Life Sciences

Product Liability in the USA Market

CHUBB®

Contents

Product Liability in the USA Market

Comprehensive planning is necessary before selling life science products into the USA. The US legal system is one of the most complex and expensive in the world in regards to litigation. A company that wishes to export to the US must take these factors into account and understand the nuances of its legal system. In order to successfully sell life science products in the US, companies must clearly understand the various regulatory approval processes and have a good knowledge of the legal issues that may result from inherent product hazards, customer use and possible misuse, and company business practices. In todays global economy, even companies that do not actively sell into the USA should consider that their products may somehow enter this marketplace.

The FDA (Food and Drug Administration) is the government body in charge of medical devices, drugs and dietary supplements in the US. All food, cosmetics, medical devices, drugs, biologics and dietary supplements are subject to approval and/or examination by the FDA when they are being imported into the United States. The FDA does not simply recognise regulatory approvals from foreign countries.

Any company who wishes to export products to the United States must first have their facility registered with the FDA. In addition, the company's products must be listed with the FDA. Drugs are restricted from importation unless they are approved under a New Drug Application (NDA) or Biologics Licence Application (BLA).

In the same way, medical devices are authorised to be sold in the US under a 510(k) or a PMA (premarket approval) according to their classification (from class I to class III) and the risk they present.

Dietary supplements also have requirements intended to protect consumers from impure ingredients and allergens. The specific rules that apply to dietary supplement manufacturing and labelling stem from the Dietary Supplement Health and Education Act (DSHEA) of 1994.

Overview of the US Market

In the US, product liability that may arise from defective products can vary from state to state, which means that each jurisdiction has its own set of legal requirements. However, there are several core legal theories that exist when dealing with products liability in the USA:

Products Liability Legal Theories

Negligence
Negligence is the failure to exercise a reasonable amount of care or to carry out a legal duty which results in injury or property damage to another.
The plaintiff needs to show that the manufacturer failed to use ordinary or reasonable care in designing, manufacturing, or selling the product and that such failure was a cause of the injury to the person bringing the claim.

Strict liability
Strict liability is based on the defect of a product which then becomes the direct cause of a bodily injury or property damage. With strict liability, the plaintiff must prove that:

- The product was defective in its design, manufacturing, or marketing
- The defect was the proximate cause of harm.

It is not necessary to prove that the manufacturer was negligent. Unlike negligence, the focus is here on the product and not on the manufacturer.

Breach of Warranty
A warranty is essentially a promise by the manufacturer that its product will have certain characteristics or perform in a certain way. Responsibility for violation of a warranty may be expressed or implied:

- Expressed warranty: "statement by the manufacturer or seller, either in writing or orally, that his product is suitable for a specific use and will perform in a specific way." Any word becoming part of the transaction between parties is sufficient to constitute an express warranty. Some rulings have expanded the concept of warranty beyond words to including graphical representations of the product and its use.

- Implied warranty: "automatic warranty implied by law that the product is suitable for ordinary use or particular use requested by the buyer during the transaction." Implied warranty includes safety warranty. For this theory, the plaintiff must show that the product did not live up to the promise or warranty made by its manufacturer, and as a result was a cause of the injury to the person bringing the claim.

Remark: Even if there are intermediary sellers (as distributors), the initial seller is not exempt from responsibility.

Key US Liability Concepts

Preemption
Preemption is the theory that products approved by a federal regulatory authority (i.e. the FDA) supersede state law based on the fact that the federal agency reviewed and subsequently approved the product. The theory of preemption is intended to protect companies from torts (lawsuits) because the product went through a federal approval process. However, preemption is a highly debated topic and it does not necessarily protect companies from claims because of nuances such as the amount of approval scrutiny that a product received during the FDA approval process and new information that was discovered after the product was approved. In addition, preemption is merely a defence and legal costs can still be spent to defend the claim in US courts

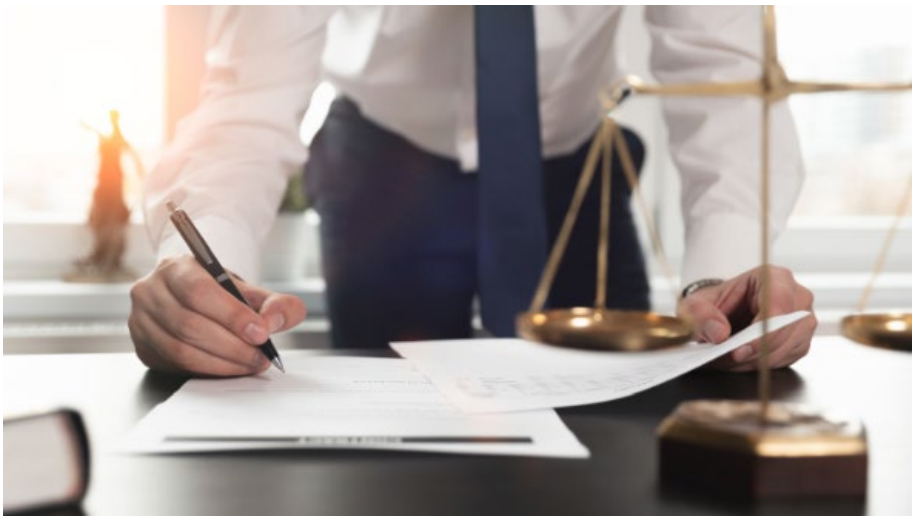
Jurisdiction
Many factors decide whether or not litigation against foreign firms will be brought about in US courts. Companies should seek their legal counsel's assistance to learn more about this issue and how a specific company's operations can affect its application to individual products sold in the US.

Punitive damages
Punitive damages is a method to allow courts to "punish" companies for egregious or other forms of "bad" behaviour. For example, the manufacturer knew the danger of its product but did not do anything to remedy the problem. Punitive damage amounts can vary from jurisdiction to jurisdiction and can increase the total amount of the claim. It should also be noted that some jurisdictions allow punitive damages to be covered by insurance while other jurisdictions make the company solely responsible for paying any and all punitive damage costs.

Jury
In US liability law, responsibilities and indemnities (including punitive damages) are mostly decided by a trial composed of a jury (for the questions of fact) and a judge (for the questions of law). Other means of deciding and assigning liability include Arbitration and Mediation.

Class action
Class action and Multi District Litigation (MDL) are techniques for suing an entity on behalf of large numbers of people whose cases involve common questions of law and/or fact. Therefore, people who did not initiate a legal action as an individual can receive their share in case of victory. American attorneys have the possibility to use different media (television, radio, Internet, letters…) to encourage consumers to join class action suits.

Prevention - some elementary rules



Planning

Managing product liability risks requires understanding the product lifecycle from initial development to clinical testing through regulatory approval and marketing. The FDA website provides a wealth of information in terms of regulatory guidance and technical resources, as well as providing data on adverse events reports. In Europe, national competent authorities' websites can also provide information on adverse events, regulation... (MHRA, AFSSAPS...). With the introduction of MDR 2017/745, a central European database will also be generally accessible in future, which will provide information on products and manufacturers as well as adverse event reports. Some other organisations can provide a good range of data that should be regularly consulted during design but also post-market phases (ECRI Institute, Pubmed, etc.). Some of these organisations may require subscription services.

When developing a life science product, certain practices should be considered as part of a products liability risk management program.

- Before marketing a drug or a medical device in the US, one of the first steps consists of **checking regulations and specific requirements** of the American market. If both European and US regulations tend to be harmonised through ICH (International Conference on Harmonisation) or GHTF (Global Harmonisation Task Force) actions, differences will likely still exist and should be considered.

- **Scientists, engineers and project management teams should be trained** to understand and assess product liability hazards in order to better anticipate this risk at the early stage of the design process. It is imperative that each step of new product development (from discovery through clinical trials) be documented and comply with the requirements of the appropriate regulatory authority. Effective **risk analysis is essential** for determination of inherent and predictable risks, as well as those that are related to reasonably foreseeable misuse. The goal should be to mitigate the potential for mistakes by achieving a comprehensive level of due diligence during the discovery, pre-clinical and clinical testing phases. These risk management principles will serve as a strong foundation when developing instructions, warnings, etc.

- During a lawsuit's discovery phase (before depositions and trial), the company will have to provide all documents regarding the product and the activities of the company. Documentation sought may include risk analysis results, design/development plans, quality metrics and results, complaints as well as internal correspondences (including electronic mails, files, etc.). It is therefore important to **implement a procedure for managing these documents** in order to prove that safety is a priority for the manufacturer. This includes all employees and not just senior management.

Examples of differences between US and Europe regulation

Drugs
Amongst differences between Europe and US drug regulation, drug development activities present substantial differences in the way amendments to Clinical Trial Applications (CTA) and Investigational New Drugs (INDs) are handled. Additionally, the enforcement mechanism for early approval of innovative therapies (accelerated approval in the US, conditional approval in Europe), and the role of the Quality Assurance function are differences to be familiar with.

Medical devices
With the introduction of the European Regulation 2017/745, the requirements for high-risk products have changed considerably and are now very much in line with US regulations. According to Article 54 and Articles 61-80, all new Class III devices and some Class IIb devices must pass a clinical trial in order to be approved for the European market.

In 70% of product liability litigation with punitive damages, the plaintiff used these documents to prove that the company knew there was a defect and that no suitable measures were implemented[1].

All documents should be written in a way that there is no sense of ambiguity on the willingness of the company to sell safe products. All affected employees should be trained on issues relevant to the hazards that come as a result of exporting products to the US.

All parties can be orally cross-examined, so this must be considered throughout the documentation process. The most important thing to remember when documenting and corresponding is to write DEFENSIVELY, as if it were being viewed or read in court. All employees should be trained in some form of defensive writing and documentation awareness training.

[1]*Goodden, Randall. «Product Safety and Liability Presentation.» Munich. 14 Feb. 2006. Lecture.*

GMPs / Quality System Regulation

As previously discussed, knowledge of US regulation is necessary for companies that wish to sell products in the United States. Amongst U.S. regulatory requirements, compliance with cGMPs is probably one of the most important ones.

The quality systems for FDA-regulated products (food, drugs, biologics, and devices) are known as current good manufacturing practices (cGMPs). cGMPs provide systems that assure proper design, monitoring, and control of manufacturing processes and facilities.

Drugs
GMP implementation is mandatory for drugs manufactured in Europe and in the US. In Europe, GMP compliance is required as part of the EU directive 91/356/EEC of 13 June 1991, as amended by Directive 2003/94/EC of 8 October 2003, and 91/412/EEC of 23 July 1991 respectively. In the US, GMP regulations for drugs are contained in the parts 210 and 211 of the title 21 of the Code of Federal Regulations (21 CFR). Focus areas of the FDA cGMPs regulations are :

- organisation & personnel,
- equipment and facilities,
- control of components, drug product containers, closures
- production and process control
- packaging and labelling controls
- warehousing and distribution controls
- laboratory controls
- documentation and records

Medical devices
In Europe, medical device manufacturers must follow Essential Requirements of the EU Medical Device Regulation 2017/745. A Quality Management System is required as part of their Essential Requirements.

Annexes of the Regulation do not stipulate the type of quality system, but it is generally agreed that compliance with ISO 13485 standards will provide a presumption of conformity with the essential requirements of the relevant directive. ISO 13485 also has relevance in the US for medical device manufacturing.

ISO 13485:2016 “Medical Devices - Quality Management Standard for Medical Devices” is a worldwide recognised quality management system standard for design & development, production, selling and other activities of medical devices.

The U.S. Food and Drug Administration supports the international harmonisation of standards and regulations governing medical devices. FDA’s Quality System Regulation (QSR) is based on ISO 9000 standards and is basically the same as ISO 13485:2016, except for a few additional requirements.

Moves are being made to recognise each other’s requirements via Mutual Recognition Agreements.

Labels - Warnings - Instructions

Labels, warnings and instructions need to be strictly managed. In the US, the goal for the manufacturer is to provide guidance to warn of hazards known about the project, which includes open and obvious hazards, as well as adverse health effects that are not readily known to the patient or their doctor.

- The company must also **forecast abnormal but predictable uses** of the product in instructions and warnings. Generally, this is stated as 'reasonably foreseeable misuse'.

- For drugs, biologics and certain types of devices, formal warnings and labelling must be submitted to the FDA for review prior to approval. When issues or problems are discovered post approval, it is **incumbent on the company to alert the regulatory agencies** to change warnings and labelling in order to protect patient safety. See 'Product Safety Surveillance' below.

- Life science companies need to be aware of the fact that the United States congress passed sweeping drug safety reforms in 2007 with legislation known as the Food and Drug Administration Amendments Act (FDAAA). FDAAA specifically addresses among other things an increased level of scrutiny for drug labelling, warnings and instructions by requiring companies to go through a process known as a **"Risk Evaluation and Mitigation Strategy"** (REMS). REMS are designed to provide a formal analysis and action plan for managing the risks of a product's safety profile.Companies who wish to market drugs with significant adverse health event potential will most likely be required to complete a REMS as part of the approval process. Depending on the severity of the drug risk, companies may be required to attach a standalone "medication guide" with the drug. They may also need to have a highly controlled doctor and pharmacy distribution system." The FDA website is the best place to learn more about FDAAA and implementing a REMS program.

- W**arning label design in the US is very different from how it is handled in Europe.** While the European approach is graphic-intensive, in the US, there is generally more text. To make sure medical devices are adequately US-centric labelled, different guides should be followed such as the FDA "guidance on medical device patient labelling" and ANSI Z535. Dietary supplements must also be properly labelled for any known allergens. This requirement is part of the FDA's Food Allergen Labelling and Consumer Protection Act of 2004.

- The strict translation of instructions is often not sufficient. It is advisable that a **local and specialised organisation checks the translation** in order to adapt the instructions to the American market requirements. All advertising and marketing documents as well as the website should be checked too.

Contractual relationships and guarantees

- Implementation of contractual documents with third parties (suppliers, clients…) should be systematic. Ideally, each interaction needs to be confirmed with a **written adequate document** mentioning **general conditions of sales and applicable conditions of sales.** These documents will have to be **reviewed by a law firm** with a good knowledge of specificities related to the American market.

- Particular attention should be paid to the preparation and validation of specifications (clarity, precision, definition of third parties' responsibilities, etc.) as well as to updates when any change occurs.

- Even if companies do not actively market their products or services in the United States, there can be reasons to believe that their products or services may reach customers in the United States. To avoid any surprises, a consultation with legal counsel is advised to develop guidance governing online contracts and adapt the limitations of warranties and liabilities in their general terms and conditions to meet the stringent requirements of U.S. law.

Marketing (over promotion / off-label use)

- **Overpromotion** can considerably limit the impact of advertising and warnings in front of a court in case of lawsuit. All marketing documents should be reviewed by legal counsel and by the research & development department in order to mitigate overpromotion issues. In the same way, sales representatives need to recognise what constitutes over promotion and understand what can and cannot be said in order to avoid express breach of warranty.

- **Off-label Promotion** has historically been a major issue in the USA, especially in comparison to Europe. When exporting to the American market, companies need to be well versed with this specific topic. 'Off-label' is defined by the Code of Federal Regulations, 21 CFR part 99, as "a new use that is not included in the approved labelling of an approved drug or device, or a use that is not included in the statement of intended use for a cleared device".

- **Off-label risk management needs to be implemented** through (not an exhaustive list):
- Analysis of off-label hazard during research & development steps
- Monitoring for off-label activity in a formalised post-market safety surveillance program
- Surveillance data collected and analysed for off-label usage received from multiple sources
- Training for all internal and external stakeholders including topics such as regulatory requirements and litigation trends
- Legal and regulatory review of marketing materials…
- Resubmission of FDA application when a new use for the product is shown to be efficacious when used in an off-label manner.

The bottom line with off label promotion is that it is generally considered an illegal activity per FDA, unless specific controls, including the ones described above are implemented. Allegations of off label use can be cited in product liability litigation and if a life science company was found to be in violation of off-label promotion regulations, this could be held against them.

Example of off-label issue:

In January 2009, the company Eli Lilly was ordered to pay more than $1.4 billion to various federal US and state agencies as part of the plea agreement and a civil settlement. The punishment stems from off-label promotion of the drug Zyprexa, a powerful drug approved by FDA for schizophrenia and bipolar disorders. Indeed, Eli Lilly encouraged primary care physicians to use Zyprexa as a treatment for sleep disorders and dementia in elderly patients and touted the drug's known side effect of significant weight gain as a therapeutic benefit (according to internal Lilly marketing material). The US Department of Justice alleged that «Eli Lilly's management created marketing materials promoting Zyprexa for off-label uses, trained its sales force to disregard the law and directed its sales personnel to promote Zyprexa for off-label uses.»

Product Safety Surveillance

- Life science companies need to implement an adequate product complaint management and safety surveillance program to capture, track, trend and ultimately take action on information based on product safety data.

- In the past, there was a significant difference between the requirements of the EU and the FDA in terms of post-marketing surveillance of products. With the new MDR 2017/745 Article 83, the manufacturer is also responsible in the EU for the post-marketing surveillance of products. However basic compliance with regulations should only be considered as a starting point and is not enough for managing an effective product safety surveillance program.

  - A dedicated safety surveillance department should be in place and responsible for managing incoming adverse events (from interaction with other products to long-term effects, off-label use, misuse…).
  - An active collection of data is advised and all staff (including sales staff and receptionist) should be trained to capture relevant adverse events (AE) data and how to record the information and forward to the appropriate department.
  - When adverse event data is substantial, a robust AE management system should be considered. In all cases, it must be able to perform sort functions to look for trends that will be reviewed on a regular basis.
  - All AE of special concern should be investigated and followed-up, and not only those considered as serious or unexpected.
  - A safety surveillance program audit should be in place (internal audits and external audits)

- As a reminder, if a manufacturer receives an adverse event report, it is required to send the report to the FDA as specified by regulations. Even more importantly, when adverse trends are identified, the company must ensure that the appropriate manager(s) be alerted and that the company take subsequent action, based on a pre-defined risk assessment process.

Recalls

- In Europe, the Directives associate systematic recall with "product problems that have led to, or could lead to, deaths or serious deterioration in state of health."

- According to the FDA, "recalls are actions taken by a firm to remove a product from the market.

- Recalls may be conducted on a firm's own initiative, by FDA request, or by FDA order under statutory authority." The FDA definition of recall does not include a market withdrawal or a stock recovery.

- The definition of a recall in Europe and US is very similar; however, when the FDA recalls a product, they also define the level of seriousness of a recall in relation to health risk:

  Class I recall: a situation in which there is a reasonable probability that the use of, or exposure to, a defective product will cause serious adverse health consequences or death.

  Class II recall: a situation in which the use of, or exposure to, a defective product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.

  Class III recall: a situation in which the use of, or exposure to, a defective product is not likely to cause adverse health consequences.

  The classification determines the FDA's expectations of the manufacturer's recall strategy. The strategy varies depending on the health risk and device type. The recall of a life-supporting or life-sustaining device may require direct contact with the user and possible assistance, including publicity, from the FDA.

- Most recalls are initiated by the firm itself on a voluntary basis. But to the case of a defective or dangerous product, the FDA can suggest or request its recall. If the company does not react, the FDA can seek a court order authorising the Federal Government to seize the product. These include seizure of available product, and/or injunction of the firm, including a court request for recall of the product.

Conclusion

Selling life science products into the United States involves stringent regulatory compliance combined with careful consideration of litigation issues.

The legal climate in the USA is highly complex and varies from state to state.

A company's evidence of risk management best practices, coupled with regulatory compliance due diligence will help to mitigate litigation potential.

Before embarking on any product export endeavour, legal counsel should be sought.

Websites

http://www.missioneco.org/etatsunis - la responsabilité civile du fait des produits défectueux aux Etats-Unis par la Mission Economique de Washington

http://www.fda.gov - Federal Drug Administration

http://www.epa.gov - Environmental Protection Agency

http://www.nam.org - National Association of Manufacturer

http://www.ansi.org - American National Standards Institute

http://www.ftc.gov - Federal Trade Commission (jointly oversees over the counter drugs with the FDA)


4.5

Contact

Chubb European Group SE
Direktion für Deutschland
Baseler Straße 10
60329 Frankfurt am Main

O +49 69 75613 0
F +49 69 746193
info.de@chubb.com
chubb.com/de

Chubb. Insured.℠

Chubb European Group SE ist ein Unternehmen, das den aufsichtsrechtlichen Bestimmungen des französischen Versicherungsgesetzes unterliegt | eingetragen unter der Registrierungsnummer 450 327 374 RCS Nanterre | eingetragener Sitz: La Tour Carpe Diem, 31 Place des Corolles, Esplanade Nord, 92400 Courbevoie, Frankreich | Direktoren: Adam Phillip Clifford, David Furby, Kenneth Koreyva, Sara Mitchell, Veronique Brionne, Jonathan Adair Turner, Sian Katharine Richards, Miriam Connole, Mark McCausland | Die Chubb European Group SE hat ein voll eingezahltes Aktienkapital von €896.176.662,-- und unterliegt der Zulassung und Aufsicht der Autorité de contrôle prudentiel et de résolution (ACPR) 4, Place de Budapest, CS 92459, 75436 PARIS CEDEX 09 sowie in Deutschland zusätzlich den Regularien der Bundesanstalt für Finanzdienstleistungsaufsicht (BaFin) zur Ausübung der Geschäftstätigkeit, welche sich von den französischen Regularien unterscheiden können | Direktion für Deutschland |Baseler Straße 10, 60329 Frankfurt am Main | Amtsgericht Frankfurt HRB 58029 | Hauptbevollmächtigter Andreas Wania | USt-IdNr.: DE240196168 | VersStNr.: 807/V90807004025 | Citigroup Global Markets Deutschland | IBAN: DE47 5021 0900 0210 1170 24 | BIC: CITIDEFF

DE-EN0903 05/21