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Medicinal product regulation and product liability in the United States: overview

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REGULATORY OVERVIEW

1. What are the main legislation and regulatory authorities for pharmaceuticals in your jurisdiction?

Legislation

The US Food and Drug Administration (FDA) enforces many statutes and rules that govern the regulation of pharmaceutical products and medical devices. 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 (*www.fda.gov*) is responsible for protecting the public health by ensuring 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, 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) (*www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/default.htm*) oversees the research, development, manufacturing and marketing of drugs.

Also within the FDA, the Center for Biologics Evaluation and Research (CBER) (*www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/default.htm*) regulates all biological and related products for human use, including blood, vaccines, allergenics, tissues, and cellular and gene therapies.

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

2. Briefly outline how biologicals and combination products are regulated in your jurisdiction.

Biological and combination products are regulated by the FDA (*see Question 1*). Within the FDA, while CBER usually regulates biologics, therapeutic biological products are considered drugs and therefore regulated by CDER.

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

3. Briefly outline how medical devices and diagnostics are regulated in your jurisdiction. Is there any specific regulation of health IT issues and mobile medical applications?

The safety, efficacy, and security of medical devices and radiation-emitting products are regulated by the FDA (*see Question 1*). Within the FDA, the Center for Drug Evaluation and Research (CDER) (*www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/default.htm*) oversees the research, development, manufacturing and marketing of drugs. CDER evaluates all new drugs before they are sold and serves as consumer watchdog for the drugs on the market, to be sure they continue to meet the highest standards.

There are three classes of medical devices based on the control necessary to assure the safety and effectiveness of the device:

- Class 1 devices are subject to the least regulation, and only "general controls". These devices are not intended to support or sustain life or be substantially important in preventing impairment to human health and cannot present an unreasonable risk of illness or injury. Examples include elastic bandages and hand-held surgical instruments (*see 21 C.F.R. § 860.3*).

- Class II devices are those devices where general controls alone cannot assure the safety and effectiveness. Special controls may include special labelling requirements, mandatory performance standards, and post-market surveillance. Examples include powered wheelchairs, infusion pumps, and surgical drapes (*see 21 C.F.R. § 860.3*).
- Class III devices are those devices for which insufficient information exists to assure safety and effectiveness solely through general or special controls. They require pre-market approval and include those devices that support or sustain human life or present a potential, unreasonable risk of illness or injury. Examples include implantable pacemakers, pulse generators, and automated external defibrillators (*see 21 C.F.R. § 860.3*).

There are two general regulatory pathways for marketing medical devices:

- The most common is the 510(k) process. In this process, the device manufacturer must demonstrate to the FDA that its device is "substantially equivalent" to a previously marketed predicate device in order to receive FDA clearance for marketing (*see 21 CFR §807.92(a)(3)*). The 510(k) pre-market notification submission identifies characteristics of the new or modified medical device as compared to a medical device with a similar intended use, which is currently legally marketed in the US, for example the so-called "predicate" device (*see 21 CFR §807.92(a)(3)*). In the 510(k) process, FDA only determines if the device is substantially equivalent to another device whose safety and effectiveness may never have been assessed.
- The second pathway is through the Premarket Approval Process (PMA), which is similar to the new drug approval (NDA) process (*see 21 C.F.R. §807.81*). In a PMA review, FDA determines if the device is reasonably safe and effective for its intended use.

Health IT Issues

The Office of the National Coordinator for Health Information Technology (ONC) is authorised to regulate health IT by the Health Information Technology for Economic and Clinical Health (HITECH) Act (*Pub. L. No. 111-5, 123 Stat. 226 (17 February, 2009*).

The HITECH Act authorises the US Department of Health and Human Services to establish programmes to improve healthcare quality, safety, and efficiency through the promotion of health IT, including electronic health records and private and secure electronic health information exchange. ONC authors regulations that set the standards and certification criteria electronic health records must meet to assure healthcare professionals and hospitals that the systems they adopt are capable of performing certain functions (*see www.healthit.gov/policy-researchers-implementers/health-it-legislation-and-regulations*).

FDA's jurisdiction extends to mobile applications (apps) that meet the definition of device in section 201(h) of the Federal, Food, Drug, and Cosmetic Act. FDA issued a final guidance in September 2013, stating that FDA intends to regulate apps that are an extension of a medical device, transform the mobile platform into a regulated medical device, and perform patient-specific analysis, providing diagnosis/treatment recommendations. FDA will regulate those apps whose functionality could pose a risk to a patient's safety if the mobile app did not function as intended. The apps that undergo FDA review will be evaluated using the same regulatory standards and risk-based approach that the agency uses for other medical devices (*see Mobile Medical Applications - Guidance for Industry and Food and Drug Administration Staff, www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM263366.pdf*).

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

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

The Patient Protection and Affordable Care Act (Affordable Care Act, or ACA) (*Pub. L. No. 11-148, 124 Stat. 119, enacted in March 2010*) provides for significant reform to the US healthcare system, including reform to healthcare insurance and funding. The law includes various provisions to be phased in over the next decade, with a number of the key reforms implemented by 2014. Starting in 2014, most citizens are required to either buy health insurance or pay a tax penalty, with certain exceptions for the poor. Additionally, the law provides incentives for employers to provide healthcare benefits for their employees.

5. 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) 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.

6. When is the cost of a medicinal product funded by the state or reimbursed? 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 covered by Medicare, regardless of income, health status, or current prescription expenses. To be eligible for Medicare, an individual must be either 65 years or older, qualify due to a disability or illness, or have kidney failure requiring dialysis or a transplant. 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 Affordable Care Act has and will continue to impact the benefits provided by Medicaid and Medicare, including prescription drug benefits. The law expands Medicare and Medicaid coverage and eligibility, and provides for certain rebates and discounts on prescription drugs under Medicaid and Medicare.

CLINICAL TRIALS

7. Outline the regulation of clinical trials.

Legislation and regulatory authorities

Clinical trials are authorised by the FDCA and must comply with good clinical practices (GCPs) (regulations are set out at *www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm*).

Authorisations

New drugs are tested for toxicity and efficacy on laboratory animals. If these tests indicate that a drug may be effective and that it is reasonable to test it on humans, the sponsor must then obtain FDA's approval to conduct human clinical trials (*21 CFR §§ 312.2(a), 312.20*). An Investigational New Drug Application (IND) must be submitted to the FDA (*21 CFR §312.23*), using FDA Form 1571 (available at *www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/default.htm*). The FDA must then 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 (*21 CFR § 312.53(c)*), including a completed, signed statement from the investigator (FDA Form 1572) (available at *www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/default.htm*).

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, the next steps before approval of a drug for marketing (*see Question 9*) include clinical testing on human subjects in the following phases (*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 approves the New Drug Application (NDA), the drug can be marketed. After then, Phase IV and other post-marketing studies can be or may be required to be conducted to collect additional information about the risks, benefits and optimal use of a particular drug (*21 CFR § 312.85*).

Consent

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

Trial pre-conditions

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

- Types of patients that can participate.
- Schedule of tests and procedures.
- Drugs to be tested.
- Dosages to be administered.
- 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 informed of known risks and that they are promptly informed of any new risks or adverse effects (the Investigator's Brochure).

MANUFACTURING

8. 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)*).

The Food and Drug Administration Safety and Innovation Act (FDASIA) was enacted in July 2012 (*Public Law 112-144*). Among other things, this legislation changes the registration process under the FDCA. Specifically, FDASIA requires the FDA to establish a unique facility identifier (UFI) system. After FDA establishes such a system, companies will be required to include a UFI for each establishment in their registrations. Further, companies will be required to include information about manufacturers of drug excipients of products listed, including the establishments used by the manufacturers to produce the excipients and the UFI of each (*section 701, FDASIA (21 USC § 360)*).

Foreign applicants

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

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.*

Key stages and timing

A manufacturer must register with the FDA as a drug establishment within five days of beginning the manufacturing, preparing, 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. A distributor of a drug manufactured or processed by a registered establishment may also submit a drug listing.

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.

Fee

Annual fees are 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), 379j-42, and 379j-52*). Annual fees are available at *www.fda.gov/ForIndustry/UserFees/default.htm*.

Monitoring compliance and imposing penalties

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 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)*).
- Require production of documents in physical or electronic form in advance of or in lieu of an inspection (*21 USC § 374(a)(4)*).

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

FDASIA amended the FDCA to replace the previous biennial schedule for inspections with a risk-based schedule for both domestic and foreign facilities based on an establishment's "known safety risks". The FDA considers factors including an establishment's compliance history, the history of recalls related to the establishment, the inherent risks of products produced at the establishment, the frequency of prior inspections of the establishment, and whether the establishment has been inspected by certain foreign governments or agencies. Establishments' manufacturing devices are subject to inspection at least once every two-year period (*21 USC § 360(h)*).

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*).

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.

MARKETING

Authorisation and abridged procedure

9. What is the authorisation process for marketing medicinal products?

Application

Manufacturers must obtain approval of a New Drug Application (NDA) from FDA before marketing a prescription drug. Biologics manufacturers must submit a Biologics License Application (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*.

A 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 about 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 for which approved NDAs and BLAs are required.

Authorisation conditions

FDA approval of a NDA depends on sufficient evidence that the drug meets the statutory standards for:

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

Likewise, 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 an assessment of the storage and testing of cell substrates used in manufacturing the biologics.

Key stages and timing

The two main stages for product approval are:

- IND review and clinical investigations.

- 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 to as many as 20 years.

Fee

Fees are set by the Prescription Drug User Fee Act (PDUFA), Medical Device User Fee Act, Generic Drug User Fee Amendments of 2012 (GDUFA), and the Biosimilar User Fee Act of 2012 (BsUFA). For fee information, see *www.fda.gov/ForIndustry/UserFees/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 FDA, or FDA withdraws its approval of a NDA or biologic licence.

Monitoring compliance and imposing penalties

FDA monitors continued compliance of a NDA approved prescription drug or a BLA approved biologic by requiring that adverse event reports, and other post-marketing reports, are filed with FDA by the respective manufacturer (*21 CFR §§ 314.80–81 and 600.80*) in order to continually assess the safety and effectiveness of the approved product.

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

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

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

10. What commitments and pharmacovigilance obligations apply after a company has obtained marketing authorisation? Are there further conditions concerning how the drug is distributed and accessible to patients?

After a NDA is approved, companies are required to report 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. Manufacturers must report adverse events quarterly for the first three years and then once annually. In addition, companies must submit annual reports that include a summary of "significant new information from the previous year that might affect the safety, effectiveness, or labelling of the drug product" (*21 CFR § 314.81(b)(2)*). Licensed manufacturers of a biologic must comply with similar adverse event reporting requirements (*21 CFR § 600.80*).

11. 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?

Various procedures can expedite review of an application, including:

- **Treatment IND.** 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.* 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 USC § 356 and 21 CFR § 312.80, et seq.).** Fast Track designation is intended to expedite FDA review of drugs designed to treat serious or life-threatening diseases or 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 a NDA in sections, and possible evaluation of studies using surrogate endpoints for Accelerated Approval (*see below, Accelerated Approval, Subpart H*). 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, and the FDA is required to determine within 60 days whether the drug meets the criteria for designation as a fast track product (*21 USC § 356(a)*).
- **Priority Review.** 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 (21 USC § 356(b), 21 CFR § 314.500, et seq.).** 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.)

- **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 (ANDA) (*21 CFR § 314.92, et seq.*). This is the procedure followed for generic drugs.
- **Biological Products.** In March 2010, the Biologics Price Competition and Innovation Act (BPCIA) was enacted as part of the Patient Protection and Affordable Care Act. The BPCIA 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. In 2012, the FDA 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.*
- **Qualified Infectious Disease Products (QIDPs).** In July 2012, the Generating Antibiotic Incentives Now Act (GAIN Act) was enacted as Title VIII of FDASIA. The GAIN Act is designed to provide incentives for the development of certain new antibacterial and antifungal products that treat certain serious infectious diseases, including drug resistant pathogens. Such drugs that are designated as Qualified Infectious Disease Products can qualify for priority review and fast track status (*sections 801 and 802, FDASIA, 21 U.S.C. §§ 355f and 356(a)(1)*).

12. Are foreign marketing authorisations recognised in your jurisdiction?

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

Parallel imports

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

The FDCA (*21 USC § 331*) prohibits interstate shipment of any unapproved new drugs. This 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.

FDASIA amended the FDCA to require commercial importers of drugs to register with the FDA and submit a unique identifier for its principal place of business. The FDA will issue regulations designed to implement the unique facility identifier requirement by 2015 (*section 714, FDASIA, 21 U.S.C. § 381(s)*). Drugs imported by unregistered importers will be considered misbranded (*section 714, FDASIA, 21 U.S.C. § 352*).

For information on pharmaceutical patents, trade marks, competition law, patent licensing, generic entry, abuse of dominance and parallel imports, visit *Pharmaceutical IP and Competition Law in the United States: overview.*

RESTRICTIONS ON DEALINGS WITH HEALTHCARE PROFESSIONALS

14. 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. 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 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.

SALES AND MARKETING

15. What are the restrictions on selling medicinal products? Are there specific regulations for the sale of medicinal products on the internet, by e-mail and by mail order?

Prescription drugs and over-the-counter drugs (OTC) are subject to different requirements. Prescription drugs must be prescribed by a physician to a particular patient, and must be purchased from a pharmacy. OTC drugs do not require a doctor's prescription and can be purchased in other stores.

Pharmaceutical products can be marketed and sold over the internet or by mail order. 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 prescribing 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

16. 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 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 Food and Drug Administration Modernization Act of 1997 (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 drugs and medical devices on the internet, focusing 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 January 2014, FDA released draft guidance on the use of interactive promotional media for prescription drugs and biologics, setting out its view regarding when a company must submit interactive internet advertising to FDA and what must be submitted (*www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM381352.pdf*). Additional guidance on internet advertising is expected from FDA in 2014.

DATA PROTECTION

17. Do data protection laws impact on pharmaceutical regulation in your jurisdiction?

The Health Insurance Portability and Accountability Act 1996 (HIPAA) regulates the use and disclosure of Protected Health Information (PHI) held by certain "covered entities". PHI is information held by a covered entity concerning health status, provision of healthcare, or payment for healthcare that can be linked to an individual patient. This includes a patient's medical records and payment history. With limited exceptions, covered entities can only disclose PHI after receiving written authorisation from the patient. Covered entities must notify individuals of their uses of PHI, and must keep track of disclosures of PHI and document privacy policies and procedures.

HIPAA permits disclosure of PHI for two purposes that are related to pharmacovigilance:

- A covered entity can disclose PHI to a person subject to FDA jurisdiction for a public health purpose related to the quality, safety, or effectiveness of an FDA regulated product, such as collecting or reporting adverse event reports (*see www.hhs.gov/ocr/privacy/hipaa/understanding/special/publichealth*).
- HIPAA permits the disclosure of PHI for research (*see www.hhs.gov/ocr/privacy/hipaa/understanding/coveredentities/research.html*).

PACKAGING AND LABELLING

18. 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 contain:

- The established name of the drug as one of its principal features (*21 CFR § 201.50*).
- The net quantity of the content (*21 CFR § 201.51*).
- A summary of the essential scientific information needed for the safe and effective use of the drug (*21 CFR § 201.56(a)(1)*).

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 for drug labels 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, FDA approves special patient materials and medication guides to instruct patients about the safe use of a 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 Subpart C*). 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*).

PRODUCT LIABILITY

19. Outline the key regulators and their powers in relation to medicinal product liability.

The FDA is the key regulator of medicinal product liability. FDA regulates the approval of drugs and medical devices as well as their labelling and marketing. Companies may also be subject to regulation by state agencies and by lawsuits brought under state laws. State statutes, regulations, and lawsuits are pre-empted where inconsistent with federal law. See also *Questions 1, 2, 16, 20, 22, and 23*.

20. Are there any mandatory requirements relating to medicinal product safety?

The FDA monitors compliance by requiring that adverse event reports are filed by the respective manufacturer after FDA approval (*see 21 CFR §§ 314.80- 81 and 600.80*). Manufacturers must report adverse events quarterly for the first three years and then once annually. Adverse events observed during clinical trials must also be reported and classified as minor or serious, unexpected or expected, and study-related, possibly study-related or not study-related (*see 21 C.F.R. § 312.64*). The FDA also requires companies to develop procedures for the surveillance, receipt, evaluation, and reporting of post-marketing adverse drug experiences to FDA before new drug approval.

Similarly, the Medical Device Reporting (MDR) regulation requires reporting of device-related adverse events and problems to the FDA (*see 21 C.F.R. § 803*). Manufacturers are required to report when they learn that one of their devices may have caused or contributed to a death or serious injury. Additionally, manufacturers must report to the FDA when they become aware of malfunctions in their device that would likely cause or contribute to a death or serious injury if the malfunction were to occur. FDA imposes numerous other requirements related to product safety. See also *Questions 8, 9, 10, and 16*.

21. Outline the key areas of law applicable to medicinal product liability, including key legislation and recent case 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 throughout the US. There is no federal tort law, while the law of each state often differs. Restatement (Third) of Torts (Restatement (Third)), drafted by the American Law Institute (ALI), provides the basis for product liability law in many jurisdictions. The Restatement (Third) establishes separate tests for manufacturing defects, design defects and warning defects. Strict liability applies only to manufacturing defects.

Under the Restatement (Third), design defect 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 exists only 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)*). Unlike fiduciary consumer products, only licensed physicians can prescribe drugs and medical devices. Accordingly, a manufacturer's duty is to warn the physician, who is referred to in case law as "the learned intermediary". A breach of warranty is a form of liability, which 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 warranty.
- Implied warranty of merchantability.
- Implied warranty of fitness for a particular purpose.

22. Who is potentially liable for defective medicinal products?

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

23. What defences are available to product liability claims?

Defences

As with product liability claims, defences are a matter of state law and, therefore, vary from jurisdiction to jurisdiction. Available defences may 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 23*) 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 the product in an unforeseeable manner, alteration of the product, negligent use of the product, and failure to properly maintain the 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 in providing its warnings to the learned intermediary.

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 complying with 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 recognised 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.

In 2011, the Supreme Court held that state law failure-to-warn claims against generic drug manufacturers are 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 their labels under the CBE regulation, while generic drug manufacturers cannot. In 2013, in *Mutual Pharmaceutical Co. v. Bartlett, 133 S.Ct. 2466 (2013)*, the Supreme Court extended the reasoning of *Mensing* to design-defect claims, noting that the design of generic manufacturers' products is subject to the same "sameness" requirement as generic warnings.

24. 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.

Still, courts routinely deny class certification in cases involving prescription medications, where individual issues predominate. See, for example, *In re Prempro, 230 F.R.D. 555, 571 (W.D. Ark. 2005)*, *In re Fosamax Prods. Liab. Litig., 248 F.R.D. 389, 396 (S.D.N.Y. 2008)*, *In re Yasmin and Yaz (Drospirenone) Mktg., 275 F.R.D. 270 (S.D. Ill. 2011)*, *In re Vioxx Prods. Liab. Litig., 2012 WL 2061883, at *5 (E.D. La. June 6, 2012)* , and *In re Celexa and Lexapro Marketing and Sales Practices Litig., 291 F.R.D. 13, at 15–21 (D. Mass. 2013)*.

The following prerequisites must be established before a class action is certified in federal courts (*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 may be 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 may differ, 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) governs US class actions. 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. 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, multi-district litigation (MDL) provides a method for consolidating multiple product liability claims filed in different federal court jurisdictions by allowing these cases to be transferred to one district court for consolidated pre-trial proceedings (*see 28 USC § 1407*). Many states' laws also provide for consolidation of related cases pending in their courts. Federal and state cases cannot be formally consolidated, but state and federal court judges hearing related cases often co-ordinate.

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 US 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.

25. 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 be awarded as a prerequisite to an award of 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 Mut. Auto. Ins. 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*, more than 1,000 cases have referred to it, resulting in varied interpretations of its ratio guideline. In some cases, 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 Indep. School Dist., 2007 WL 1073850 (N.D. Tex. April 10, 2007)* (upholding a 100:1 ratio in a case involving nominal damages).
- *Ariz. Dep' t of Law, Civil Rights Div. v. ASARCO, LLC*, 798 F. Supp. 2d 1023, 1047–50 *(D. Ariz. Jul. 13, 2011)* (upholding punitive damages of US$868,750 where compensatory damages were a nominal US$1, and stating that ratios in excess of single digits are not necessarily unconstitutional where only nominal compensatory damages are awarded).

Varied interpretations of *State Farm* have resulted in inconsistent punitive damage awards. To limit inconsistent punitive damages, many states have enacted some measure of punitive damage reform.

REFORM

26. 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, and several key provisions to be 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 those 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 with more than 50 employees must provide health insurance for their employees or pay a fine.
- Prohibiting insurers from denying insurance coverage due to pre-existing conditions.

On 28 June 2012, the US Supreme Court upheld the constitutionality of most of the Patient Protection and Affordable Care Act in *National Federation of Independent Businesses v. Sebelius, 125 S. Ct. 2566 (2012)*.

For information on pharmaceutical patents, trade marks, competition law, patent licensing, generic entry, abuse of dominance and parallel imports, visit *Pharmaceutical IP and Competition Law in the United States: overview*.

ONLINE RESOURCES

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