From Biotechnology to Nanotechnology: Parallels in State Regulatory Review

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ABSTRACT

A critical juncture for any emerging technology is the transition from research and development to commercial production. For many companies, particularly smaller ones, opaque state and local permitting processes and environmental regulations can hamper progress to market by imposing unforeseen and possibly high additional resource burdens. The prospect of navigating a convoluted state and local government regulatory system may prompt companies to look elsewhere to site their manufacturing and production operations.

This case study of the process by which Massachusetts reviewed and revised environmental regulations pertaining to the biotechnology industry provides useful insights into the potential regulatory issues facing the nanotechnology sector broadly defined and offers lessons for how industry representatives may need to work with state officials to adapt regulatory frameworks to sector-specific needs.

Keywords: regulation

Economic Potential of Biotechnology

Biotechnology, broadly understood, is the use of cellular and molecular processes from living systems to make or assist in making an array of pharmaceuticals and other products with therapeutic or human enhancement properties.[1] It has become a significant sector of the Massachusetts economy with at least 280 firms and 30,000 employees, making it one of the largest regional concentrations of biotech companies in the world. [2]

Massachusetts is attractive for biotech research and development (R&D) because of its well-educated workforce, first-rate research universities and medical centers, availability of venture capital, and concentration of legal, technical, workforce development and support services. Beyond current strengths in R&D, biotechnology is seen as crucial to the Commonwealth's *future* economic viability through job creation, job retention, commercial product innovation, and production.

The Massachusetts Biotechnology Council (MBC), the industry's trade association predicted in 2002 that if conditions remained good the ten percent growth seen in biotech over the previous ten years could continue with an additional 100,000 new instate jobs by 2010 and more that $1 billion in cumulative personal income tax revenue.[3]

The Biotechnology Industry: Catalyst for Action

The MBC represents over 500 companies, academic institutions and service organizations involved in the life sciences and healthcare industries and has the financial capacity to make its views known, with gross receipts in FY2005 of $3.8 million and total assets just over $3 million. [4]

In 2002, the MBC published *MassBiotech 2010: Achieving Global Leadership in the Life-Sciences Economy,* perhaps its most influential work to date. The report was the culmination of a three month-long study of the Massachusetts biotech industry conducted jointly by the MBC and the Boston Consulting Group (BCG), and was intended as a call to action for policy makers in Massachusetts. The report outlined a vision of growth for the state's biotech industry, and recommended a course of action for achieving that vision. The report and its recommendations were informed by interviews and working committees involving numerous industry leaders, academics, and government leaders, a collaborative process between government and industry that apparently helped to ensure an audience invested in its findings.

According to the report, while Massachusetts exhibited great strengths in biotechnology related R&D leading to start up of new companies, as biotech companies aged they were less likely to remain in Massachusetts. The report found that while biotech companies typically kept eighty percent of their workforce in the state during their initial five years of existence, that percentage drops to about half by the time a company is more than 16 years old. [5] The report did not provide a definitive explanation for this drop off but pointed to a comparatively high cost of manufacturing and production, along with what it argued was a low array of economic incentives and the perceived complexity of the Commonwealth's regulatory rules, all of which the report's authors argued made a profitable and efficient product to market transition more difficult in comparison to other states.

Retaining such production is important, the MBC report argues, because as "activities move down the value chain, a much wider range of job opportunities becomes available—for example, positions as lab technicians, in manufacturing or quality control and assurance. Such jobs spread the benefits of biotech employment to a far broader range of the population."[6] According to the report, the industry perception was that siting a production plant in Massachusetts was often problematic due to an array of state and local zoning and permitting delays, exacerbated by the absence of a standardized statewide approval process.

The Commonwealth of Massachusetts has a strong legacy of home rule going back to colonial times, and its 351 cities and towns have varied and often complex zoning and planning requirements. Navigating these diverse rules can be time consuming and thus costly in terms of construction and operation delays. In addition, state government permitting requirements related to air and water pollution and solid waste were seen as overly burdensome and complex, and construction delays as a function of permit issues translated into longer product time-to-market and a substantial opportunity cost for biotech firms.

A notable exception to what the industry considered an opaque and unwieldy process was the 1992 effort to assist Genzyme in obtaining a site for a new manufacturing plant in Boston's Allston Landing section. Then-Governor William Weld worked closely with local, state, and federal agencies ranging from the Boston Redevelopment Authority (BRA) to the Massachusetts Turnpike Authority, and even, Conrail, to expedite the permitting process and thereby lower the opportunity costs of siting the facility in a complex urban environment. But it took a governor and the political capital of key actors to ensure that a locally based company was able to find and acquire a local site for manufacturing operations.

The MBC report concluded with a call to streamline the Commonwealth's regulatory system and create an expedited state and local permitting process to smooth the transition to manufacturing for current and future biotechnology operations. The analysis and objectives outlined in the MBC report received important initial support from key state government leaders.

Biotech Rules Proposal

In the year following the report's release the MBC, working with MassDevelopment (the Commonwealth's development finance agency), the Executive Office of Environmental Affairs (EOEA), and the Executive Office of Economic Development (EOED), brought together stakeholders from industry and state government to explore specific ways by which Massachusetts could improve state regulations affecting the biotech industry. In April 2004 the MBC submitted a set of draft recommendations to the state that included a broad education and technical assistance program, state and local zoning and planning program revisions, regulatory improvements, and innovative models to expedite siting new biotech facilities.

At the direction of then-Governor Mitt Romney, DEP responded with a multi-program review in which it pulled together department staff with significant interactions with the biotech industry and solicited input on how to streamline and clarify DEP's interface with the industry.[7] In March 2005 the agency released its "Proposal to Streamline and Strengthen Environmental Requirements for Biotechnology Facilities" for public comment. The proposal outlined specific regulatory revisions and additions designed to retain and attract biotech manufacturing in the Commonwealth.

The proposal began with a regulatory definition of biotechnology important for current and future regulatory review as "the use of cellular and molecular processes from living systems to make or assist in making products" and biotech operations as those "that manufacture products regulated by the FDA as medical devices, drugs, or biologics, and for which appropriate Investigational Notices or Applications have been filed with FDA."[8] Specifically, DEP proposed amendments to air quality standards and industrial wastewater regulations that would be available only to biotechnology companies which manufacture products regulated by the U.S. Food and Drug Administration (FDA) as drugs, biologics, or medical devices such that these exemptions would apply to those companies just as they reach the manufacturing scale. A third proposal relative to hazardous waste regulation applied broadly to industries beyond biotechnology.

Air Pollution Control **[310 CMR 7.00]**
All industries that emit airborne waste from power production or manufacturing operations must record and track all air pollutant emissions and calculate facility-wide totals, including any low level emissions otherwise exempted from DEP permit and regulation requirements. The amendments to the Air Pollution Control regulations added two exemptions from permit requirements specifically for biotechnology operations that may emit volatile organic compounds (VOCs), which broadly encompass most compounds containing carbon.

Preconstruction Waiver: Unconditional exemption that codifies emissions caps and best management practice requirements otherwise applied through individual permits. In enacting this revised rule, DEP reasoned there was little likelihood that an affected laboratory would exceed the current permitting threshold of one ton of VOC emissions per year.

Surface Disinfection: Conditional exemption or "permit by rule" for activities that produce more than a *de minimis* (in this instance far less than one ton per year) level of emissions but less than permitting options with higher minimum thresholds, such as those under U.S. EPA's New Source Review (NSR) preconstruction permitting program authorized by the U.S. Clean Air Act. Mass DEP had precedent in granting conditional exemptions to air pollution regulations, having previously proposed similar treatment for general use of engines and turbines frequently installed for back-up electric power generation by many industries, biotech included.

***Hazardous Waste* [310 CMR 30.000]**
Massachusetts General Laws (M.G.L. c21C) allow DEP to waive certain requirements when it has determined a particular hazardous waste or activity to be insignificant as a potential hazard. Proposed amendments apply to all generators of hazardous waste and include the hazardous waste component of mixed waste.

Case by Case Waiver permits hazardous waste generators to apply for a case-by-case waiver of any or all of the requirements under 310 CMR 30.00 that are *more* stringent than the minimum federal requirements promulgated under the federal Resource Conservation and Recovery Act (RCRA) [9] which avoids inconsistency between state and federal laws.

The applicant must prove, and DEP must verify, the wastes and activities are insignificant as a potential hazard to public health, safety, welfare or the environment, or adequately regulated by another government agency consistent with the RCRA. This waiver was technically permitted under existing regulations but seen as opaque and thus under-utilized.

Blanket Waiver: Blanket waiver of the treatment licensing requirement to conduct elementary neutralization (or pH adjustment) of aqueous corrosive waste in tanks or containers. Here, federal hazardous waste programs allowed such treatment without a license while Massachusetts statutes did not.

The revised regulation created a waiver from the licensing requirement to allow companies to treat small amounts of corrosive aqueous waste on site but stipulated management and testing standards and required notification to DEP of waste levels and amounts. This exclusion from licensing *elementary neutralization* (pH adjustment of aqueous corrosive waste) over other forms of treatment is due it being a relatively simple, low-risk procedure, and the corrosive waste would be managed as a hazardous waste until it is made non-hazardous by elementary neutralization.

***Water Pollution Control & Industrial Wastewater* [314 CMR 17.00] & [257 CMR 2.00]**
DEP proposed a new section to existing water pollution control regulations providing a comprehensive standard applicable solely to biotechnology operations.

The new section would serve as a permit-by-rule in setting minimum effluent limits and management standards for certain biotechnology operations that discharge industrial wastewater to the sewer system of a Publicly Owned Treatment Works (POTW) with an EPA approved Industrial Pretreatment Plan (IPP) other than the Massachusetts Water Resources Authority (MWRA). At the time of the proposal in 2005 this applied to 47 of the 130 POTW's in the state. Those operations discharging to a non-approved POTW or to ground and surface waters would remain subject to state permits. The stricter limit would apply in cases where municipal authorities set effluent limits for chemicals that overlap with this proposed regulation.

The proposed regulations also classified seven industrial wastewater treatment systems commonly used by biotech operations along with set staffing and reporting requirements for each.

Public Comment & Revisions

Release of the DEP proposal in June 2005 triggered a standard thirty day process for seeking public comment from industry, local, state, and federal government agencies, interested public and nonprofit organizations, and, in theory, individual citizens. DEP advertised a public comment period to run June to July 2005 and held six public hearings in different regions of the state to receive oral and written testimony.

Comments were received from the MBC and other industry representatives, several state agencies and special authorities such as the Massachusetts Water Resources Authority (MWRA). A number of public interest advocacy organizations submitted comment including the Environmental League of Massachusetts, Healthcare without Harm, Sciencecorp, and the Toxics Action Center.

Comments from the biotech industry included several calls for greater expansion in the applicability of the amended regulations. Hazardous waste comments focused on the need to ensure clarity of language in the revisions and to include participation by the Hazardous Waste Advisory Committee (HWAC) and the public in establishing criteria by which to determine the waivers.

The water pollution and industrial wastewater proposals elicited the greatest volume of concerns. The proposed effluent limits for mercury generated especially hostile responses from environmental and public health groups

since they were set at 0.08 mg/l (80 ppb), 80 times higher than that allowed under existing regulations. In light of such significant opposition, DEP decided not to include the effluent limits in the final version of the amendments and expressed its commitment to continuing work with key stakeholders to examine the feasibility of including state-wide minimum effluent limits in the future.

DEP published final air, water and waste amendments in November 2005.

However, in January 2007 DEP promulgated revisions that streamlined state permit and approval requirements for sewer connections, sewer extensions, and industrial wastewater management contained in 314 CMR 7.00. This revision negated the need for biotechnology specific provisions [314 CMR 17.00] because it covers all defined industrial users and industrial waste. These revisions define "Industrial User" as a source of indirect discharge and "Industrial Waste" as any liquid, gaseous, or solid waste substance or a combination thereof resulting from any process of industry, manufacturing, trade or business or from the development or recovery of any natural resources.

In March 2007 DEP announced *further* revision to 310 CMR 7.00 (Air Pollution Control) as part of a broader "revision to the Massachusetts State Implementation Plan (SIP) to be submitted to the EPA to attain and maintain certain National Ambient Air Quality Standards. [10] In this case, the revisions encompassed more of the air pollution regulations that apply to all industries. The changes made minor technical corrections and updates. Minor revisions to the biotechnology operations [310 CMR 7.03(25)(b)] clarified that the owner / operator of the facility is responsible to the regulations and added a new organic material emission cap (<10 tons per year) to provide small facilities a mechanism to limit their facility's potential emissions.[11]. DEP promulgated the amended regulations in June 2007 with no further changes expected.

Parallels for Nanotechnology

The applicability of this case to the nanotechnology sector, broadly understood, is clear. States are critical players, both as primary enforcers of federal environmental, health, and safety regulations and as regulatory innovators in their own right. States also seek a balance between encouraging economic development and ensuring public and environmental health and safety. The role of states as regulatory agents will loom larger as nanotechnologies move to commercial production. This case study of the process by which Massachusetts reviewed and revised environmental regulations pertaining to the biotechnology industry provides useful insights into the potential regulatory issues facing the nanotechnology sector and lessons about how industry representatives may need to work with state officials to adapt regulatory frameworks to sector-specific needs.

The Massachusetts Department of Environmental Protection, under current statute, has regulatory authority over all industrial users, which can and does extend to any nanotechnology based manufacturing operation that produces or emits air, water, and hazardous waste pollutants. DEP permitting requirements relate to minimum thresholds such as tons per year or parts per billion. Given that the size and related risk of nanoparticles and structures remain untested relative to many health, safety and environmental standards, it is unclear how DEP and other state and federal regulatory authorities will manage these new products and associated waste and production operations.

However, DEP is paying attention to research and development as well as best practices emerging from industry, other states, and academic research. DEP maintains a Emerging Contaminants Workgroup of which a staff led subcommittee on nanotechnology brings together both high and field level staff from an array of offices within the agency. DEP also hosts and conducts cooperative conferences and information sessions with industry and government leaders to share knowledge and build partnerships. Such early collaboration may be key to producing regulatory responses that are relevant, effective, efficient, and transparent.

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[1] Amendments to 310CMR 7.0, Massachusetts DEP http://www.mass.gov/dep/air/laws/regulati.htm#bio
[2] Massachusetts Biotechnology Council and The Boston Consulting Group, *MassBiotech 2010: Achieving Global Leadership in the Life-Sciences Economy* (2002), 11.
[3] *MassBiotech 2010*: 8.
[4] U.S. Internal Revenue Service Form 990 (2005), at www.guidestar.org.
[5] *MassBiotech 2010*: 33.
[6] *MassBiotech 2010*: 33.
[8] Department of Environmental Protection, "Proposal to Streamline and Strengthen Environmental Requirements for Biotechnology Facilities," (2005), 2.
[9] RCRA is 42 U.S.C. s/s 6901 et seq. (1976) and gives the EPA the authority to control hazardous waste from the "cradle-to-grave." RCRA also set forth a framework for the management of non-hazardous wastes.
[10] Massachusetts Department of Environmental Protection, "Background for the Amendments to Regulations 310 CMR 7.00 for the Control of Air Pollution" (March 2007), 1.
[11] Massachusetts Department of Environmental Protection "Draft Amendments to Regulations 310 CMR 7.00 for the Control of Air Pollution" (March 2007), 5.