

How to Avoid Becoming a Biotech Zombie

Part 2 Moving from Principles to Systems

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Putting business principles to work in biotech requires careful implementation of nine critical business systems.



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The first article in this three-part series aimed at helping companies avoid becoming one of the biotech zombies—companies that have never turned a profit or marketed a drug but somehow managed to survive for decades—presented some general business principles:

- Slow and steady wins the race: pursue careful, systematic growth.
- Stick to your core capability while remaining open to its strategic possibilities.
- Weave together the business plan and the commercialization process.
- Prepare for the unique stakeholder pressures at each stage of company evolution.
- Drive the strategic vision in daily decision-making.

Putting those principles to work requires careful installation of some critical business systems. However, in the biotech industry there is no one-size-fits-all organizational design, as there is in many other industries. Each biotech, depending on the relevant science and the product area—from pure biopharmaceuticals to hybrids, vaccines, technology platforms, or devices—is unique, requiring business systems designed for its particular purpose. Moreover, because a biotech company requires an enormous diversity of skills, extra care must be taken to integrate all of these systems to ensure that they work smoothly together.

The issue of vitality evoked by the zombie metaphor is particularly apt in this case—a biotech is more of an organism than an organization, more like a living

Business and regulatory intelligence gathering systems should be integrated to provide comprehensive scenarios.

thing than like a machine. Although we speak of systems like marketing and investor relations, it should be remembered that despite the familiar terminology, these systems aren't like the traditional organizational superstructure of departments and functions sitting atop the company's core activity. Rather, they must uniquely meld business and science as well as work tightly together if the company is to achieve profitability and scientific viability required for a biotech to thrive. Therefore, think first of what the system must do: what challenges are peculiar to the industry, the science, the company it must address, and then make sure all of the elements are firmly in place.

ALIGNING THE BUSINESS MODEL WITH THE SCIENCE: THE STRATEGY SYSTEM

Many companies fail to align the business model, including the commercialization plan, with the scientific platform. For example, a company may have a product that

has potential applications in many therapeutic areas, but instead of pursuing the more profitable path of outlicensing this intellectual property to companies that can pursue those applications, the company produces the product itself for a single, comparatively low-return application.

As products move through the commercialization plan and new doors open and others close as a result of the product performance, the strategy should be subject to constant review and, when necessary, adjusted through an ongoing strategy development system. Strategy review and formulation should not be relegated to the annual budget review process, as it is in more traditional industries, but should be addressed by the top management team, including the chief executive officer (CEO), chief financial officer (CFO), chief scientific officer (CSO), and chief regulatory affairs officer (CRAO), who regularly convene explicitly for that purpose.

Keeping the progress of the business plan and the science simultaneously in view, the strategy group is responsible for short- and long-term objectives, contingency planning, and developing strategic alternatives. For example, the group might ensure that clinical trials are designed to demonstrate product value in multiple patient subgroups and that protocols examine and uncover the cost and benefits of products in populations that represent future target markets.

Above all, the strategy group should remain flexible enough to go where the science leads, while creating business value. This is

sometimes easier said than done. For example, the scientists and inventors who establish and lead some biotechs may believe so fervently in their original vision for their innovation that they resist redirecting the company's efforts along a path that is much more likely to pass regulatory muster.

A high-performing strategy system that neither lets the business ride roughshod over the science nor makes of the science a disinterested, academic pursuit, can make all the difference between a scientifically and financially healthy company and the empty shells that are the industry's zombies.

SCANNING THE HORIZON: THE BUSINESS AND REGULATORY INTELLIGENCE GATHERING SYSTEM

Business intelligence gathering and regulatory intelligence gathering differ sharply, and require distinct capabilities and skills. Business intelligence focuses on market behavior, competitor actions, and threats such as the encroachment of offshore companies. Its practitioners are typically industry and business generalists. Regulatory intelligence focuses on the actions and intentions of regulators, and their likely effects on the company. Its practitioners are highly focused specialists, with extensive experience in the regulatory arena. Despite these differences, however, the two systems should be integrated to provide comprehensive, nuanced business, or regulatory scenarios.

Business intelligence gathering is relatively well understood and the skills and processes required to institute it are familiar. This is, however, not the case for regulatory intelligence gathering. Knowing how to monitor and analyze US Food and Drug Administration (FDA), European Medicines Agency Home (EMA), Japanese Ministry of Health, Labor, and Welfare rulings, and International Conference on

Quick Recap

- **The science** should be aligned with the business model.
- **The greatest** opportunities for creating a value-added quality system lie in non-mandatory standards and guidelines.
- **Crises can be survived** if you have an effective risk management system.
- **Hiring the right people** can mean the difference between a successful product and a blockbuster product.

Harmonisation (ICH) guidelines is a craft that requires great familiarity and strong working relationships with the relevant regulatory bodies. Companies that lack the subtle ability to correctly interpret communications and guidance from regulators often fall victim to hearing what they wish a regulatory agency had said rather than what the agency really meant. Such wishful thinking and selective hearing has more than once been responsible for overly optimistic press releases or investor guidance that was entirely unwarranted and which, in the long run, created reputation-damaging volatility in a company's valuation. Just as much as superior business intelligence, the ability to read accurately the regulatory tealeaves confers significant competitive advantage.

The combined business and regulatory intelligence system should include, in addition to business and industry experts, a first-rate scientific officer and seasoned regulatory affairs professionals, who really understand where the regulatory chips are likely to fall. The system should also include feedback mechanisms to alert leadership to competitive, scientific, medical, operational, or regulatory problems. An integrated business and regulatory intelligence gathering system gives the company the ability to outflank the competition, pre-empt problems, maintain an efficient and realistic commercialization plan, and absorb regulatory information—favorable or unfavorable—and translate it into opportunities.

STAYING ALIVE: THE INVESTOR RELATIONS SYSTEM

In large, publicly traded companies, investor relations means dealing with analysts, oversee-

ing US Securities and Exchange Commissions (SEC) filings and annual reports, and satisfying shareholders. In start-up and emerging biotechs, however, it means far more: securing the significant, regular infusions of funding that are the lifeblood of the company. Further, the CEO, other top officers, and sometimes board members must be actively involved

in interactions with venture capitalists (VCs), potential alliance partners, and other investors. In a landscape where biotechs are competing for funding with many other investment opportunities that routinely come the way of VCs, the failure to maintain a systematic, intellectually honest, investment-savvy approach to potential investors can be disastrous.

Concepts such as PAT, QbD, and design space encourage greater scientific understanding of processes and products.

Simply trying to dazzle investors with science and limitless market possibilities no longer suffices. The investor relations system must be able to provide compelling answers to the questions that today's investor will ask about risk-adjusted value, investment horizons, commercialization strategy, intellectual property, the reimbursement environment, company culture, business and operating systems, supply strategy, and more. Not to mention the science, which is a potential minefield for biotechs that assume potential investors won't understand the science underlying the opportunity or be able to analyze it adequately. Being able to answer all of those questions requires not simply occasional intensive efforts devoted to developing investment pitches, but a dedicated system that keeps the evolving investment rationale fresh. There is perhaps no better way to maintain the marriage of business and science than to be able at every stage of the company's lifecycle to answer this question in the most detailed way: "Why should an investor give me money now?"

ACHIEVING EXCELLENCE AND COMPLIANCE: THE QUALITY SYSTEM

Some of the components of an effective quality system should be designed based on the company's business model, others are mandated by law, and still others should be designed with widely recognized standards and non-mandatory regulatory guidance in mind.

For a company whose business

model is vertical integration—taking a drug from discovery to market—the quality system should be designed to interface with other key departments for mutual problem-solving and communication, in addition to handling field monitoring. By contrast, a company whose business model depends on outlicensing must have a quality system capable of transferring its innovation to a licensee and then continuing to monitor the product's performance in the market to ensure that the company can respond appropriately and quickly to any adverse developments. The company's quality system should also include a mechanism for retrieving information on performance from licensees and may also entail having personnel on-site at the licensees' facilities. The quality system for a company that intends to outlicense but has not yet done so should be focused on Quality by Design (QbD) to ensure that they get it right from the first.

Quality components mandated by law include compliance, customer service, and product design. Further, manufacturers of devices and hybrids are required by law to establish design controls and meet quality systems regulations (QSRs) pertaining to purchasing controls. They must also meet the requirements for management responsibility, which are laid out in 21 *CFR* 820. Nonbinding standards and guidelines that can help shape the quality system include those promulgated by the International Standards Organization (ISO), ICH, FDA, and EMEA.

Because the quality components

necessitated by the business model and by law are likely to be obvious, familiar, and inescapable, the greatest opportunities for creating a significantly value-added quality system lie in non-mandatory standards and guidelines. Achieving ISO certification for your quality management system signals your company's commitment to quality and international standards and helps establish valuable credibility with industry partners, government authorities, and the public. Further, concepts such as process analytical technology (PAT), QbD, and design space (DS), which figure prominently in ICH Q8 and ICH Q9, encourage greater scientific understanding of processes and products and hold out the promise of a lighter regulatory burden for companies that adopt them. But because the regulatory agencies don't spell out precisely how to go about it, some companies fail to take advantage of the opportunities those principles offer for reducing compliance risk, establishing more robust processes, continuously improving and creating more regulatory room in which to operate. Companies that take advantage of these opportunities will not only establish greater trust with regulators but also gain additional advantage over competitors whose quality systems lack such capabilities and therefore slow their progress to market, enmesh them in compliance issues, and bog them down in costly rework.

ADDRESSING EXPOSURE: THE RISK MANAGEMENT SYSTEM

Regulatory hurdles, complex uncertainties, and the difficulty of doing something that's never been done before make each biotech a uniquely risky business both scientifically and financially. A comprehensive risk management system should be designed to perform four critical tasks: identify risks, calcu-

late their impact, mitigate their potential effects, and recover from crisis.

The system should be able to identify internal and external risks, including gaps in core competencies, management bandwidth, product development risks, times to various gates in development, regulatory hurdles, competitive risks, and many other factors. It must also quantitatively calculate the likely risks and their effect on cash flow.

The system should also be able to determine which risks are critical—the “killer concerns” that could seriously derail the company—and develop plans to mitigate those potentially disastrous occurrences. For example, if you’re in a race with a competitor to get to market first, anything that slows down commercialization could severely diminish the lifecycle sales of the product. To minimize the risk of being second, you might decide to go after only one indication for therapeutic treatment. You could then pursue only a narrow segment in Phase 3 clinical trials, requiring only about one year plus the six months required for an expedited review. But if you chose to pursue three indications instead of one, you might be tied up in clinical trials for as long as four years or more.

When it comes to crisis recovery, the challenges for life sciences companies are extraordinarily acute because the lives of patients are often at stake. The risk management system should therefore include a fully agreed on action plan that can be rapidly and comprehensively implemented in the event of a major crisis. It should be designed to address the crisis immediately and in full, with the ultimate goal of re-establishing genuine trust with the public and regulators. Moreover, it should be designed with the underlying science of the product in mind,

which allows you to project worst-case scenarios and plan your responses to them.

MAKING THE MOST OF INTELLECTUAL CAPITAL: THE KNOWLEDGE MANAGEMENT SYSTEM

Many companies lack first-rate problem-solving and decision-making capabilities because of deficiencies in the way knowledge is managed, circulated, and executed throughout the company, not because of deficiencies in their personnel. The solution lies in a cross-functional knowledge management system that delivers critical business, scientific, and operations intelligence when and where it’s needed. Such intelligence should include metrics for quality, risk, manufacturing failures, compliance, and all of the other key parameters of the operation. An enterprise resource planning (ERP) system should be implemented to provide instant answers to basic business questions. Superior knowledge management helps integrate functions, facilitates faster and better decisions, and produces greater return on intellectual capital.

GETTING THE WORD OUT: THE MARKETING SYSTEM

The overwhelming importance of marketing in the life sciences has been generally recognized, but in biotech, the focus should be widened to include, not only the competitive landscape, but also the reimbursement environment. Reimbursement, of course, can’t begin until product approval, but you shouldn’t wait until then to address the issue. As early as Phase 2 of drug development, the marketing system should be geared up to undertake the advocacy of the innovation across government and private payers who want to understand the likely business implications, as well as healthcare providers who

want to understand the science.

Unfortunately, this early alignment of marketing with securing reimbursement rarely happens, sometimes because the company’s founding scientist or inventor, with great faith in the idea, believes that the rationale for reimbursement will be perfectly obvious. Companies that make reimbursement an early concern of marketing will achieve product profitability quickly, while those that don’t may find reimbursement lagging by as much as four years from the time the product is approved by the FDA.

GETTING BETTER ALL THE TIME: THE CONTINUOUS IMPROVEMENT SYSTEM

Because there are so many competing improvement methodologies—from Six Sigma to Lean, Baldrige assessments, ISO 9000, and more—organizations often get bogged down in unproductive discussions about which to use. Experience shows that the better approach is to use whichever tool is most appropriate for the problem at hand while integrating all of the tools under the umbrella of a holistic system for continuous improvement. Such a system should work in all types of processes, functions, businesses, and cultures. It should provide a common language, tool set, and roadmaps for improvement. Management systems must be in place to support and guide improvement. Finally, it must address the three key aspects of process management: process design and redesign, process improvement, and process control.

COMPETING ON TALENT: THE HUMAN RESOURCES SYSTEM

As the primary source of value creation has shifted in most major industries over the past 20 years from tangible assets to knowledge and innovation, companies have

come to recognize that they are ultimately competing on the basis of talent. Nowhere is that truer than in biotech, where people are critically important because their unique skills—in manufacturing, development, scale-up, technology transfer, and regulatory strategy—create much of the value. For example, not many people know how to make stem-cell products or nucleotide-based products. Biotech requires not merely workers, but craftspeople who can make vaccines, combination products, therapeutic proteins, and cell and tissue products. In fact, having the right people can make the difference between a threefold return on investment and a tenfold return.

The human resources (HR) system therefore stands at the critical intersection of strategy and execution. The HR function must of course still fulfill its transactional

functions: payroll, benefits, and the like. But now more than ever it must take the lead in developing a human capital strategy that is tied to the company's business model and the science. That means that the chief human resources officer (CHRO)—a new C-level position rapidly spreading across industries—must be granted a seat at the top leadership table. It should be noted, however, that finding strategically minded HR executives with biotech experience can be difficult, but it is worth the trouble to ensure that you have the HR system that talent-based competition requires and a leader who is empowered to make it work.

The systems, from strategy to human resources, however, are only part of the story. They are the structure—the anatomy, so to speak—of the living company. Those systems must also be infused with life through the critical

processes that create a genuinely vital company. Those life-giving processes are the functions—the physiology of the company—that are the subject of the next article in this series. ♦

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