United States

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1. Please give a broad overview of the structure and funding of the national healthcare system.

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

2. What is the definition of a pharmaceutical product?

Pharmaceutical products regulated by the US Food and Drug Administration (FDA) (*see Question 3*) are defined as follows:

- Drugs. Products intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in humans, or products (other than food) intended to affect the structure or function of the body *(21 United States Code (U.S.C.) § 321(g)(1))*.
- Biological products. Any virus, therapeutic serum, toxin, antitoxin or analogous product applicable to the prevention, treatment or cure of diseases or injuries of man *(21 Code, Federal Regulations (C.F.R.) § 600.3(h))*.

3. For each of the key regulators (pharmaceutical, medicinal, medical device, GMO) please give:

- Their name.
- Contact details (including website address).
- A summary of their areas of responsibility.

- **Name.** The US Food and Drug Administration (FDA).
- **Contact details.** HFE-88, 5600 Fishers Lane,
  Rockville, Maryland 20857
  Tel: +1 888 463 6332
  Fax: +1 301 443 3757
  Website: *http://www.fda.gov*
- **Areas of responsibility.** The FDA administers the statutes and regulations that govern the regulation of pharmaceutical products (*Federal Food, Drug and Cosmetic Act (FDCA), 21 U.S.C. § 301,et seq).*

  International enquiries related to setting up a pharmaceutical establishment should be sent to: International Affairs Staff (HFY-50),
  Food and Drug Administration,
  5600 Fishers Lane,
  Rockville,
  Maryland 20857
  Tel: +1 301 443 4480
  Fax: +1 301 443 7539.
- **Name.** Center for Drug Evaluation and Research (CDER).
- **Contact details.** HFD-210, Room 12B-31,
  5600 Fishers Lane,
  Rockville,
  Maryland 20857
  Tel: +1 301 827 4573
  Fax: +1 301 827 3056
  Email: druginfor@cder.fda.gov
  Website: *http://www.fda.gov/cder/*
- **Areas of responsibility.** CDER has regulatory responsibility for all drugs for human use except biological products.
- **Name.** Federal Trade Commission (FTC).
- **Contact details.** 600 Pennsylvania Ave NW,
  Washington, DC 20580
  Tel: +1 202 326 2222
  Email: usptoinfo@uspto.gov
  Website: *http://www.ftc.gov*
- **Areas of responsibility.** The FTC and FDA are responsible for regulating the marketing of pharmaceutical products. The FDA exclusively regulates labelling and advertising for prescription drugs. The FDA regulates the labelling of over the counter (OTC) drugs; the FTC regulates their advertising.
- **Name.** US Patent and Trade Mark Office (PTO).
- **Contact details.** Crystal Plaza 3, Room 2C02,
  Washington, DC 20231
  Tel: +1 800 786 9199
  Email: upstoinfo@upsto.gov
  Website: *http://www.uspto.gov*

- **Areas of responsibility.** The PTO governs patents and trade marks for pharmaceutical products.

4. Is authorisation required for marketing approval of pharmaceutical products? If so, please give a broad overview of the authorisation process, in particular:

- To whom should the application be made?
- What are the key stages and timing of the process?
- Is there an abridged procedure?
- What fee is payable?
- Is authorisation given for a fixed period? If so, for how long and what is the renewal procedure?
- In what circumstances can authorisation be revoked?

- **Application.** An Investigational New Drug Application (IND) must be submitted to the FDA to test a drug on human subjects. Once adequate safety and efficacy information is developed for a drug through pre-clinical laboratory and animal studies and well-controlled clinical studies, the sponsor (manufacturer) must obtain FDA approval of a New Drug Application (NDA) before the drug can be marketed.

  After approval of the NDA, there are ongoing requirements for the reporting of post-marketing adverse drugs experiences (*21 C.F.R. § 314.80*). Annual reports must be filed (*21 C.F.R. § 314.81(b)(2)*).

- **Key stages and timing.**

  IND review. New drugs are tested for toxicity and efficacy on laboratory animals (see *http://www.fda.gov/cder/handbook/develop.htm* for flowchart on the new drug development process). If those tests indicate that a drug may be efficacious and it is reasonable to test it on humans, the sponsor must obtain FDA approval before doing so (*21 C.F.R. §§ 312.2(a), 312.20*).

  An IND application (forms FDA 1571 and 1572, obtainable from *http://www.fda.gov*) must be made to the FDA (*21 C.F.R. § 312.23*) (*see http://www.fda.gov/cder/handbook/ind.htm* for flowchart on IND Review Process).

  The FDA must review a sponsor's IND application within 30 days of submission and take appropriate action (*21 C.F.R. § 312.40(b)*). If the FDA responds negatively, the IND does not take effect. If the FDA responds favourably or fails to respond, the sponsor may proceed with clinical testing on human subjects.

  NDA review. Once adequate safety and efficacy information is developed for a drug, the sponsor must obtain FDA approval of a NDA (Form FDA 356h, available at *http://www.fda.gov*) before it can market the drug (*U.S. 21 U.S.C. § 355(a)*). Drug companies can submit their NDAs electronically.

  The FDA has 180 days to respond after an NDA is filed (*21 C.F.R. § 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 sponsor.

  An NDA must contain a broad range of information (*21 C.F.R. Part 314*). The scope of this information exceeds that required in an IND.

  The application must include a form with the information mentioned in 21 C.F.R. § 314.50.

  The time from product conception to approval can range from a few years to 20.

- **Abridged procedures.**

  Treatment IND. This programme allows physicians to prescribe experimental drugs before approval under certain circumstances (*21 C.F.R.§ 312.34(a)*). Under this programme, drugs may be available for use after Phase II testing is complete.

  Fast track programmes. (*21 C.F.R. § 312.80, et. seq.*) "Fast Track" refers to a programme in which a sponsor interacts with the FDA to expedite the FDA review process for drugs designed to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs. The benefits of Fast Track include meetings with the FDA for its input into development plans, the option of submitting an NDA in sections rather than all components simultaneously, and of requesting evaluation of studies using surrogate endpoints for Accelerated Approval (*see below "Accelerated Approval (Subpart H)"*). The Fast Track designation is for a product and claim that addresses an unmet medical need, but is independent of Priority Review and Accelerated Approval. An applicant may use any or all of the components of Fast Track without the formal designation. Fast Track designation does not necessarily lead to a Priority Review or Accelerated Approval. Sponsors may request Fast Track designation at the time of the original submission of their IND, or any time afterwards, before approval.

  Priority review. The FDA assesses each application as either Standard or Priority. The FDA seeks to perform an accelerated, six-month review on Priority drugs. 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 Priority review. All non-priority drugs are considered Standard applications.

  Accelerated Approval (Subpart H). This is intended to make promising products for life threatening diseases available on the market on the basis of preliminary evidence before formal demonstration of patient benefit. The studies of products are made to measure and the FDA evaluation is performed on the basis of a surrogate marker (a substitute

measurement for the clinical measurement of interest, usually prolongation of survival) that is considered likely to predict patient benefit. The approval that is granted is provisional, with a written commitment to complete clinical studies that formally demonstrate patient benefit.

Parallel track approval. Under this FDA policy, AIDS patients whose condition prevents them from participating in clinical trials can receive investigational drugs that have been shown to be potentially useful.

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. Such supplements can be reviewed on a priority basis of six months or less.

Listed drugs versus generic drugs. Manufacturers of drugs that are identical, similar or related to listed drugs (FDA approved drugs) can circumvent the extensive NDA approval process and file an Abbreviated New Drug Application (ANDA) (*21 C.F.R. § 314.92,et seq*). This is the procedure followed for generic drugs.

- **Fee.** For fee information see *http://www.fda.gov/oc/pdufa/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 approved NDA.
- **Revocation.** The FDA has broad powers to withdraw marketing licences (*21 U.S.C. § 355(e)*). Reasons for drug recalls include:
  - failure or inability to validate drug analysis methods;
  - subpotency;
  - stability data failing to support expiry date;
  - failure or inability to validate manufacturing processes;
  - deviations from good manufacturing practices;
  - failure of drug to dissolve properly;
  - labelling mix-ups;
  - marketing without a new or generic approval;
  - lack of assurance of sterility;
  - cross-contamination with other products.

5. Is a distinction made between over the counter drugs and drugs that can only be obtained on prescription? If so, how is the distinction made and what impact does this have on the process for authorisation?

The FDA regulates most OTC drugs by a monograph system (*21 C.F.R. § 330.1, et seq*) designed to establish which active ingredients may be marketed in OTC drugs without additional product approval, and for what recommended uses. The system covers acceptable ingredients, doses, formulations and labelling for each class of OTC drugs.

OTC products that conform to the monograph can be marketed without further review by the FDA. Products that do not conform to the monograph, or contain an ingredient that would be OTC for the first time, must go through the NDA process. Typically such products are approved as prescription drugs and later switched to OTC status.

6. Is there a mutual recognition procedure? (For EU countries only.)

N/A

7. Is there a separate procedure for determining whether the cost of a pharmaceutical product will be funded/reimbursed by the state? If so, please give details (including how pricing is determined in these circumstances).

The federal government does not directly intervene in the pricing of prescription drugs. There are complex laws and regulations regarding pricing and reimbursements for pharmaceutical products under the Medicare and Medicaid programmes, which each have their own procedures.

Medicare coverage for pharmaceutical products is limited primarily to in-patient use. There is very limited coverage for outpatient drugs. Medicare reimburses providers who administer the drugs. States set their own reimbursement rates, subject to upper limits set by the federal government, as a basis for reimbursing for drug prescriptions. Currently, several pharmaceutical companies, as well as several states, have established prescription drug card programmes to help senior citizens and people with lower incomes with the cost of prescription drugs. These programmes are not funded by the Medicare programme. For further information see The Department of Health and Human Services' website at *http://cms.hhs.gov/*.

Title XIX of the Social Security Act requires that in order to receive federal matching funds, certain basis services must be offered in any state Medicaid programme. States may also receive Federal funding if they elect to provide other optional services, including prescribed drugs. Created by the Omnibus Budget Reconcilliation Act (OBRA) of 1990, the Medicaid Drug Rebate Programme requires a drug manufacturer to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services for states to receive federal funding for qualifying outpatient drugs dispensed to Medicare and Medicaid patients. The drug rebate programme is administered by Centers for Medicare and Medicaid Services (CMS). For further information see the CMS website at *http://cms.hhs.gov/*.

8. Is authorisation required to manufacture pharmaceutical products? If so, please give a broad overview of the authorisation process, in particular:

- To whom should the application be made?
- Are there any specific restrictions on foreign ownership?
- What are the key stages and timing of the process?
- What fee is payable?
- Is authorisation given for a fixed period? If so, for how long and what is the renewal procedure?
- In what circumstances can authorisation be revoked?

- **Application.** A manufacturer must register with the FDA as a drug establishment (*see Question 3*).
- **Restrictions on foreign ownership.** There are specific procedures set out for foreign drug establishments (*21 C.F.R. § 207.40*).
- **Key stages and timing.** Within five days of beginning the manufacturing, preparation, compounding or processing of a drug or biological product, a manufacturer must register with the FDA as a drug establishment using FDA Form 2656 *(21 C.F.R. § 207.20-21)*. The registration must include a list of every drug of the establishment that is in commercial distribution. The drug listing information 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 NDA applicant for each "prescription drug establishment" named in an NDA for a prescription drug (*21 U.S.C. § 379h(a)(2)(A)*). (For information on the amount of annual fees for each establishment that manufactures prescription drugs, see *http://www.fda.gov/oc/pdufa/default.htm.*)
- **Period of authorisation and renewals.** Each drug establishment must re-register annually on receipt of registration forms from the FDA (*21 C.F.R. § 207.21(a)*). Drug listing information must be updated every June and December (*21 C.F.R. § 207.21(b)*). Changes in the manufacturing of drugs and their packaging are reviewed by the FDA.

  Manufacturers should notify the FDA in advance of changes by filing a manufacturing supplement to a new or generic drug application. A global manufacturing supplement that applies to multiple products and requires only one review can be filed.
- **Revocation.** A manufacturer that utilises a facility in contravention of good manufacturing practices (GMPs) will not have its NDA approved, or if already approved, will have its approval withdrawn until corrections are made.

9. Are clinical trials regulated? If so, please give an overview of necessary consents, authorisations and procedural requirements.

A study sponsor must submit an IND and obtain FDA approval before it can begin a clinical investigation of a new drug in human subjects (*21 C.F.R. §§ 312.2(a), 312.20* and *21 C.F.R. § 312.50*).

No investigator can participate in a clinical trial until he or she provides the sponsor with a completed, signed statement of investigation (Form FDA 1572) (*21 C.F.R. § 312.53(c)*). The investigator must commit to conduct the study in accordance with the protocol, report any adverse experiences, and maintain adequate and accurate records. Informed consent must be obtained from each study subject who will be administered the investigational drug (*21 C.F.R. § 312.60*).

An Institutional Review Board (IRB) must review and approve all clinical studies before an investigator begins conducting research (*FDA regulations*).

After submission of an IND, pre-approval clinical testing on human subjects consists of (*21 C.F.R. § 312.21*):

- Phase I (small studies to determine toxicity and pharmacological information).
- Phase II (small studies to determine safety and efficacy).
- Phase III (large studies to determine safety, efficacy and dosage).

After the FDA has approved a drug, Phase IV post-marketing studies may be conducted to collect additional information about the risks, benefits and optimal use of a particular drug.

10. Please give a broad overview of provisions relating to the packaging and labelling of pharmaceutical, biotechnology and GMO products.

General labelling provisions. These provisions are applicable to all drug labels and mandate that a variety of information be included (*21 C.F.R. Part 201*). Information included on drug labels must be prominent and conspicuous. No other wording can be given materially greater conspicuousness, and the label must be in English *(21 C.F.R. § 201.15)*.

There should be no misleading statements on a drug label with regard to another drug, device, food or cosmetic (*21 C.F.R. § 201.6*). A drug label must conspicuously bear the name and place of business of the manufacturer, packer or distributor *(21 C.F.R. § 201.1)*. Directions for use must be included. They must include (*(21 C.F.R. § 201.5)*):

- Statements of all purposes for which the drug is intended.

- Quantity of doses for different age groups.
- Frequency 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 C.F.R. § 201.50*). The label must also include the net content (*21 C.F.R.§ 201.51*).

The labelling should 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 C.F.R. § 201.56*).

The label for a prescription drug must contain the following in the order shown:

- Description.
- Clinical pharmacology.
- Indications and usage.
- Contra-indications.
- Warnings.
- Precautions.
- Adverse reactions.
- Drug abuse and dependence.
- Overdosage.
- Dosage and administration.
- How supplied.

The following categories may also be used if appropriate:

- Animal pharmacology and/or animal toxicology.
- Clinical studies.
- References.

Information that must be included under each heading is also mandated by the FDA (*21 C.F.R. § 201.57*).

For some prescription medicines, the FDA approves special patient materials to instruct patients about the safe use of the product. These patient package inserts may 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 (FDA-approved patient information) for selected prescription drugs that pose a serious public health concern. Medication Guides are compulsory if the FDA determines that one or more of the following circumstances exist:

- Patient labelling could help prevent serious adverse effects.
- The drug has a serious risk or risks (relative to benefits) of which patients should be made aware because information concerning the risk or risks could affect patients' decision to use, or continue to use, the product.
- The drug is important to health, and patient adherence to directions for use is crucial to the drug's effectiveness.

Labelling requirements for OTC drugs. OTC drugs are used without the supervision of a physician, so they have additional labelling requirements (*21 C.F.R. Part 201).*

In 1999, the FDA issued new regulations to provide easy-to-understand labelling for OTC drugs. The regulations require a standardised format that will improve the labelling on drugs Americans use most; non-prescription, or OTC drugs. The intent is to clearly show a drug's ingredients, dose and warnings, and make it easier for consumers to understand information about a drug's benefits and risks, as well as its proper use.

Specific labelling requirements for specific drug products. Certain drugs have specific labelling requirements and all relevant regulations should be consulted concerning these drugs *(21 C.F.R. §§ 201.300-320).*

11. Are the prices of pharmaceutical products regulated?

Pharmaceutical companies are free to set their own prices within market demands. Antitrust regulations overseen by the FTC apply to the marketing of pharmaceuticals. Generally, manufacturers and wholesalers negotiate with Health Maintenance Organisations (HMOs), large chain pharmacies, and smaller independent pharmacies to set prices.

There is indirect influence through government control of drug reimbursements in federal and state Medicaid programmes.

12. Are there any restrictions on marketing practices such as gifts or "incentive schemes" for healthcare establishments or individual medical practitioners? Are any such practices commonly used?

In their marketing efforts, representatives of drug manufacturers may provide healthcare providers with promotional materials of various types. Federal anti-kickback statutes regulate remuneration that may be provided. The American Medical Association (AMA) has set AMA Guidelines on Gifts to Physicians from Industry. Similarly, Pharmaceutical Research and Manufacturers of American (PhRMA) has the PhRMA Code on Interactions with Healthcare Professionals.

Marketing campaigns typically involve a variety of promotional pieces. The 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 DDMAC has requested, in guidance to industry, 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 DDMAC will provide comments on these pieces in due course.

13. How are parallel imports regulated?

Wholesalers can re-import US made drugs (*Medicine Equity and Drug Safety Act, 2000*) (*see 21 U.S.C. § 384*). This law will also allow importation of drugs made abroad.

Imported drugs must still have FDA approval for marketing and labelling, and there are geographical restrictions that only allow importation from countries that have regulatory regimes similar to that of the FDA (*see 21 U.S.C. § 384*).

14. Is it possible to market pharmaceutical products online, by email and/or mail order?

Pharmaceutical products can be 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 internet websites (where a doctor may prescribe drugs after a consumer enters brief information relevant to his or her medical condition) by enacting laws that make it illegal for a doctor to prescribe a drug without an examination. The AMA has stated that it is an ethical violation to sell drugs without a face-to-face consultation. A bill is currently before both houses of Congress that would require internet pharmacies to disclose their licensing information (*106 H.R. 2763* and *106 S. 3208*). The bill would allow for national injunctions and forced compliance with FDA regulations and laws.

15. Are there any restrictions on advertising pharmaceutical products (available over the counter or on prescription)?

FDA regulations concerning prescription drug advertising are designed, in part, to ensure that claims are supported by credible scientific evidence (*21 C.F.R. § 202.1*). The FDA has published a number of comparative drug advertising guidelines to assist manufacturers in complying with its advertising regulations. Advertisements can also be submitted to the FDA before publication for comment.

The Lanham Act permits false advertising claims (*15 U.S.C.§ 1051,et. seq*). Competitors of the defendant have standing to sue to challenge advertising as false or misleading (*§ 43(a), the Lanham Act, 15 U.S.C. § 1125(a)(1)(B)*).

The FDA Modernisation Act of 1997 (FDAMA) (*Pub.L. 105-115, Nov. 21, 1997, 111 Stat. 2296*) abolished the prohibition on dissemination by manufacturers of information about unapproved uses of drugs and medical devices, known as off-label use.

The FDAMA allows manufacturers to disseminate peer-reviewed journal articles about off-label use of a product to healthcare providers. However, the manufacturer must commit itself to file within a certain time a supplementary application to establish the safety and efficacy of this use.

Regulations involving direct to consumer advertising are extensive. The manufacturer must present a fair balance between the information relating to efficacy and the information regarding side effects and contraindications (*21 C.F.R. § 202.1*). (*See 21 C.F.R. §§ 200.200 and 202.1 for exemptions to these regulations.*) New regulations require that drug manufacturers 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 C.F.R. § 208.1*).

16. Please give a broad overview of product liability law. In particular:

- Under what legal provisions can liability arise (eg contract, tort, statutory)?
- Who is potentially liable for a defective product?
- What is the substantive test for liability?
- What defences are available?
- What is the scope of potential liability and sanctions?

- **Legal provisions.** Causes of action against drug manufacturers primarily lie in tort and breach of warranties claims (quasi-contractual in nature). Criminal liability may arise on the part of a manufacturer for producing or marketing a product with either a defective design or inadequate warning.
- **Who is liable?** The pharmaceutical manufacturer is usually the defendant in civil court actions, but the plaintiff can also sue a distributor, pharmacist and/or pharmacy. The plaintiff can also sue his or her physician for malpractice within the same lawsuit.
- **Substantive test.**

  Restatement (Third) of Torts. The tort law applicable in product liability cases involving drugs varies from jurisdiction to jurisdiction. The Restatement of Torts, drafted by the American Law Institute, provides the basis for tort law in many jurisdictions (*see http://www.ali.org*).

Under the approved Restatement (Third) of Torts, a three-tiered analysis replaces the Restatement (Second) of Torts § 402A analysis that had been adopted in many jurisdictions.

The Restatement (Third) sets separate tests for manufacturing defects, design defects and defects in warnings. Strict no-fault liability applies only to manufacturing defects. Design defect claims require risk-utility balancing, as well as proof of a reasonable alternative design, the lack of which renders the product not reasonably safe.

Design defect liability for prescription drugs and medical devices is limited (*see section 6, the Restatement (Third)*). 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)*).

- **Liability for breach of warranties.** Warranty theories represent a strict form of liability, but they are limited by the contractual concepts of disclaimer and notice. Warranty theories are governed by the Uniform Commercial Code (UCC), which has been adopted in 49 of the 50 states.

  The UCC recognises three different types of warranties:

  - express;
  - the implied warranty of merchantability; and
  - the implied warranty of fitness for a particular purpose.

- **Criminal liability.** Criminal prosecution involves a high burden of proof (beyond a reasonable doubt). Although prosecution is theoretically possible under general criminal statutes, there is no current trend to impose such liability.

- **Defences.** The learned intermediary doctrine; generally, a pharmaceutical manufacturer has no duty to provide information directly to patients, and discharges its duty to warn by providing sufficient and adequate information to physicians who use their individual medical judgment to prescribe the drug and inform patients. Subject to certain exceptions, this doctrine is recognised in almost all jurisdictions. Exceptions to the doctrine involve situations where there is no close physician/patient relationship. As direct-to-consumer advertising and patient package inserts become more common, the doctrine may provide manufacturers with decreased protection.

- **Scope of liability.** The limitation period for a product liability action 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 plaintiff had no reason to know of his or her injury or that the drug may have caused it (the discovery rule).

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

17. Are class actions permitted for product liability claims? If so, how common are they?

Class actions are permitted for product liability claims in both state and federal courts. They are common in the product liability context because of the ease with which each individual can assert a claim and the potential that exists for large damage awards.

There are prerequisites to a class action in federal courts (*Rule 23, Federal Rules of Civil Procedure*). While state court rules can differ, the class action requirements in many states parallel those set out in the Federal Rules.

18. Does any regulatory body monitor compliance with authorisation and/or consumer protection regulations? If so, what are its powers?

The FDA has enforcement powers to ensure product safety and effectiveness and compliance with GMPs (*see Question 8, "Revocation"*).

The FDA has statutory authority to (*21 U.S.C. § 374(a)(1); see also FDA Enforcement Manual, ¶300*):

- 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 after such introduction to enter any vehicle being used to transport or hold such products.

- Inspect at reasonable times and within reasonable limits and in a reasonable manner that facility or vehicle and all pertinent equipment, finished and unfinished materials, containers, and labelling.

The FDA also has authority to inspect records, files, papers, processes, controls and facilities related to drug products (*21 U.S.C. § 374(a)(1)*) and collect samples of products it regulates (*21 U.S.C. § 372(b)*).

FDA inspections, procedures and policies are described in the FDA's Investigations Operations Manual (IOM).

Several federal statutes give the FDA power to impose fines after an administrative hearing (*21 C.F.R.17.1*).

19. What is the test for a pharmaceutical product to be capable of patent protection? Are there separate tests for biotechnology, medical device or GMO products?

A pharmaceutical product must be new and non-obvious in light of existing prior art to obtain patent protection.

20. What is the procedure for obtaining patent protection? In particular:

- To whom should the application be made?
- What are the key stages of the process and timing?
- What fee is payable?
- For how long is protection given?
- What is the renewal process?
- In what circumstances can a patent be revoked?
- Is your country a party to any international conventions on patent protection?

- **Application.** An application for a patent is sent to and processed by the PTO.

  Address. Box Patent Applications,
  Assistant Commissions for Patents,
  Washington, DC 20231 (*35 U.S.C. § 111*) (*see http://www.uspto.gov and Question 3*).

- **Process and timing.** The timetable for the issue of a patent ranges between 18 and 30 months from application to issue. The PTO will answer an applicant's enquiries regarding the status of the application. If the applicant is represented by a lawyer or agent, all comments concerning the application should be addressed through them.

  Rejected applications can be appealed to the Board of Appeals of the US Patent Office. (*See 35 U.S.C. § 111 and §112for further details of the application process.*)

- **Fee.** The basic fees for obtaining a patent include:

  - application fee: US$750 (about EUR704);
  - utility issue fee: US$1,300 (about EUR1,221).

  (For a complete fee schedule, see *http://www.uspto.gov*).

- **Duration of protection.** A patent term is 20 years from the date of original filing (*35 U.S.C. § 154(a)(2)*). Drug manufacturers receive five years of exclusivity for innovator products, and three years of exclusivity for new indications.

- **Renewal process.** An extension of the patent term of up to 14 years from the time of product approval is available for pharmaceuticals to offset FDA regulatory delay preventing commercialisation during the regular patent term *(35 U.S.C. §156).*

  Maintenance fees are:

  - US$890 (about EUR836)(due at 3.5 years);
  - US$2,050 (about EUR1,925) (due at 7.5 years);
  - US$3,150 (about EUR2,958) (due at 11.5 years).

  (For a complete fee schedule, see *http://www.uspto.gov.*)

- **Revocation.** A patent can be revoked if facts come to light indicating that the idea was not unique when the patent was issued or that the patent was procured by fraud.

- **International conventions.** The US is a party to international conventions on patent protection, including the Paris Convention and the Patent Cooperation Treaty.

21. Are drug patents commonly infringed? What is the process for enforcement?

Drug patents are frequently infringed. When this happens, the enforcement process is generally the same as when any other patent is infringed (*see 35 U.S.C. §§ 271-297 for the patent infringement and remedy process*).

22. Can the brand of a pharmaceutical/medical device/GMO product be protected by registration as a trade mark? If so, what is the test for obtaining trade mark protection?

A trade mark is any word, name, symbol, or device, or any combination thereof used by a person, or which a person has a *bona fide* intention to use in commerce and applies to register on the principal register to identify and distinguish his or her goods, including a unique product, from those manufactured or sold by others and to indicate the source of the goods, even if that source is unknown (*15 U.S.C. § 1127*).

A trade mark application can be submitted in three situations:

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

23. What is the procedure for obtaining registration of a trade mark? In particular:

- To whom should the application be made?
- What fee is payable?
- For how long is protection given?
- What is the renewal process?
- What are the key stages of the process and timing?
- In what circumstances can a trade mark be revoked?
- Is your country a party to any international conventions on trade mark protection?

- **Application.** An application for a trade mark is made to the Assistant Commissioner for Trade marks (*15 U.S.C. § 1051, et seq.*).

  Address. 2900 Crystal Drive,
  Arlington, VA 22202-3513
  (see http://www.uspto.gov).

- **Process and timing.** The Trade Mark Assistance Center provides general information about the trade mark registration process and responds to enquiries about the status of specific trade mark applications and registrations (Tel: +1 703 308 9000).

- **Fee.** The basic fees for obtaining a trade mark include:

  - application fee for registration: US$335 (about EUR315) per class.
  - application fee for renewal: US$400 (about EUR376) per class.

  (For a complete fee schedule, see *http://www.uspto.gov.*)

- **Duration of protection.** A trade mark can last indefinitely as long as the owner continues to use the trade mark to identify the goods.

- **Renewal process.** *See above "Process and timing".*

- **Revocation.** A trade mark's registration can be cancelled if either (*15 U.S.C. § 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.

  If the trade mark's registration is revoked, the aggrieved party may either appeal to the US Court of Appeals for the federal circuit or file a civil action within 60 days of the decision.

- **International conventions.** The US is a party to international conventions on trade mark protection, including the Paris Convention.

24. What is the process for enforcing brand or trade mark infringement?

This is done through an action for trade mark infringement. The action can be based on a registered trade mark or on common law rights in a trade mark.

25. Are homeopathic products specifically regulated? If so, please give details.

Homeopathic drugs must meet the standards for strength, quality and purity established in the Homeopathic Pharmacopeia of the US (HPUS).

If a homeopathic remedy is offered for the cure, mitigation, prevention or treatment of disease symptoms, it is classified as a drug and subject to regulation by the FDA. Although homeopathic drugs fall under the authority of the FDA, they are regulated differently from other drugs.

Manufacturers of homeopathic drugs are not required to submit NDAs. Homeopathic drugs do not have to undergo finished product testing for identity and strength because they contain little or no active ingredients. There are no toxicity or poison-control issues. Unlike conventional drugs, they may contain more than 10% alcohol.

Companies that manufacture, prepare, propagate, compound or otherwise process homeopathic drugs must register as drug establishments and conform to current GMPs.

Homeopathic drugs that claim to treat a serious disease can only be sold by prescription. Only homeopathic drugs for minor health problems, such as colds or headaches, can be sold without a prescription.

26. Please summarise any impending developments in the field of life sciences (regulatory/legal/popular).

Products liability litigation continues to be a threat to life sciences companies doing business in the US. One of the main forces driving the current litigation frenzy is the constant threat of punitive damages and excessive punitive damage verdicts. Punitive damages are awarded not to compensate a plaintiff, but are intended to punish a defendant for intentional or malicious misconduct and to deter similar future misconduct. These verdicts often bear no relationship

to the injuries the plaintiff actually sustained or the amount of compensatory damages awarded. Excessive punitive damage verdicts are not only a threat themselves, but they also drive up the perceived value of pending cases, affecting litigation decisions and potential settlements. Currently, almost half of the states in the US are without any statutory or common law limits on punitive damages awards.

The growth of civil litigation in the US is also supported by the strength and organisation of the plaintiffs' bar. US plaintiffs' attorneys are a strong special interest group in the political arena and, as a group, one of the largest contributors to candidates for political office in the US. Their political influence affects not only the success or failure of statutory reform efforts and legal challenges to such legislation, but also other issues that affect the US civil litigation system, such as judicial elections, nominations and confirmations.

There are significant efforts towards tort reform being made at both the federal and state level. Currently, the US Chamber of Commerce is supporting a Class Action Fairness Act in Congress. The Class Action Fairness Act (*H.R. 2341*) was passed in the House of Representatives in March, 2002. Although the Senate Judiciary Committee held a hearing on its version of the bill (*S.1712*) in July, 2002, no further action occurred in the 107th Congress. The proposed law would make it easier to move large, multi-state class actions from state to federal court, preventing widespread venue-shopping by trial lawyers. Advocates are poised to reintroduce the legislation again in 2003 and will continue their efforts to build bipartisan support. Several states have enacted various Civil Justice Reform measures. However, there remain many states where tort reform is needed.