
Risk Management + Post-Market Safety Strategies = Improved Financial Ratings

By: Barbara Schneider, PhD, MBA
WATERMARK Research Partners, Inc.
www.watermarkdsmb.com

Enterprise Risk Management (ERM) is the new buzz, but not new news. In the pharmaceutical, biotech, and device world, risk is not a new idea. There have always been risks at each step of a products life. In fact, the simple use of a product that involves people is a risk. So, what has changed with regard to risk in this industry? The answer: financial penalties associated with poor safety risk strategies.

Risks to the pharmaceutical and device industry

There are several areas of risk for the sponsor company that will be discussed. This paper takes you through the product life cycle and the changes in risk and financial investment.

- **Research & Development**

There are many risks associated with development. These risks include, but are not limited to, risk of failure of the product, financial risk, risk to the research subjects, risk of competition, risk of technology transfer, and others. The risk continues to rise as more subjects are exposed to the new product. At the same time, with continued research and development, the financial investment becomes deeper.

- **Launch**

As the product continues through the life cycle, the next major milestone is product launch. As the product goes to market, the risks change again. Now the product is put into the hands of physicians who were not involved in the clinical trial and is used in patients who are not restricted by strict inclusion/exclusion criteria. Once a product is launched and is available, physicians can use the product with any patient that they feel may benefit. As a result, many products may be used off label or are used incorrectly.

At launch, increases in risk as more are patients exposed to the product and the conditions for product use are less restrictive. At the same time, the product is now being marketed so there may be some additional financial investment in the marketing and launch of the product. But the financial benefits will begin to be seen as it is adopted in the medical community.

- **Market**

During this phase of the product life cycle, financial investment continues in the marketing of the product, but the financial benefits are recognized. The goal of the sponsor is to raise a profit for the product that recoups the investment in research and development with the greatest opportunity in the initial marketing push at launch.

The longer the product is on the market and the more experience with the product in the physician community, the potential risk decreases for the patients. The risk is never completely gone as the risk of off-label use, competition and patent expiration continue. During this on-going marketing phase the financial gains should continue.

- **Product Retirement**

The expiration of a product can be voluntary or may mark the end of a patent. This is a strategic time when a company decides if they should continue with the product, reenter R&D to improve the product, sell the product to another company, or retire the product. As this time in the product life cycle is reached, the financial benefit will decrease due to newer technology, and the risk to patients may continue to decrease as well.

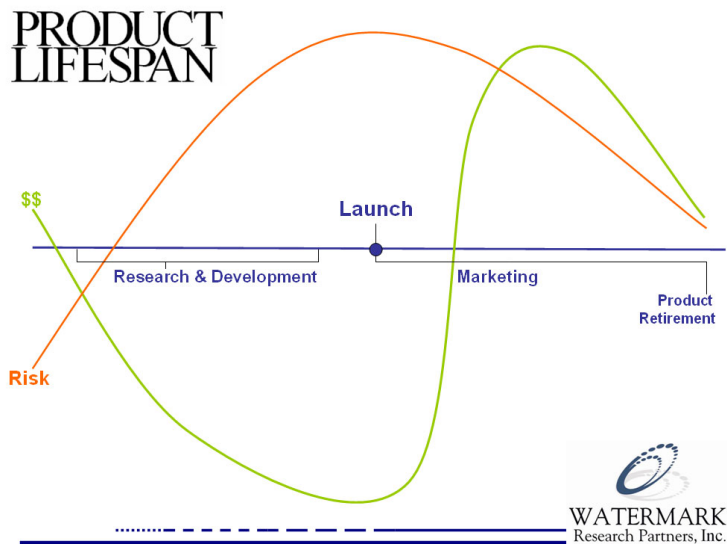


Figure1: A graphic representation of financial investment and risk of a product lifespan.

Regulatory Groups Involved

Risk management in the pharmaceutical, biotech, and device industry is required throughout the life cycle of the product. In addition to managing the risk of R&D, launch, marketing, and product expiration; sponsors must also manage regulatory and governmental groups that may impact the profitability of the product and ultimately the company.

- **FDA**

In the health care industry, a big component of product development is the Food and Drug Administration (FDA). The FDA is charged with ensuring the safety of products that come into contact with people. These include food, drugs, medical devices, biologics, animal feed and drugs, cosmetics, radiation emitting products, and combination products. This is no small challenge for the agency. As a way to ensure safety, the FDA will issue guidance documents or enact legislation to be followed by sponsor companies. Most recently the FDA enacted the FDA Amendment Act of 2007.

The focus of the post-market safety provision is addressed in Title IX of the FDAAA 2007. There are three specific areas to be discussed; Post-Market Safety Surveillance, Studies and Clinical Trials, and Risk Evaluation and Mitigation Strategies. During an FDA media teleconference on Sept. 27, 2007 regarding the *FOOD AND DRUG ADMINISTRATION AMENDMENTS ACT OF 2007 (FDAAA2007)* a FDA spokesperson stated “that this bill and its provisions are very consistent with what has been our FDA philosophy of being engaged in the total life cycle of these products to ensure their quality on the front end as they come in, in the pre-application process and to continue to stay engaged as they are now being utilized in larger populations that we continue to learn from that experience.”

- **Post-Market Safety Surveillance**

Post-marketing safety surveillance is designed to ensure that a product’s safety profile does not significantly differ from the marketing profile granted for approval. Recent safety related product withdrawals, lawsuits, and regulatory scrutiny have significantly increased the pressure on pharmaceutical and device companies to track adverse events well into a product’s post-launch lifecycle.

- **Studies and Clinical Trials**

The Act, enables the FDA to require sponsors to conduct post-approval clinical trials or studies to assess risk related to the product, assess signals of risk, and identify expected serious risk based on data. The FDAAA2007 also authorizes the FDA to require labeling changes if the agency becomes aware of new safety information it believes should be included in the label.

- **Risk Evaluation and Mitigation Strategies**

Under the act, the FDA may require a risk evaluation and mitigation strategy to ensure the benefits outweigh the risk of the product.

- **Medicare/Medicaid**

For a product to be successful, physicians and patients must be reimbursed for expenses. Medicare, Medicaid, and other third party reimbursement is the means by which products are used by physicians and paid for by patients. Most recently, Medicare revised their guidance for national coverage determinations to include evidence development.

The specific data developed through the coverage and evidence development process may help ensure that the care provided to a particular beneficiary is “reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member,” which is the standard set by law for Medicare coverage. To review the guidance for Medicare, go to: www.cms.hhs.gov/coverage.

- **Standard & Poor’s**

Standard & Poor’s is the world’s foremost provider of independent credit ratings, indices, risk evaluation, investment research and data. They supply investors with independent benchmarks they need to feel more confident about their investment and financial decisions. In November 2007, Standard & Poor’s released a new enterprise risk management analysis for credit ratings to be used by non-financial companies’.

There are four major analysis components regardless of the company or sector. The components include:

- Analysis of risk-management culture and governance
- Analysis of risk controls
- Analysis of emerging risk preparation
- Analysis of strategic risk management

Included in the analysis were risk types that are seen in the pharmaceutical and device sector. These risk types that may easily be applied to new pharmaceutical and device products include: market environment, liability lawsuits, physical damage, political risk, regulatory/legislative, financial market risk, reputation, technology failure, and data security.

Mitigating Risk

Mitigating risk is a complex process as the balance between product availability, liability, and safety is measured. One of the tools that are critical to this process is one of data collection. It is impossible to mitigate risk for FDA, Medicare/Medicaid, or Credit Rating if you have not collected product metrics.

- **Post-Market Safety Surveillance and Patient Outcome Registries**

In the pharmaceutical and device industry, post-market safety surveillance and patient outcome registries can play a critical part in mitigating risk. If we think back to the groups that govern the industry we can see the need for on-going safety surveillance and patient outcome registries.

- **Medicare/Medicaid and other Third Party Reimbursement**

Collecting additional patient data as part of the coverage process is critical to establishing or broadening insurance coverage for a product. Coverage with Evidence Development (CED) generates data on the utilization and impact of the item or service evaluated in the National Coverage Determinations (NCD) so that Medicare can 1) document the appropriateness of use of that item or service in Medicare beneficiaries under current coverage; 2) consider future changes in coverage for the item or service; and 3) generate clinical information that will improve the evidence base on which providers base their recommendations to Medicare beneficiaries regarding the item or service⁶.

- **Standard & Poor**

Critical data elements collected can provide information on safety and efficacy. Risk Control Processes cited by Standard and Poor's which may be directly related to the pharmaceutical and device industry include external disclosure, monitoring, internal reporting, training and prevention⁷.

Benefits of Mitigating Risk with Post-Market Safety Surveillance and Patient Outcome Registries

From a Marketing Perspective It's the perfect way to engage your customers and discover real-time and actionable insight into how your product is performing.

From a Clinical Perspective It's a unique and powerful method for the collection of observational or epidemiologic data, and it is becoming a widely adopted business tool in the pharmaceutical, medical device, biotechnology, academic and private healthcare settings.

From a Reimbursement Perspective Medicare and other third party payers use clinical evidence to make determinations about reimbursement.

From a Private Provider and Academic Medical Center Perspective It's an effective tool for gathering post-approval research to accelerate innovation, produce faster knowledge gains, and alert companies to potential problems quicker than any other available tool.

Strategic Reasons of Post-Market Safety Surveillance and Patient Outcome Registries

- Allows a company to collect demographic, observational, and treatment data from across many different clinical sites and institutions in real-time.
- Helps with predicting future revenues and with third-party reimbursement.
- Allows a company to identify and remedy product issues pro-actively.
- Provides marketing support by understanding the impact of your product in the marketplace, understanding impact of your competition, and building a physician community around the product.
- Collects information on off-label use.
- Can help identify where additional physician product training may be needed.
- Provides information on patient population trends and patterns which allows strategic planning by the sponsor company.
- Saves money by providing information on safety, efficacy, and utilization.
- Shows the companies efforts for risk mitigation which may impact the company credit rating.

Implementation Strategy

The problem is that even the development of applications by a sponsor company to address safety and outcomes can be considered a risk. The risks involved are financial resources to develop the tools, IT services such as employee time to develop/ program the software and provide support for end users (which are not internal), a security risk of hosting on an internal server, supportive services such as statistical support and adjudication support and most importantly the ability of the sponsor to show independence and completeness in reporting.

One of the key strategies is how to implement these tools and who should administer. As you read through the volumes of FDA information and guidances, one common theme is the completeness of reporting, favorable and unfavorable information. One of the ways to ensure complete reporting is through an independent group. The goal is to identify a group that is independent, provides ease of use technology, can link safety surveillance and outcomes together, provide clear and usable database reports, and can offer ancillary support services such as independent statistical, adjudication, and audit support. Understanding of the regulatory process and experience interacting with clinicians and sponsor companies is imperative.

References

1. Senate and House of Representatives of the United States of America in Congress. “Food and Drug Administration Amendments Act of 2007”, September 27, 2007.
2. U.S. Department of Health and Human Services, Food and Drug Administration. Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), “Guidance for Industry: Providing Regulatory Submissions in Electronic Format - Postmarketing Expedited Safety Reports.” May 2001.
3. Center for Devices and Radiological Health. “Ensuring the Safety of Marketed Medical Devices: CDRH’s Medical Device Postmarket Safety Program.”, January 18, 2006.
4. U.S. Department of Health and Human Services, Food and Drug Administration. Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), “Guidance for Industry: Postmarketing Adverse Experience Reporting for Human Drug and Licensed Biological Products: Clarification on What to Report”, August 1997.
5. U.S. Department of Health and Human Services, Food and Drug Administration. Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), “Guidance for Industry: Reports on the Status of Postmarketing Study Commitments — Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997”, February 2006.
6. DEPARTMENT OF HEALTH AND HUMAN SERVICES, Centers for Medicare & Medicaid Services. “Medicare Program: Review of National Coverage Determinations and Local Coverage Determinations”, Federal Register / Vol. 68, No. 216 / Friday, November 7, 2003 / Rules and Regulations.
7. Standard & Poor’s RatingsDirect. “Enterprise Risk Management Analysis For Credit Ratings of Nonfinancial Companies”, November 15, 2007.
8. Treasury & Risk: The Future of Finance Today, “Risk Management, Rating Risk Practices” January 2007.