WIGGIN AND DANA

Counsellors at Law

BioInsights

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Wiggin and Dana and its Clients in the News

- **Wiggin and Dana** was selected by *PLC Which Lawyer?* and *PLC Cross-Border Life Sciences Handbook* as one of only eight "highly recommended firms" in the United States for Commercial and Partnering in the Life Sciences Industry for 2006.
- **Santaris Pharma A/S** entered into a collaboration with **Enzon Pharmaceuticals, Inc**. to co-develop and commercialize a series of innovative RNA Antagonists based on Santaris Pharma's LNA® (Locked Nucleic Acid) technology and utilizing Enzon's drug development expertise.
- **Alexion Pharmaceuticals, Inc.** acquired the former **Dow** manufacturing facility in Smithfield, Rhode Island. The biopharmaceutical manufacturing facility will be used primarily to produce Soliris (TM) (eculizumab), Alexion's lead product candidate for Paroxysmal Nocturnal Hemoglobinuria (PNH).
- **Q-Med AB** executed license and supply agreements with **Smith & Nephew Orthopaedics Trauma & Clinical Therapies**, under which Q-Med AB has granted Smith & Nephew Inc. the global exclusive right to market, sell and distribute DUROLANE® and other products intended for the management of orthopedic conditions and diseases.
- **VeroScience LLC** acquired rights in Cycloset® (a phase III drug for Type II diabetes) and entered into a marketing and distribution partnership for Cycloset® with **Wyeth Pharmaceuticals**.
- **Nerviano Medical Sciences S.r.l. (NMS)**, an Italian company owned by the Vatican and the largest pharmaceutical *read more*

United States Pharmaceutical Product Liability: Current Trends and Risk Management

The life sciences industry is operating in a more litigious and aggressive environment than ever before. With increasing numbers of high profile product liability cases and the attendant costly negative publicity, pharmaceutical and biotechnology companies at all stages of product development and commercialization must now carefully consider strategic risk management steps and procedures to identify, prevent, reduce and shift product liability risk.

strict liability

Most product liability claims in the U.S. are based on the doctrine of strict liability, in addition to negligence and other fault-based theories. The strict liability doctrine holds sellers of defective products responsible for injuries caused by products without a showing of negligence or other fault. Defects may be based on, among other causes, design, manufacturing, sales promotion practices, failure to warn, and failure to comply with regulatory requirements. In addition, the product must be found to have been capable of causing the alleged injury and in fact did so in the particular case. The concepts of general and specific causation are key issues in a number of high profile drug cases.

failures to warn claims

A drug free from manufacturing and design defects may nevertheless give rise to a successful lawsuit if the patient was not adequately informed of potential adverse events and other risks arising from the use of the pharmaceutical product. The scope of instruction and warning claims has been a complex and continually evolving area of product liability law over the past decade. Pharmaceutical manufacturers often rely on the "learned intermediary" defense, which protects the manufacturer if it properly warns or instructs a physician who prescribes the drug. As mentioned below, recent FDA rules may further protect pharmaceutical manufacturers if they fully report all adverse events to the FDA and comply with labeling regulations. However, the "learned intermediary" defense may be eroded when the manufacturer engages in "direct-to-consumer" advertising and may not be taken advantage of by a drug company if the plaintiff can demonstrate that the warnings on the label were either inadequate or diluted by marketing activity directed to the prescribing physician that, for example, encouraged off-label use.

preemption

One of the most controversial and frequently litigated issues in U.S. product liability law is the preemption defense. Preemption is the defensive claim that a federal law or regulation under which product safety standards are *read more*

Published periodically by Wiggin and Dana, a 135 attorney law firm with offices in New Haven, Stamford, New York, Hartford and Philadelphia (USA). Wiggin and Dana Biotechnology & Life Sciences expertise includes M&A, licensing and other transactions, public and private financing and intellectual property assistance.

established (for example, the U.S. Food, Drug and Cosmetic Act) supersedes any conflicting state law on the subject, including state common law tort principles. Unless preemption applies, compliance with governmental standards does not bar a common law product liability claim but is relevant evidence that a jury may consider when deciding liability.

Preemption has become a more common liability shield for drug companies since the FDA issued a recent rule allowing labels to be simplified. The FDA formally stated its long held view that compliance with FDA regulations preempts manufacturers from state law product liability claims. The FDA also recently filed a brief arguing that a state law failure to warn claim was preempted by the FDA's determination that a warning of the alleged side-effect in the drug's product label was unwarranted. Courts are not required to follow this view, but often defer to governmental rule making agencies, like the FDA, and a few courts have already dismissed product liability claims on this basis.

punitive damages

No aspect of the American legal system is potentially more frightening to drug manufacturers than punitive damages awards. Punitive damages are awarded relatively infrequently. According to one recent estimate, they have been awarded in only about 2% of product liability cases over the past 25 years, although the trend has increased sharply (both in frequency and amount of awards) over that period. Furthermore, many large awards are reduced by the trial court or on appeal. Nevertheless, many are still enormous, especially in a legal system that permits plaintiffs' attorneys to collect their fees on a contingency basis—usually amounting to at least one-third of the award.

For example, in the Vioxx litigation where thousands of cases have been brought against Merck throughout the U.S., state court juries in Texas and New Jersey have made large awards of punitive damages, over $200 million in at least one Texas case. The Texas awards will be reduced by an applicable state statute limiting such awards to a fixed multiple of the compensatory damages. Regardless, the awards in each of these cases have been or will be appealed by Merck.

class actions

Many high-profile product liability cases in U.S. courts are brought as class actions, from tobacco and asbestos to pacemakers and diet drugs. What began as a procedure for aggregating multiple claims in complex civil litigation has evolved into an immensely complicated and unwieldy form of litigation, in which an attorney actively offers representation to a class of consumers who have allegedly been harmed by a product, files a lawsuit on behalf of the class, and if the suit is successful, the individual class members receive a very small share of a huge damages award, while the attorney takes one-third. While personal injury class actions often are not certified in drug cases due to the prevalence of case-specific factual issues, there is a growing trend of courts certifying classes in consumer fraud cases brought by third party-payors, such as health plans and insurance companies, seeking refunds of moneys spent on allegedly defective drugs. Recent federal legislation expanded the jurisdiction of Federal courts in class action suits and is expected to reduce some of the abusive cases brought in some state courts.

potential criminal and other governmental claims

Civil and criminal investigations and complaints by the government are becoming increasingly common and proceed in parallel to private personal injury claims. Brought by state and federal authorities these cases often concern claims for reimbursement of Medicaid and Medicare expenditures, violations of federal and

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R&D facility in Italy, entered into an agreement with **Bristol-Myers Squibb Company** under which NMS will identify and conduct early stage development of active compounds against new oncology targets provided by Bristol-Myers Squibb. Terms of the multi-year risk sharing collaboration include the potential for up to $150 million in clinical and regulatory milestones in addition to royalty payments.

- **Advanced BioHealing, Inc.** acquired assets and rights associated with advanced wound care products, Dermagraft® and TransCyte®, from **Smith & Nephew Wound Management (La Jolla)**.
- **Biovitrum AB** executed a co-development and commercialization agreement with **Symphogen A/S** for Symphogen's lead product, a combination of recombinant polyclonal antibodies, for the treatment of certain blood disorders, and **Biovitrum AB** also executed an agreement with **Syntonix Pharmaceuticals, Inc.** for the co-development and commercialization of Syntonix' long-acting, recombinant Factor IX product for Hemophilia B.
- **PhotoCure ASA** licensed **GE Healthcare** the exclusive global rights outside of the U.S. and the Nordic region to market and distribute PhotoCure's product Hexvix® (hexaminolevulinate), an optical molecular imaging agent intended for the diagnosis and monitoring of bladder cancer.

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- **BioInvent International AB** entered into a collaboration with **Immusol, Inc.** for the development of a fully human n-CoDeR® antibody for the treatment of age related macular degeneration (AMD) and other ophthalmic disorders.
- **Biolipox AB** executed a collaboration agreement with **Boehringer Ingelheim GmbH** to develop and commercialize a new class of drugs with a novel mechanism of action for the treatment of pain and inflammation.
- **HistoRx Inc.** entered into a collaboration with **Eli Lilly and Company** to apply the HistoRx AQUA™ platform for quantitative pathology analysis to generate in situ protoomic information.
- **NatImmune A/S** licensed **Enzon Pharmaceuticals, Inc.** rights in NatImmune's lead development product, recombinant human Mannan-Binding Lectin, a protein therapeutic being developed for the prevention of severe infections in MBL-deficient individuals undergoing chemotherapy.
- **Karo Bio AB** was awarded U.S. Patent Nos. 7,005,538 and 6,989,402 directed to thyroid receptor ligands useful for treating conditions such as cardiac arrhythmias, thyrotoxicosis, and subclinical hyperthyroidism.
- **Affibody AB** was awarded U.S. Patent No. 6,955,877 directed to methods for in vitro selection and identification of engineered or natural polypeptides using solid support carriers.

state anti-kickback laws, and consumer fraud and misrepresentation. Coordination between private litigants and state and federal authorities is frequent. Also added into the mix of product liability litigation are whistle-blower cases brought by disgruntled employees claiming that their employer, the pharmaceutical company, has defrauded the government by withholding important information regarding their drug or misrepresenting important safety or benefit qualities. Defending the private personal injury litigation becomes exponentially more difficult while addressing this kind of ancillary litigation.

litigation of foreign personal injury suits in u.s. courts

Lawsuits filed in U.S. courts by foreign plaintiffs seeking redress for personal injuries they claim to have sustained from the use of U.S. products in their home countries is a growing trend. The foreign plaintiffs argue that the conduct at issue is "American misconduct", that the events that gave rise to the litigation occurred in the U.S., and that U.S. courts thus have the greatest interest in protecting consumers of defective products manufactured by U.S. businesses. U.S. product manufacturers have challenged the propriety of litigating these lawsuits in the U.S. and have advanced various jurisdictional arguments against these claims by foreign plaintiffs. The U.S. Circuit Court of Appeals for the 7th Circuit is currently scheduled to hear oral argument on whether negligence claims brought against four American manufacturers of blood-clotting products by hemophiliacs and their spouses, who are citizens and residents of the U.K., were properly dismissed on the grounds of forum non conveniens (*In re: Factor VIII or IX Concentrate Blood Products Litigation*).

risk management practice tips

Pharmaceutical manufacturers and sellers employ a wide range of risk management steps to identify, prevent, reduce, shift to a third party or provide financial resources to cover product liability risks. Indeed, many insurance companies and others have extensive consulting organizations to support life sciences companies in identifying and managing these risks.

The specific measures adopted by a company depend on many factors, including the extent to which the company is involved in the clinical development, manufacture and sale of a drug, the nature of the drug and its therapeutic area, and the prescribing audience.

Consider the following measures to manage product liability risks:

- Establish and maintain internal compliance programs to assure compliance with GLP, GCP, GMP and other applicable regulatory and legal requirements
- If involved in manufacturing, establish and maintain appropriate QA procedures and compliance
- Manage risks during the conduct of clinical trials and identify potential risks that should be managed in the commercialization of the drug, including:
  - Proper protocol design, including patient eligibility, dosages and data monitoring (e.g., cardiovascular effects)
  - FDA and IRB approval of protocols
  - Proper investigator relationships, including compliance with conflict of interest rules
  - Proper informed consents
  - Appropriate data monitoring
  - Appropriate clinical trial insurance

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- Establish and maintain appropriate adverse event (AE) reporting procedures, including medical support to patient and physician inquiries, sales representatives training and procedures, and compliance with regulatory reporting requirements
- Evaluate and, where appropriate, implement the use of biomarkers or other pharmacogenomic testing to avoid use of the drug by patients who may be especially susceptible to serious AE's
- Identify and educate physicians about appropriate patient monitoring programs, such as follow up visits and liver function tests for statins
- For drugs with a narrow therapeutic index, address as appropriate, educational software, patient monitoring and a patient registry
- Identify and develop relationships with experts and opinion leaders, including coordination of and participation in expert advisory meetings
- Maintain appropriate warnings on all labeling and promotional materials
- Maintain appropriate sales promotional practices, including proper training of sales representatives, assure compliance with proper promotional practices (including AMA and PhRMA guidelines), avoid off-label promotion, and provide appropriate medical liaisons and other medical support
- Maintain appropriate document retention practices
- Maintain product tracking systems and establish procedures to handle recalls or product withdrawals, including public relations issues
- Obtain contractual indemnification from third parties where appropriate—e.g., from the manufacturer if you are only selling or distributing the drug
- Maintain appropriate insurance, including clinical trial, product liability and, where available and appropriate, product recall insurance; the scope of coverage, co-insurance levels and policy limits is highly differentiated for each product and company, and must be reviewed periodically with insurance companies and other risk management advisors
- When product rights are acquired from a third party, consider:
  - Proper due diligence of AE experience and of all risk management steps undertaken by the seller
  - Assurances that the seller will continue to maintain appropriate insurance for an extended reporting period for occurrences arising out of products sold or manufactured by the seller
  - Contractual representations, warranties and indemnification