Commission (FTC) (*see box, The regulatory authorities*) apply to the marketing of pharmaceuticals. Manufacturers and wholesalers generally negotiate with Health Maintenance Organisations

(HMOs), large chain pharmacies and smaller independent pharmacies to set prices. There is also indirect influence through government control of drug reimbursements in Medicare and Medicaid programmes (*see Question 4*).

**4. When is the cost of a medicinal product funded by the state or reimbursed to the patient? How is the pharmacist compensated for his dispensing services?**

Medicaid is a joint federal and state programme that provides medical assistance (including prescription drugs) for low income individuals who meet certain criteria. Under the federal Medicaid Drug Rebate Program, drug manufacturers must grant discounts on prescription drugs to state Medicaid programmes if they want to be eligible for Medicaid reimbursements. No federal funds are reimbursed to drug manufacturers although there is indirect governmental influence.

Medicare prescription drug plans are available to all individuals with Medicare, regardless of income, health status, or current prescription expenses. Insurance companies and other private companies work with Medicare to offer these drug plans and prices. Like other insurance, Medicare prescription drug plans require payment of monthly premiums, deductibles and part of the prescription cost. Assistance with payments associated with the Medicare prescription drug plans is available for individuals with limited resources.

The healthcare reform legislation enacted in March 2010 will impact the current benefits provided by Medicaid and Medicare, including prescription drug benefits. Over the upcoming years, the legislation is scheduled to expand Medicare and Medicaid coverage and eligibility, and provide for certain rebates and discounts on prescription drugs under Medicaid and Medicare (*see Question 35*).

## MANUFACTURING

**5. What is the authorisation process for manufacturing medicinal products?**

### Application

Companies that manufacture drugs and human biological products must register their establishment(s) and submit to the FDA a listing of every product in commercial distribution (*section 510, FDCA (21 USC § 360)*).

### Conditions

The FDA Division of Compliance Risk Management oversees the drug establishment registrations and listings, which must be submitted electronically unless a waiver is granted. Instructions regarding the FDA's electronic drug registration and drug listing are available at *www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/DrugRegistrationandListing/ucm078801.htm*.

### Restrictions on foreign applicants

All foreign drug establishments involved in the manufacturing, preparation, compounding, or processing of drugs or devices for importation into the US must register with the FDA (*21 USC § 360(i)*). Specific procedures for the registration of foreign drug establishments are set out in 21 Code of Federal Regulations (CFR) § 207.40.

### Key stages and timing

A manufacturer must register with the FDA as a drug establishment within five days of beginning the manufacturing, preparation, compounding, or processing of a drug or biological product (*21 CFR § 207.20-21*). The registration must list every drug that is in commercial distribution by the establishment. The drug listing can also be submitted by the distributor of a drug manufactured or processed by a registered establishment.

### Fee

An annual fee is allocated to each prescription drug or biological product establishment named in a New Drug Application (NDA) or Biologics License Application (BLA) (*21 USC § 379h(a)(2)(A)*). Annual fees are available at *www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/default.htm*.

### Period of authorisation and renewals

Each drug establishment must renew its registration annually (*21 CFR § 207.21(a)*). Drug listing information must be updated every June and December (*21 CFR § 207.21(b)*). Any changes in the manufacturing of drugs and their packaging are reviewed by the FDA. Manufacturers must notify the FDA in advance of these changes by filing a manufacturing supplement to a new or generic drug application.

**6. What powers does the regulator have in relation to manufacturing authorisations?**

### Monitoring compliance

The FDA has enforcement powers to ensure product safety, effectiveness and compliance with current good manufacturing practices (CGMPs). The FDA has statutory authority to:

- Seize any drug that is adulterated or misbranded when initially introduced into the market, while in interstate commerce or while held for sale (*21 USC § 334*).
- Enter any factory, warehouse or establishment in which food, drugs, devices or cosmetics are manufactured, processed, packed or held for introduction into interstate commerce, or to enter any vehicle being used to transport or hold such products (*21 USC § 374(a)(1)*).
- Inspect at reasonable times, within reasonable limits and in a reasonable manner, that facility or vehicle (*see bullet point above*) and all relevant equipment, finished and unfinished materials, containers and labelling (*21 USC § 374(a)(1)*).
- Collect samples of drug products (*21 USC§ 372(b)*).
- Inspect records, files, papers, processes, controls and facilities related to drug products (*21 USC § 374(a)(1)*).

FDA inspection procedures and policies are described in the FDA's Investigations Operations Manual (*see www.fda.gov/ICECI/Inspections/IOM/default.htm*).

Biologics are subject to stringent manufacturing regulations, and each manufacturing facility must meet CBER guidelines to ensure safety of that particular biologic product (*21 CFR § 601.20*). FDA must be notified of any changes to the manufacturing process of any biologic product (*see 21 CFR § 601.12 and 21 USC § 356a*).

### Imposing penalties

If a company fails to comply with CGMPs or biologic manufacturing guidelines, the FDA can:

- Issue a warning letter.
- Initiate regulatory actions.
- Impose fines after an administrative hearing.
- Suspend, revoke or fail to approve an application to market a drug or biologic.

## CLINICAL TRIALS

**7. Outline the regulation of clinical trials.**

### Legislation and regulatory authorities

Clinical trials are authorised by the FDCA (*see 21 CFR Part 355(i)*) and must comply with good clinical practices (GCPs) (regulations are set out at *www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm155713.htm*).

### Authorisations

New drugs are tested for toxicity and efficacy on laboratory animals. If the tests indicate that a drug may be effective and that it is reasonable to test it on humans, the sponsor must first obtain the FDA's approval for human clinical trials (*21 CFR §§ 312.2(a), 312.20*).

This is done by submitting an Investigational New Drug Application (IND) application to the FDA (*21 CFR §312.23*), using FDA Form 1571 (available at *www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/default.htm*).

The FDA must review IND applications within 30 days of submission and take appropriate action (*21 CFR § 312.40(b)*). If the FDA responds negatively, the IND does not take effect and human trials cannot proceed. If the FDA responds favourably or does not respond, the manufacturer can proceed with human trials.

An investigator cannot participate in a clinical trial on human subjects until it provides the sponsor with specific information, including a completed, signed statement of investigation (FDA Form 1572) (*21 CFR § 312.53(c)*).

The investigator must agree to conduct the study according to the protocol, report any adverse experiences, and maintain adequate and accurate records. An Institutional Review Board (IRB) must also review and approve all clinical studies before an investigator begins conducting research.

After submission of an IND, before approval of a drug for marketing (*see Question 8*), clinical testing on human subjects consists of (*21 CFR § 312.21*):

- **Phase I.** Small studies of 20 to 80 patients to determine toxicity and pharmacological information.
- **Phase II.** Small studies of several hundred patients to determine safety and efficacy.
- **Phase III.** Large studies of several hundred to several thousand patients to determine safety, efficacy and adequacy of labelling.

After the FDA has approved a drug for marketing, Phase IV and other post-marketing studies can be conducted to collect additional information about the risks, benefits and optimal use of a particular drug (*21 CFR §§ 312.85 and 355(o)(3)*).

### Consent

Informed consent must be obtained from each study subject who will be administered the investigational drug (*21 CFR § 312.60*).

### Trial pre-conditions

Before beginning a clinical trial, a protocol must be established, describing the:

- Types of patients that can participate.
- Schedule of tests and procedures.
- Drugs.
- Dosages.
- Length of the study.
- Outcomes to be measured.

### Procedural requirements

Sponsors of clinical trials involving human drugs, biological products, and combination products have numerous procedural requirements and obligations while conducting a clinical trial (for example, 21 CFR Parts 50, 54, 56, and 312). These obligations require that sponsors (*21 CFR §§ 312.50*):

- Select qualified investigators.
- Provide the information required to conduct a proper investigation.
- Monitor the investigation.
- Ensure that investigators are promptly informed of any new risks or adverse effects.

## MARKETING

***Authorisation and abridged procedure***

**8. What is the authorisation process for marketing medicinal products?**

### Application

Manufacturers must obtain approval of an NDA from the CDER before marketing a drug. Biologics manufacturers must submit a BLA and obtain a biologics licence from CBER before placing the biologic into interstate commerce. FDA Form 356h is used for both an NDA and BLA and can be found at *www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/default.htm*.

An NDA must include the information set out in 21 CFR § 314.50, which generally includes:

- An application form.
- Index.
- A summary.
- Five or six technical sections.
- Case report tabulations of patient data.
- Case report forms.
- Drug samples.
- Labelling.

A BLA must include the information set out in 21 CFR § 601.2, which includes information on the:

- Manufacturing processes.
- Chemistry.
- Pharmacology.
- Clinical pharmacology.
- Medical effects of the biologic product.

According to a Congressional mandate, FDA has attempted to minimise the differences in the review and approval of products required to have approved BLAs and NDAs.

### Authorisation conditions

The FDA will approve an NDA after it is satisfied that the drug meets the statutory standards for:

- Safety and effectiveness.
- Manufacturing and controls.
- Labelling.
- Bioequivalence (where applicable).

The FDA will issue a biologics licence after it determines that the product, manufacturing process, and manufacturing facilities meet applicable requirements to ensure the continued safety, purity and potency of the product. This includes assessment of the storage and testing of cell substrates used in manufacturing the biologics.

### Other conditions

See below, *Post-marketing commitments and pharmacovigilance obligations.*

### Key stages and timing

The two main stages are:

- IND review and clinical investigations (*see Question 7*).
- NDA or BLA review and approval for marketing or licensure. Once adequate safety and efficacy information is developed for a drug, the manufacturer must obtain FDA approval by submitting an NDA or BLA (*see above, Application*). Companies can submit their NDAs or BLAs electronically. The FDA has 180 days to respond after an NDA is filed (*21 CFR § 314.100(a)*). The FDA interprets filed to mean when it is considered approvable by the FDA rather than when it was initially submitted by the manufacturer. The time from product conception to approval can range from a few years to 20 years.

### Fee

Fees are set by the FDA Prescription Drug User Fee Act. For fee information, see *www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/default.htm.*

### Period of authorisation and renewals

Authorisation to market a drug continues unless and until it is withdrawn from the market, either voluntarily by the manufacturer or by the FDA, or the FDA withdraws its approval of an NDA or biologic licence.

### Post-marketing commitments and pharmacovigilance obligations

After an NDA is approved, there are ongoing requirements for the reporting of post-marketing adverse drugs experiences (*21 CFR § 314.80*). For example, the manufacturer must report each serious and unexpected adverse drug experience, whether foreign or domestic, as soon as possible, but no later than 15 days after initial receipt of the information. Annual reports must also be filed (*21 CFR § 314.81(b)(2)*). Licensed manufacturers of a biologic must comply with similar adverse event reporting requirements (*21 CFR § 600.80*).

## 9. Which medicinal products can benefit from the abridged procedure for marketing authorisation and what conditions and procedure apply? What information can the applicant rely on?

There are various procedures that can expedite application review including:

- **Treatment IND.** A Treatment IND allows physicians to prescribe experimental drugs showing promise in clinical testing for serious or immediately life-threatening conditions before approval. In 2009, FDA revised its regulations regarding Treatment INDs to expand treatment use of an investigational drug under a treatment protocol, or treatment IND, outside of a clinical trial (*21 CFR § 312.300, et seq.*).
- **Fast Track programmes (21 CFR § 312.80, et seq.).** Fast Track designation is intended to expedite the FDA review of drugs designed to treat serious or life-threatening conditions and that show potential to address unmet medical needs. This is accomplished through increased interaction between the manufacturer and the FDA. Fast Track designation provides for more frequent meetings and correspondence with the FDA for its input, the ability to submit an NDA in sections, and possible evaluation of studies using surrogate endpoints for Accelerated Approval (*see below, Accelerated Approval, Subpart H*). In addition, Fast Track designation is independent of Priority Review (*see below, Priority Review*) and Accelerated Approval. Manufacturers can request Fast Track designation at the time of the original submission of the IND or any time afterwards, before approval.
- **Priority Review.** The FDA designates each application as either Standard Review or Priority Review. A drug is given Priority Review if it offers major advances in treatment, or provides a treatment option where adequate therapy is not currently available. The FDA attempts to review Priority drugs within a six-month time frame. While the review time for Priority drugs is shortened, the process is essentially the same, with the same

supporting data required for safety and efficacy as drugs classified as Standard. Products submitted for Fast Track approval are typically designated for Priority Review. All non-priority drugs are considered standard applications.

- **Accelerated Approval, Subpart H.** Accelerated approval is intended to make promising products for life-threatening diseases available on the market as a result of preliminary evidence. This preliminary evidence is usually based on a surrogate endpoint (a substitute measurement for the clinical measurement, such as prolongation of survival or symptom improvement) that is considered likely to predict patient benefit. Accelerated approval is also appropriate when it is determined that safe use of the promising product is based on restriction of the product's distribution or use. Accelerated approval is provisional and a written commitment to complete clinical studies to formally demonstrate patient benefit is required. (See also 21 CFR Part 601, Subpart E, with the requirement for accelerated approval of biological products for serious or life-threatening illnesses.)
- **Parallel track approval.** Under this FDA policy, patients with AIDS/HIV-related diseases who cannot participate in clinical trials due to their condition receive investigational drugs that show promise in preliminary studies. This differs from a Treatment IND in that it applies only to patients with AIDS and HIV-related diseases, with the investigational drugs possibly being made earlier in the development process.
- **New or expanded use review.** Applications for a new or expanded use of an existing drug are received as efficacy supplements to the original NDA. The FDA's goal is to review standard supplements in ten months and priority supplement in six months or less.
- **Listed drugs versus generic drugs.** Manufacturers of drugs that are identical, similar or related to listed drugs (that is, FDA approved drugs) can circumvent the extensive NDA approval process and file an Abbreviated New Drug Application (*21 CFR § 314.92, et seq.*). This is the procedure followed for generic drugs.
- **Expanded access to investigational drugs.** In 2009, the FDA revised its regulations to clarify the methods available to patients interested in access to investigational new drugs, despite the fact that they are not eligible to participate in a clinical trial. The revised regulations also make investigational new drugs more accessible and clarify how costs can be charged for such drugs. See *www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm172492.*
- **Biological products.** In March 2010, the Biologics Price Competition and Innovation Act (BPCI Act) was enacted as part of the Patient Protection and Affordable Care Act. The BPCI Act establishes an abbreviated approval pathway for biological products that are "highly similar to" or "interchangeable with an FDA-approved biological product", also known as biosimilar products. The sponsor must demonstrate that there are no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency. The FDA recently issued three draft guidance documents setting forth its current thinking about the development and licensure of biosimilar products. See *www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm291232.htm.*

**10. Are foreign marketing authorisations recognised in your jurisdiction?**

Foreign marketing authorisations of medicinal products are not recognised in the US.

**11. What powers does the regulator have in relation to marketing authorisations?**

### Monitoring compliance

The FDA monitors compliance with NDA approval or a biologics licence by requiring that adverse event reports, and other post-marketing reports, are filed by the respective manufacturer (*21 CFR §§ 314.80-81, 600.80*). This ensures that drugs and biologics remain safe and effective.

### Imposing penalties

If the FDA no longer believes that the data supports the safety and efficacy of an approved drug or biologics licence, it can:

- Issue a written notice or warning.
- Suspend or withdraw the approval or licence.
- Seize the drug or biologic.

In addition, violation of the FDCA can result in both civil and criminal penalties.

## *Parallel imports*

**12. Are parallel imports of medicinal products into your jurisdiction allowed?**

The FDCA (*21 USC §§ 331*) currently prohibits interstate shipment of any unapproved new drugs. This also includes foreign-made versions of US-approved drugs that have not received FDA approval. Importers must show that any drugs offered for importation have been approved by the FDA.

## *Restrictions*

**13. What are the restrictions on marketing practices such as gifts, sponsoring, consultancy agreements or incentive schemes for healthcare establishments or individual medical practitioners?**

Federal anti-kickback statutes regulate the remuneration that can be provided. Offering any type of remuneration, directly or indirectly, to any person or entity in a position to purchase, lease, order or prescribe (or influence such) a service or item reimbursed by a federal healthcare programme could violate the federal Anti-Kickback Statute (*42 USC §1320a-7b(b)*), if the purpose of the payment or gift to the healthcare professional is to induce federal healthcare programme business. Pharmaceutical manufacturers must, therefore, carefully scrutinise sales and marketing practices involving gifts, donations or other forms of remuneration that may be given to medical professionals and/or facilities.

No gift can generally be given to healthcare providers in exchange for prescribing products or a promise to continue prescribing products. Gifts provided to physicians should primarily be for the benefit of the patient. In January 2009, the Pharmaceutical Research and Manufacturers of America (PhRMA) revised its Code on Interactions with Healthcare Professionals. The revised code:

- Prohibits non-educational gifts of any value, including pens, mugs and medical equipment.
- Allows for the distribution of materials of minor value (that is, less than US$100) that are intended for the education of patients or healthcare personnel.
- Allows for occasional modest meals to be provided to doctors in conjunction with an educational presentation, but only in the office or hospital setting.

The American Medical Association (AMA) provides guidance to physicians as to the gifts it considers acceptable in its Gifts to Physicians from Industry (*Council on Ethical and Judicial Affairs, Opinion 8.061*). Similar to the PhRMA's revised Code, the AMA's Opinion sets out the guiding principles that gifts given to physicians should:

- Primarily benefit the patient.
- Not be of substantial value.
- Not influence the physician.

The AMA indicates that gifts of minor value that serve an educational purpose are appropriate, including textbooks and modest meals. The AMA finds that a physician can receive modest meals at educational functions, but does not set location limitations similar to the PhRMA Code. Unlike the PhRMA, the AMA allows for physicians to receive gifts of minimal value related to their work (for example, pens and notepads) and also medical equipment of non-substantial value. The PhRMA and AMA agree that items intended for the personal benefit of the physician, including cash or cash equivalents, are considered inappropriate (except as compensation for bona fide services).

Under the FDCA, representatives of drug manufacturers have traditionally been banned from promoting the use of medications for uses that have not been approved by the FDA (known as off-label use). The FDA permits manufacturers to lawfully distribute material concerning off-label use in certain circumstances (*see Question 15*). Manufacturers can respond to unsolicited requests for information about FDA-regulated products by providing truthful, balanced, non-misleading and non-promotional scientific or medical information that is responsive to the specific request, even if it includes unapproved or uncleared indications.

The FDA's Office of Prescription Drug Promotion (OPDP) (formerly Division of Drug Marketing, Advertising and Communications (DDMAC)) advises the pharmaceutical industry on proposed advertising and promotional labelling (*21 CFR § 202.1(j)(4)*). The OPDP has requested that launch campaigns be submitted voluntarily to the DDMAC for comment before dissemination. Companies can request an advisory opinion on non-launch promotional pieces before they use them (*21 CFR § 10.85*).

The Foreign Corrupt Practices Act (FCPA) prohibits improper payments to government officials outside the US. The anti-bribery portion of the FCPA prohibits US-based companies, including drug and device manufacturers, from influencing government officials or gaining improper advantage by offering, paying, or promising to pay foreign officials anything of value.

**14. What are the restrictions on marketing medicinal products on the internet, by e-mail and by mail order?**

Pharmaceutical products can be marketed and sold over the internet. However, a patient must have a prescription from a physician to purchase a prescription drug. Given the difficulties of regulating the internet and uncertainty over who exactly has the authority to regulate it, many people may be purchasing prescription drugs without prescriptions.

Some states have attempted to regulate the prescription of drugs on the internet by enacting laws that make it illegal for a doctor to prescribe a drug without an examination. For further information, see *www.fda.gov/ForConsumers/ProtectYourself/default.htm*.

## ADVERTISING

**15. What are the restrictions on advertising medicinal products?**

### Legislation and regulatory authority

FDA regulations concerning prescription drug advertising are designed, in part, to ensure that claims are supported by credible scientific evidence (*21 CFR § 202.1*). FDA's OPDP is responsible for ensuring truthful advertising and promotion of prescription drugs. A drug is considered "misbranded" if an advertisement fails to satisfy the requirements of the FDCA and FDA regulations (*21 USC § 352*). Generally, prescription drug advertisements do not require prior FDA approval (*21 USC § 352(n)*). In the case of accelerated approval products, however, all promotional materials intended for dissemination within 120 days of approval must be submitted to the FDA during the pre-approval period (*21 CFR § 314.550*). Advertisement pre-approval may also be required, in special circumstances, as part of an enforcement action.

All advertisements must be submitted to the OPDP when the advertisement is initially published (*21 CFR § 314.81(b)(3)(i)*). The OPDP also offers comments on any adverts submitted before publication.

The Lanham Act (*15 USC § 1051, et seq.*) allows lawsuits based on claims of false advertising. Competitors of the defendant can sue to challenge advertising as false or misleading (*§ 43(a), Lanham Act, 15 USC §1125(a)(1)(B)*).

### Restrictions

Regulations involving direct advertising to consumers are extensive. The manufacturer must present a fair balance between the information relating to efficacy and the information concerning side effects and contraindications. Drug manufacturers must also distribute patient labelling or medication guides when the FDA determines that a prescription drug or biological product poses a serious and significant public health concern (*21 CFR § 208.1*).

The FDAMA abolished the prohibition on dissemination by manufacturers of information about off-label uses (use of an FDA-approved drug for an indication other than that for which it was

approved) of drugs and medical devices. Manufacturers are permitted to disseminate peer-reviewed journal articles about off-label use of a product to healthcare providers. Specifically, they can provide information concerning the safety and efficacy of a drug for a use not included in FDA-approved labelling. For further information, see FDA's Guidance for Industry, *Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices*, January 2009, available at *www.fda.gov/oc/op/goodreprint.html*.

In 2010, FDA launched the "Bad Ad Program" designed to educate healthcare providers about their ability to ensure that drug advertising and promotion is truthful and not misleading. This programme is designed to give healthcare providers an easy way to report any misleading prescription drug advertising or promotion to FDA.

### Internet advertising

FDA applies the same regulations to the advertising and promotion of drug and medical devices on the internet as it does with print and television. In November 2009, FDA held a public hearing concerning the advertising and promotion of drug and medical devices on the internet, which focused on how to apply existing regulations to this emerging technology. Recently, FDA has increased its scrutiny of internet advertising and promotion, including manufacturer-sponsored websites, third-party websites funded by the manufacturer, social media sites and blogs. In April 2011, FDA issued a Notice for Comment soliciting comments regarding the examination of online direct-to-consumer prescription drug promotion.

## PACKAGING AND LABELLING

**16. Outline the regulation of packaging and labelling of medicinal products.**

### Legislation and regulatory authority

FDA requires that specific requirements are met for drug labelling to be approved. The general labelling provisions are applicable to all drug labels and a variety of information must be included (*21 CFR Part 201*).

### Information requirements

**General labelling provisions.** Information included on drug labels must be prominent and conspicuous. There must be no misleading statements on a drug label with regard to another drug, device, food or cosmetic (*21 CFR § 201.6*). A drug label must clearly bear the name and place of business of the manufacturer, packer or distributor (*21 CFR § 201.1*). Directions for use must be included and provide the following information (*21 CFR § 201.5*):

- Statements of all conditions, purposes or uses for which the drug is intended.
- Quantity of doses for different age groups.
- Frequency and duration of administration.
- Time of administration in relation to meals or other time factors.
- Method of administration and preparation for use.

**Labelling requirements for prescription drugs.** A prescription drug label must:

- Bear the established name of the drug as one of its principal features (*21 CFR § 201.50*).
- Include the net quantity of the content (*21 CFR § 201.51*).
- Contain a summary of the essential scientific information needed for the safe and effective use of the drug.

This information should be based on data derived from human experience whenever possible (*21 CFR § 201.56(a)(3)*).

The required format and content of the label for prescription drugs are set out in *21 CFR §§ 201.56* and *201.57*. The requirements require these drug labels to include three overarching sections:

- Highlights of Prescribing Information.
- Full Prescribing Information (Contents).
- Full Prescribing Information.

The information that must be included under each of the above sections is also mandated by the FDA (*21 CFR § 201.57*).

For some prescription medicines, the FDA approves special patient materials and medication guides to instruct patients about the safe use of product (*see 21 CFR Part 208*). These patient package materials can be given to patients by their healthcare provider or pharmacist and are considered part of FDA-regulated product labelling. The FDA may require distribution of medication guides to consumers for selected prescription drugs that pose a serious public health concern.

**Labelling requirements for over-the-counter (OTC) drugs.** As OTC drugs are used without the supervision of a physician, additional labelling requirements apply (*21 CFR Part 201*). The FDA has issued regulations to provide easy-to-understand labelling for OTC drugs (*21 CFR § 201.66*). These regulations require use of a standardised format that clearly shows a drug's ingredients and warnings, and makes it easier for consumers to understand information about a drug's benefits and risks, as well as its proper use.

**Specific labelling requirements.** Certain drugs have specific labelling requirements and all relevant regulations must be consulted concerning these drugs (*21 CFR §§ 201.300-325*).

### Other conditions

In most circumstances, the label must be in English (*21 CFR §201.15*).

## TRADITIONAL MEDICINES

**17. Outline the regulation of the manufacture and marketing of alternative or complementary medicinal products.**

Complementary and alternative medicine (CAM) encompasses a wide range of healthcare products, therapies and practices that are either used together with or in place of conventional medicine. The manufacture and marketing of CAM products, therapies or practices may be subject to FDA regulation as a biological product, cosmetic, drug, device, or food, depending primarily on

the context of its use. If the product claims to diagnose, cure, treat or prevent a disease it will be treated as either a drug or medical device and subject to FDA regulation.

Due to the many different types of CAM products and practices, it is impractical to address each one individually. However, the FDA has published the Draft Guidance for Industry on Complementary and Alternative Medicine Products and Their Regulation by the Food and Drug Administration (see *www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM145405.pdf*) about the regulation of CAM products and practices.

## PATENTS

**18. What are the legal conditions to obtain a patent and which legislation applies? Which products, substances and processes can be protected by patents and what types cannot be patent protected?**

### Conditions and legislation

Patent laws are generally codified in Title 35 of the US Code. The laws, regulations, policies, and procedures that apply to the patent process are available at *www.uspto.gov/patents/law/index.jsp*.

Any of the following can be patented, if it is new and useful:

- Process.
- Machine.
- Manufacture.
- Composition of matter.
- An improvement of any of the above.

The requirements to obtain a patent include:

- Novelty.
- Non-obviousness.
- Utility.

Novelty and non-obviousness are assessed based on the prior art at the time of filing a patent application and the level of skill of ordinary skilled artisans.

### Scope of protection

Patent protection can be applied to practically every man-made product and the processes for making products, provided those products and processes satisfy the legal requirements. Pharmaceutical and medicinal products generally fall within the scope of patentable subject matters. The following cannot be patented:

- Laws of nature.
- Physical phenomena.
- Abstract ideas.
- Mere ideas or suggestions.
- Literary, dramatic, musical or artistic works.
- Non-useful inventions.
- Inventions that are offensive to public morality.

**19. How is a patent obtained?**

### Application and guidance

Patent applications can be filed electronically with the US Patent and Trademark Office (USPTO) through the Electronic Filing System (EFS-Web) at *www.uspto.gov/patents/process/file/efs/index.jsp*. The USPTO website provides guidance and resources to assist with the patent application process. The USPTO fee schedule can be found at *www.uspto.gov/about/offices/cfo/finance/fees.jsp*.

### Process and timing

The timetable to issue a patent can vary a great deal, but the average patent application time is currently about 24 months. Once a patent application is filed it undergoes an examination process by the USPTO, which includes formal reviews and a substantive examination of the application. The status of a patent application and associated documents can be accessed through the USPTO's Patent Application Information Retrieval (PAIR) System. Rejected applications can be appealed to the Board of Appeals and Inferences, and even to the courts (for further details of the application process, see *35 USC §§ 111 and 112*).

### Deposit system

A patent application undergoes an examination process by the USPTO, which includes formal reviews and a substantive examination of the application (*see above, Process and timing*).

**20. How long does patent protection typically last? Can monopoly rights be extended by other means?**

### Duration and renewal

A patent's duration is usually 20 years from the date of original filing (*35 USC § 154(a)(2)*), subject to payment of maintenance fees. Once a patent expires, the inventor loses exclusive rights and the patent cannot be renewed.

### Extending protection

In certain circumstances, the duration of patent protection can be extended or adjusted. For example, in some cases where delay is due to the USPTO or FDA approval process, a patent's term can be extended or adjusted to offset the delay.

**21. How can a patent be revoked?**

Patent protection can cease due to various reasons, including the:

- Patent can be held unenforceable.
- Patent can be held invalid.
- Owner may not comply with required post-grant activities.

A patent can be held unenforceable if those who sought and participated in its prosecution are found to have engaged in inequitable conduct before the USPTO. Invalidity can stem from a post-grant issue by showing (to a court or even the USPTO by way of re-examination):

- Lack of novelty.
- Obviousness.
- Lack of enablement.
- Lack of written description (the patent lacks sufficient disclosure to show that the inventors had possession of their invention at the time of filing).

If an owner does not pay its required maintenance fees, or fails to respond to a re-examination request, the patent may be cancelled. Laches can also prevent patent rights enforcement, such as when a patent owner knows about infringing activity but waits a long period of time to enforce its rights.

**22. How is a patent infringed? How is a claim for patent infringement made and what remedies are available?**

### Conditions for infringement

A patent is infringed on the unauthorised making, using, importing into the US, offering for sale or selling of any patented invention during the term of the patent.

### Claim and remedies

If a patent is infringed, the patent holder can sue in federal court for damages and also seek an injunction to stop the infringing activity (for the patent infringement and remedy process, see *35 USC §§ 271-297*).

**23. Are there non-patent barriers to competition to protect medicinal products?**

Drug manufacturers receive five years of exclusivity for new chemical entities and three years of exclusivity for new indications. The Biologics Price Competition and Incentive Act provides for a 12-year exclusivity period for biological products (*42 USC § 262*).

## TRADE MARKS

**24. What are the legal conditions to obtain a trade mark and which legislation applies? What cannot be registered as a trade mark and can a medicinal brand be registered as a trade mark?**

### Conditions and legislation

A trade mark must be capable of distinguishing goods or services from those of another and it must be in use (and in interstate commerce for federal protection). A trade mark application can be submitted in three situations:

- The applicant has already begun using a mark in commerce.
- The applicant has not yet used the mark but intends (in good faith) to use it in commerce.
- There is a foreign applicant who has an application or registration in another country (under certain international agreements).

While trade mark law is regulated by federal and state law, federal law provides the primary source of trade mark law (*Trademark Rules of Practice, 37 CFR Part 2 and Lanham Act, 15 USC § 1051, et seq.*).

### Scope of protection

A trade mark typically protects brand names and logos used on goods and services. Trade mark law generally applies to pharmaceutical and medicinal products in the same way it does to other products. The USPTO may refuse a trade mark registration for a number of reasons, including that the mark is:

- Likely to cause confusion with an existing mark.
- Merely descriptive.
- Immoral or scandalous.
- A surname.
- A geographic term.

**25. How is a trade mark registered?**

### Application and guidance

Trade mark applications can be filed electronically with the USPTO through the Trademark Electronic Application System (TEAS) at *www.uspto.gov/teas/index.html*. The USPTO website provides guidance and resources to assist with the trade mark application process. The USPTO fee schedule can be found at *www.uspto.gov/about/offices/cfo/finance/fees.jsp*.

### Process and timing

If an application is submitted online through the TEAS, the applicant receives an initial summary and assigned serial number almost immediately. The total time for an application to be processed can vary from one year to several years. The application timing depends on the basis for filing and the legal issues that may arise. Current status information on trade mark applications is available through the Trademark Applications and Registrations Retrieval (TARR) database at *http://tarr.uspto.gov/*.

**26. How long does trade mark protection typically last?**

### Duration and renewal

The initial and extendable duration of a trade mark registration is ten years.

A trade mark holder must file a Declaration of Continued Use or Excusable Nonuse (§8 Declaration) during the 5th or 6th year after the registration date or within the subsequent six-month grace period (*15 USC §1508*). Failure to file a §8 Declaration results in cancellation of the trade mark registration.

During the 9th or 10th year after the registration date, and before the end of every additional ten-year period, the holder must file a combined §8 Declaration and §9 Application for Renewal (*15 USC §1509*). The combined declaration can also be filed within a six-month grace period after then. Failure to make these required filings will result in cancellation of the registration.

### Extending protection

A trade mark can last indefinitely provided the owner (*15 USC §§ 1058-59*):

- Continues to use the trade mark in connection with all of the goods or services identified in its application.
- Renews its registration.
- Pays the applicable fees.

**27. How can a trade mark be revoked?**

A trade mark's registration can be cancelled in any of the following circumstances (*15 USC § 1064*):

- The trade mark becomes a generic name for the goods or services.
- The trade mark has been abandoned.
- Registration was obtained fraudulently.
- The trade mark is used to misrepresent the source of the goods or services with which it is connected.
- A trade mark is cancelled by an opponent (subject to a quasi-judicial cancellation proceeding administered by the USPTO).

**28. How is a trade mark infringed? How is a claim for trade mark infringement made and what remedies are available?**

### Conditions

The use of a registered trade mark in connection with the sale of goods constitutes infringement if it is likely to cause consumer confusion as to the source of those goods or as to the sponsorship or approval of such goods. In deciding whether consumers are likely to be confused, the courts typically look to a number of factors, including the:

- Strength of the mark.
- Proximity of the goods.
- Similarity of the marks.
- Evidence of actual confusion.
- Similarity of marketing channels used.
- Degree of caution exercised by the typical buyer.
- Defendant's intent.

### Claim and remedies

Enforcement of a trade mark is achieved by bringing an action for trade mark infringement in civil court. The action can be based on a registered trade mark or on common law rights in a trade mark.

The remedies available for trade mark infringement include:

- Injunctive relief.
- Monetary relief.
- Treble damages.
- Attorneys' fees.
- Destruction of infringing items.

*Patent and trade mark licensing*

**29. Does a patent or trade mark licence agreement and payment of royalties under it to a foreign licensor have to be approved or accepted by a government or regulatory body?**

There is no requirement for patent or trade mark licence agreements to be approved by a government or regulatory body.

There is no governmental or regulatory approval required for royalties payable to a foreign licensor as a result of a patent or trade mark licence agreement.

*Patent and trade mark conventions*

**30. Is your jurisdiction party to international conventions on patent and trade mark protection?**

The US is party to international conventions on patent and trade mark protection, a few of which include:

- Patent Cooperation Treaty 1970.
- WIPO Paris Convention for the Protection of Industrial Property 1883.
- WIPO Protocol Relating to the Madrid Agreement Concerning the International Registration of Marks 1989.

## PRODUCT LIABILITY

**31. Outline the scope of medicinal product liability law.**

### Legal provisions

Actions against drug manufacturers for producing or marketing a product with either a defective design or inadequate warning primarily lie in tort (negligence or strict liability) and breach of warranty claims (quasi-contractual in nature).

### Substantive test

The tort law applicable in product liability cases involving drugs varies from jurisdiction to jurisdiction. The Restatement (Third) of Torts (Restatement (Third)) drafted by the American Law Institute provides the basis for tort law in product liability cases in many jurisdictions. The Restatement (Third) establishes separate tests for manufacturing defects, design defects and defects in warnings. Strict liability applies only to manufacturing defects.

Under the Restatement (Third), design defects claims require a foreseeable risk of harm posed by the product that could have been reduced or avoided by the adoption of a reasonable

alternative design. Design defect liability for prescription drugs and medical devices is limited (*see § 6, Restatement (Third) of Torts*). A design defect only exists if the risk of harm from the drug or device is so great when compared with the therapeutic benefits that doctors would not prescribe the drug for any class of patients.

Drug and medical device manufacturer liability is essentially limited to defects in manufacturing and failure to warn. The risks about which manufacturers must warn are foreseeable risks (*Restatement (Third) of Torts: Products Liability § 6(d)(1) (1998)*). A breach of warranty is a strict form of liability. However, it is limited by the contractual concepts of disclaimer and notice. Warranty theories are governed by the Uniform Commercial Code (UCC), which has been adopted in some form by each state.

The UCC recognises various warranties, including:

- Express.
- Implied warranty of merchantability.
- Implied warranty of fitness for a particular purpose.

### Liability

The pharmaceutical manufacturer is usually liable in civil actions, but all parties involved in the business of selling or distributing a product are subject to liability for harm caused by a defect in that product. A claimant can also sue its physician for malpractice in the same lawsuit.

## 32. How can a product liability claim be brought?

### Limitation periods

The limitation period varies from state to state and can range from one year to six years. The time generally begins to run from the date of injury. It can be extended where the claimant had no reason to know of his injury or that the drug may have caused it (the discovery rule).

Although state laws vary, there is a general four-year limitation period on actions for breach of contract arising out of the sale of goods (*UCC 2-725(1)*). This period begins to run when delivery is tendered (*UCC 2-725(2)*). The discovery of a latent defect some time after delivery would not affect the limitation period.

### Class actions

Class actions are permitted for product liability claims in both state and federal courts. They are commonly filed in the product liability context because of the ease with which each individual can assert a claim for personal injury and the potential that exists for large damage awards. Claimants in product liability cases can also file class actions seeking damages for medical monitoring, as well as seeking drug refunds or disgorgement of profits, alleging deceptive trade practices for drugs withdrawn from the market.

That being said, courts routinely deny class certification in personal injury cases involving prescription medications. See for example, *In re Prempro, 230 FRD 555, 571 (WD Ark. 2005)*, *In re Fosamax Products Liability Litigation, 248 FRD 389, 396 (SDNY 2008)*, and *In re Yasmin and Yaz (Drospirenone) Marketing, 275 F.R.D. 270 (SD Ill. 2011)*.

There are prerequisites to a class action in federal courts including (*Rule 23(a), Federal Rules of Civil Procedure*):

- The class is so numerous that joinder of all members is impracticable.
- There are questions of law or fact common to the class.
- The claims or defences of the representative parties are typical of the claims or defences of the class.
- The representative parties fairly and adequately protect the interests of the class.

Once these prerequisites are established, a class action is maintained as long as it meets one of the requirements set out in Rule 23(b), such as prosecuting separate actions by or against individual class members would create a risk of inconsistent adjudications that would establish incompatible standards of conduct for those opposing the class.

While state court rules can differ, the class action requirements in many states parallel those set out in the Federal Rules. While class actions are commonly used in product liability cases, courts still refuse to certify classes that do not meet the requirements for a class action.

The Class Action Fairness Act (CAFA) was enacted in February 2005. The CAFA contains two primary components, both of which are intended to reform class action practice as it currently stands. The first component expands federal jurisdiction over interstate class actions, allowing claimants to file certain class actions in federal court and defendants to remove certain class actions to federal court. The CAFA expands federal jurisdiction over any class action in which:

- There are at least 100 class members.
- The aggregate amount in issue exceeds US$5 million.
- Any member of a claimant class is one of the following:
  - a citizen of a US state different from any defendant;
  - a foreign state, or a citizen or subject of a foreign state, and any defendant is a citizen of a US state;
  - a citizen of a US state, and any defendant is a foreign state or a citizen of a foreign state.

In addition to class actions, Multidistrict Litigation (MDL) provides a method for consolidating multiple product liability claims filed in different federal court jurisdictions by allowing litigation pending in multiple federal districts to be transferred to one district court for consolidated pre-trial proceedings (*see 28 USC § 1407*).

### Foreign claimants

Foreign claimants can bring claims in the US depending on whether jurisdiction and venue are proper. Manufacturers can be sued in any state where its products are distributed, as the manufacturer is therefore subject to the product liability laws of that state. While many states have adopted "long-arm statutes" that govern personal jurisdiction over defendants in their courts, the exercise of jurisdiction cannot violate due process. The Supreme Court has developed the following two-part test to determine if the requirements of due process are met:

- The defendant must have sufficient contacts with the forum.
- The exercise of personal jurisdiction must be reasonable.

Courts can invoke the common-law doctrine of *forum non conveniens* to decline to adjudicate a case when the defendant or the judicial system would be inconvenienced, even though jurisdiction and venue are proper.

### 33. What defences are available to product liability claims?

As with product liability claims, defences are a matter of state law and, therefore, vary from jurisdiction to jurisdiction. Available defences include:

- **Statutes of limitation.** For personal injury claims, statutes of limitation can range from one year to six years. Many states employ the discovery rule (*see Question 32*) to determine when the statute of limitations begins to run.
- **Statutes of repose.** This requires a claimant to bring a claim within a certain period of time after the product is manufactured or sold. While statutes of repose are usually longer than statutes of limitation, they are not subject to the discovery rule and represent an absolute bar to a product liability claim.
- **The learned intermediary doctrine.** This doctrine provides that a prescription drug manufacturer discharges its duty by adequately warning the claimant's prescribing physician (the manufacturer has no duty to warn the consumer directly). The physician, therefore, acts as the learned intermediary between the patient and the manufacturer.
- **Intervening/superseding cause.** If a claimant's injury is caused by the intervening conduct of another and such conduct is also a superseding cause, a defendant may avoid liability in most jurisdictions. An intervening act is a superseding cause when a manufacturer could not reasonably be expected to protect against it, and includes such things as:
  - criminal acts;
  - use of a product in an unforeseeable manner;
  - alteration of the product;
  - negligent use; and
  - failure to properly maintain a product.
- **Contributory negligence/comparative fault.** According to the theory of contributory negligence, a claimant is barred from recovery if his own negligence caused or contributed to his injury. Most jurisdictions, however, have abandoned contributory negligence in favour of comparative fault. Under comparative fault, a claimant's recovery is reduced if his own negligence (or fault) contributed to his injury.
- **Assumption of the risk.** In some jurisdictions, a claimant can also be barred from recovery if he is aware of a product defect and the accompanying dangers, but proceeds to use the product anyway. Therefore, this defence is based on what the claimant actually knew and not what a reasonable person would know.
- **State of the art.** If a manufacturer can establish that a product was manufactured according to the scientific and technical achievement in the relevant field (the state of the art), such evidence can be used to show the manufacturer acted with due care.

## THE REGULATORY AUTHORITIES

### US Food and Drug Administration (FDA)

**W** *www.fda.gov*

**Main areas of responsibility.** The FDA:

- Is responsible for ensuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products, medical devices, the nation's food supply, cosmetics, dietary supplements, and products that give off radiation.
- Regulates tobacco products.
- Advances public health by helping to speed product innovations.
- Helps the public get accurate, science-based information to ensure their health.

### Center for Drug Evaluation and Research (CDER)

**W** *www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/default.htm*

**Main areas of responsibility.** The CDER has regulatory responsibility for the safety and efficacy of drugs, including prescription, generic, and OTC drugs.

### Center for Biologics Evaluation and Research (CBER)

**W** *www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/default.htm*

**Main areas of responsibility.** The CBER has regulatory responsibility for biological and related products, including blood, vaccines, allergenics, tissues, and cellular and gene therapies.

### Federal Trade Commission (FTC)

**W** *www.ftc.gov*

**Main areas of responsibility.** The FTC is responsible for promoting consumer protection and preventing anti-competitive business practices. This includes regulating the marketing and advertising of over-the-counter (OTC) drugs (*Updated FTC-FDA Liaison Agreement Advertising of Over-the-Counter Drugs, 4 Trade Reg. Rep. (CCH) 9,851 (1971)*).

- **Pre-emption.** When governmental statutes, rules and regulations control certain aspects of product safety, some jurisdictions have held that product liability claims imposing different or additional requirements on manufacturers are pre-empted. This attempts to prevent manufacturers from being subject to different and conflicting standards. The pre-emptive effect of a statute or regulation can be expressly stated or implied from the comprehensive nature of the enactment. The US Supreme Court addressed pre-emption in the medical device context in *Riegel v Medtronic, 552 U.S. 312 (2008)*.

In *Riegel*, the US Supreme Court held that tort claims against manufacturers were pre-empted if the device was approved by the FDA through the pre-market approval (PMA) process. The ruling in *Riegel* set the stage for *Wyeth v Levine* (*555 U.S. 555 (2009)*), which presented the issue of pre-emption in the context of prescription drugs.

In *Levine*, the Supreme Court held that federal law did not pre-empt the claimant's claims based on the facts of the case. The Supreme Court found that while federal law requires FDA to approve all prescription drug labels, the changes being effected (CBE) regulation permits certain pre-approval changes to strengthen a drug's warnings. Without clear evidence that the FDA would not have approved a specific label change, the Court concluded that it was not impossible for Wyeth to comply with both the federal and state requirements.

While the Supreme Court rejected the application of pre-emption to the facts of *Levine*, its analysis recognises that there could be situations where it is impossible for a drug manufacturer to comply with both state law warning duties and FDA approval requirements.

Despite not completely precluding pre-emption, the *Levine* decision has had a considerable influence on subsequent FDA pre-emption cases. Most lower courts have applied the reasoning in *Levine* and concluded that failure to warn claims against drug manufacturers are normally not pre-empted.

On 23 June 2011, the Supreme Court held that state law failure-to-warn claims against generic drug manufacturers were pre-empted by federal law (*PLIVA, Inc. v. Mensing (131 S.Ct. 2567 (2011)*). The Court found that the FDA required generic drug labelling to always be the same as the name-brand medication, therefore the CBE regulation only allowed generic manufacturers to change a label to match the brand-name label. It also ruled that the generic manufacturers could not have unilaterally issued "Dear Doctor" letters that provided additional warnings. Ultimately, the Court concluded that the generic drug manufacturers could not comply with their state-law duty by unilaterally changing their label or issuing "Dear Doctor" letters without violating federal law.

The Court distinguished *Levine* on the basis that brand-name drug manufacturers can take unilateral action to change its label under the CBE regulation, while generic drug manufacturers cannot.

**34. What remedies are available to the claimant? Are punitive damages allowed for product liability claims?**

Various remedies, including monetary damages and equitable remedies, are available to a claimant in a product liability claim.

Most jurisdictions allow for recovery of punitive damages for product liability claims. Accordingly, punitive damages are often claimed in civil litigation. To recover punitive damages, a claimant must typically prove, by clear and convincing evidence, that a defendant acted wilfully, wantonly or with malice. Many jurisdictions also require that actual damages are awarded, in order to award punitive damages. The frequency and size of punitive damage awards have grown in recent years. Predicting whether punitive damages will be awarded in a particular case, along with the size of any punitive damage award, has proven difficult in light of inconsistent outcomes.

The US Supreme Court struck down a punitive damages award that was 145 times the amount of the compensatory damages award, on the ground that such an award was an arbitrary deprivation of property in violation of the defendant's constitutional right to due process (*State Farm Mutual Automobile Insurance Co. v Campbell, 538 U.S. 408 (2003)*). The Court noted that any award ten times the amount of compensatory damages or larger is likely to be unconstitutional on due process grounds.

Since the Supreme Court's decision in *State Farm*, there have been hundreds of cases that refer to it, yet result in varied interpretations of its ratio guideline. Other courts circumvent the single-digit ratio guideline or interpret the ratio guideline as a suggestion rather than a requirement. See for example:

- *Mathias v Accor Economy Lodging, Inc., 347 F.3d 672 (7th Cir. Oct. 21, 2003)* (interpreting State Farm's ratio guideline as a suggestion rather than a rule).
- *Santamaria v Dallas Independent School District, 2007 WL 1073850 (N.D. Tex. April 10, 2007)* (upholding a 100:1 ratio in a case involving nominal damages).

These varied interpretations of *State Farm* have resulted in inconsistent punitive damage awards. To limit the awarding of inconsistent punitive damages, many states have enacted some form of punitive damage reform.

## REFORM

**35. Are there proposals for reform and when are they likely to come into force?**

In March 2010, after significant debate, two pieces of healthcare reform legislation were enacted comprising the Patient Protection and Affordable Care Act (*Public Law 111-148*), which was amended by the Health Care and Education Reconciliation Act of 2010 (*Public Law 111-152*). This legislation provides for a number of reforms between 2010 and 2019, with a number of the key provisions being implemented by 2014. Some of the many provisions of the healthcare reform legislation include:

- Mandating that everyone buys health insurance, with exceptions for the poor and in limited other circumstances. If an individual does not buy health insurance, a tax penalty is imposed on that individual.
- Expanding Medicaid coverage and eligibility.
- Establishing health insurance exchanges.
- Increasing and expanding the Medicaid drug rebate.
- Implementing an annual fee for drug manufacturers.
- Providing various prescription drug rebates and discounts under Medicare and Medicaid.
- Providing incentives for employers to provide healthcare benefits. Specifically, employers of over 50 employees must provide health insurance for its employees or pay a fine.
- Prohibiting insurers from denying insurance coverage due to pre-existing conditions.

Although the healthcare reform legislation has been enacted and certain provisions have been put in place, the legislation continues to cause great debate, including numerous lawsuits regarding the legality of certain provisions.

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