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Lynn L. Bergeson is managing partner at Bergeson & Campbell, P.C. She can be contacted on +1 (202) 557 3801 or by email: lbergeson@lawbc.com.

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The importance of regulatory diligence in funding

BY LYNN L. BERGESON

Lawyers counselling companies in the biotechnology, biopesticide and related crop protection and industrial biotechnology areas appreciate the critically important role federal agencies play in ensuring the success of start-up businesses.

Federal agencies, including the US Environmental Protection Agency (EPA) and the US Food and Drug Administration (FDA), among others, wield enormous power over businesses that require premarket product approval. While we product approval practitioners know this, it comes as a bit of a surprise when investors, poised to make multimillion-dollar investments in start-up businesses, neglect to focus on the regulatory integrity of the start-up. This lack of focus invites costly mistakes. This article explains why, and how to avoid making these mistakes.

Start-ups and product approvals

Promising innovations of any sort are exciting, and we need innovations in the industrial and agricultural chemical technology space now more than ever. Well-informed investors know that funding a promising new biopesticide that enhances crop yields with minimal environmental impact offers great potential for significant return on investment. These new products can only do so, however, if they are competently stewarded through the gruelling regulatory gauntlet of premarket product approval.

With respect to products intending to prevent, destroy, repel or mitigate any pest, for example in the US, the US Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) applies. FIFRA's jurisdictional reach is broad. A "pest" under FIFRA means all the critters suggested by the common understanding of the term (insects, rodents and weeds, among others).

The term also encompasses less well-known pests, including any other form "of terrestrial or aquatic plant or animal life or virus, bacteria, or other micro-organism (except viruses, bacteria, or other micro-organisms on or in living man or other living animals)". This latter category includes innovations, such as biologically produced pesticides that optimise the inherent pest-fighting abilities of existing plants and microbes, as well as more conventional technologies that modify the genetic composition of micro-organisms for plant protection purposes.

Unsurprisingly, the EPA's Office of Pesticide Programs has been overwhelmed with new product approval applications in response to coronavirus (COVID-19). Many innovators have correctly optimised the urgent need for products and have developed new surface disinfectants with emerging viral pathogen claims for SARS-CoV-2, the novel coronavirus that causes COVID-19, in response to COVID-19. The EPA must approve all such products as a condition of their commercial distribution and use. The approval process is demanding and time- and resource-consuming, and the outcome is uncertain.

These inconvenient facts are often not well understood by innovators or investors.

A detailed overview of the product approval process is beyond the scope of this article. There are a few key points, however, that are helpful in understanding the importance of regulatory diligence.

First, that chemical innovations require product approval under FIFRA (or industrial chemical innovations under FIFRA's counterpart, the Toxic Substances Control Act) seems not in all cases to be part of the commercialisation roadmap. Hot start-ups are quick to patent their innovations, but often neglect to appreciate the EPA's role as a commercial gatekeeper. It is not patent protection, however, that greenlights commercialisation – it is the EPA's legal finding that a new product, whether agricultural, antimicrobial or industrial, poses no unreasonable risk to human health or the environment. The EPA can only make this legal finding after engaging in a rigorous, and often indeterminate in terms of length, review of the intrinsic hazard and potential risk properties of the chemical innovation, expected conditions of use, and toxicological and environmental fate data and information.

The EPA undertakes this review in the context of an administrative process that carefully defines the terms and rules of engagement that apply to innovators seeking product approval. If the rules are not well understood or followed, or the timetable not met, the agency can delay or deny the product's approval. Even if administrative or judicial review options were more promising than they are (and they are not promising), the delay to market can cripple or eliminate any expected return on investment the innovation promises.

Second, the rules of engagement are nuanced and generally require an experienced understanding to appreciate their material influence on product approvals. Diligence in Series A, B or C funding opportunities may elicit answers to questions that command yes or no answers, but the truth behind the answer may offer a different narrative entirely. Yes, a FIFRA registration or other product notification may have been made, but the timing and quality of the application dictate the success of the submission. A poorly supported application guarantees failure or significant delay, and any administrative determination can be prejudicial to later approval filings.

An example may be helpful. Assume a start-up business engineered a promising new biopesticide active ingredient, with food uses, and is looking for $20m in Series B funding. Under the EPA's timetable, established under the Pesticide Registration Improvement Extension Act of 2018 (PRIA 4), this product would be classified as a B580 submission and the EPA's decision review time would be 20 months from application submission. This means once the start-up submits to the EPA a detailed and technically compelling FIFRA application, it will take no less than 20 months for the EPA to review and make a legal determination under FIFRA whether the product can be sold or distributed for the product's intended purposes. The time, testing and investment needed to prepare the application predate the 20 months. In short, the process takes anywhere from two to four years post proof of concept.

Diligence may elicit the answer 'yes' when an application is submitted, but the regulatory trajectory may be different than the category suggests for any number of reasons, and of course, the response is agnostic as to probability of success. The start-up can have all the proof of concept information and promising efficacy data in the world, but if the stringent EPA guideline data are not conducted according to good laboratory practice standards, or the application is lacking a study the EPA believes is needed, or the data are ambiguous, or a dozen other variables play out, the EPA's review will be delayed, or worse, will elicit an adverse result.

The probability of delay correlates with the novelty of the innovation. The less experience the EPA has with a particular molecule, new active ingredient or new use pattern, the greater the likelihood of delay. If the start-up is unfamiliar with the regulatory process, there are enormous opportunities for significant delays, demands for new data, new testing protocols, or other regulatory demands that add significantly to the bottom line and delay market entry, thus denying return on investment. There are other, less obvious but consequential, costs. Transaction costs can be steep, and the reputational damage, as between the start-up and the EPA or other regulatory agency, and the start-up and potential customers, can be irrevocably damaged.

Third, those unfamiliar with the process, including start-ups and investors new to this commercial space, may not know that the EPA often 'renegotiates' PRIA 4 deadlines. Agency glitches can also confound the review process. It is not unheard of, for example, that an EPA front-end processing glitch can add several months or more to the review process. As a result, a new deadline can extend far beyond the limit of the PRIA 4 category. Sometimes the negotiation occurs late in the timeline and only after a problem has surfaced. Careful diligence demands a thorough review of the regulatory trajectory. A delay to market can translate into multimillion-dollar losses in seasonal markets, brand damage and commercial disruptions that could mature into lawsuits. Recourse against the government is seldom an option, and even when options exist, the path is long and costly, and the outcome is uncertain.

Avoiding problems

The EPA and other regulatory agencies are under increasing scrutiny to review carefully new chemical technologies. This will be especially true under the Biden administration. Standards are high, and government agencies are very good at what they do. Investors may wish to reassess the diligence they devote to regulatory issues in funding start-up businesses whose success or failure is contingent upon premarket government approval.

Three points are critical. The first is recognising that regulatory diligence is essential, and investors should not trivialise it. There seems to be a view in the investment community that regulatory product approvals are less consequential than they are. Where this view comes from is unclear, but it is dead wrong. This area demands careful scrutiny.

Second, if the entity seeking funding employs in-house or external expertise in managing regulatory approvals, due diligence demands that this person or expert be carefully questioned about the regulatory trajectory of any product approval that may be driving the investment opportunity. It is important to dig in and understand the nature of the product and the scrutiny the government is directing to it.

Third, investors should know their limitations and retain expert assistance in evaluating the wisdom of an investment that is heavily dependent upon government approval. Truth-testing the documents in the data room and the interpretation of those documents with regard to product approval are essential components of due diligence. ■