Commentaries

An Analysis of TSCA Reform Provisions Pertinent to Industrial Biotechnology Stakeholders

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Introduction

The Frank R. Lautenberg Chemical Safety for the 21st Century Act, P.L. 114-182, significantly amends the Toxic Substances Control Act (TSCA). The Act was signed into law by President Obama on June 22, 2016. The date of signature is both the date of enactment and of entry into force of amended TSCA (referred to in this article as ''new'' or ''amended'' TSCA to refer to Pub. L. No. 114-182 and ''old TSCA'' when referring to the prior version (Pub. L. No. 94-469)).[1] New TSCA fundamentally changes the U.S. Environmental Protection Agency's (EPA) approach to evaluating and managing industrial chemicals, including genetically engineered microorganisms. The body of changes, the careful balancing of countless competing needs and interests, and artful drafting yield a statute that has been greatly strengthened and addresses virtually all of the deficiencies that have impeded TSCA's effectiveness over the years.

The changes are consequential, and stakeholders in the industrial biotechnology community could be greatly impacted by them, depending upon how EPA interprets and discharges its new authorities. This article highlights key changes of which stakeholders should be aware, sets forth the law's schedule by which EPA is to implement the changes, and identifies opportunities for stakeholders to engage in rulemaking or other activities to help influence the implementation process to ensure that it is firmly rooted in a clear understanding of the science, and of the risks and benefits offered by products of industrial biotechnology.

Overview

TSCA gives broad authority to EPA to regulate industrial chemicals, including genetically engineered microorganisms that are considered chemical substances under TSCA.[2] ''Chemical substance'' is defined broadly to include ''any organic or inorganic substance of a particular molecular identity.''[3] EPA issued regulations in 1997 implementing its review of ''intergeneric microorganisms'' (which include bacteria, fungi, algae, viruses, protozoa, and related microorganisms formed by combining genetic material from organisms in different genera) under TSCA.[4] Summarized below are key TSCA provisions and a discussion of changes occasioned by new TSCA of most significance to industrial biotechnology stakeholders.

TSCA Section 2

TSCA Section 2(b)[5] sets forth U.S. policy regarding industrial chemical management under TSCA. Importantly, new TSCA does not change U.S. industrial chemical policy except to the extent the term ''data'' in Section 2 was replaced and arguably broadened by inclusion of the term ''information.'' Thus, it continues to be the policy of the U.S. that adequate information be developed on the effects of chemicals (and that industry is responsible for such testing), and that adequate regulatory authority exists to enable EPA to identify and control chemicals presenting ''unreasonable risks'' to health and the environment, but that this authority ''be exercised in such a manner as not to impede unduly or create unnecessary economic barriers to technological innovation while fulfilling the primary purpose of this Act to assure that such innovation and commerce in such chemical substances and mixtures do not present an unreasonable risk of injury to health or the environment.''[6] TSCA Section 2(c)[7] states that it is the intent of Congress that, in implementing TSCA, EPA ''shall consider the environmental, economic, and social impact'' of any actions taken.

TSCA Section 3 Definitions

Old TSCA's definitions remain intact, but new TSCA contains two important new definitions that can be expected to impact industrial biotechnology stakeholders. The first new term is ''conditions of use,'' which serves as a centralizing concept under which EPA determines how a chemical is made, processed, used, and disposed. The results of this EPA determination become the central focus of evaluations EPA conducts on existing chemicals under TSCA Section 6, and, to a lesser extent, under Section 5 where the ''conditions of use'' focus is a bit different, as discussed below.

The second new term is ''potentially exposed or susceptible subpopulation.'' As used in context, this term is intended to ensure that EPA, in conducting evaluations of unreasonable risk or in determining the need for and nature of control actions, considers and evaluates the risks presented to such populations (including pregnant women, infants, the elderly, and workers) when they are identified as relevant by EPA. How EPA will identify these populations, based on what data and information, how health effects will be correlated with what populations, and what control actions can be expected to be considered as a result are new and crucially important concepts that will invite highly consequential implications that stakeholders will need to engage with EPA in understanding and addressing. If, for example, ''sensitive subpopulations'' is broadly defined, immune-compromised individuals could

become the default subpopulation that must be protected depending upon the specific conditions of use that are relevant in any given situation.

TSCA Section 4 Testing

New TSCA gives EPA new authority to compel the development of data and submission of information. New TSCA Section 4(a)(2) authorizes EPA to use orders, in addition to test rules and consent agreements, to develop new hazard or exposure information, including information needed to review a notice under Section 5, perform a risk evaluation under Section 6(b), implement requirements imposed under Sections 5(e) or (f) or Section 6(a), or prioritize chemicals under Section 6. In using the new order authority, EPA must explain the basis and reasoning for the action, and is required to use tiered testing approaches, unless it can justify going directly to advanced testing.

Amended TSCA also retains and expands the scope of TSCA Section 4(f) under which EPA is required to take expedited action when new information indicates that a chemical presents a significant risk to humans. Old TSCA had limited this provision to cases involving cancer, gene mutations, and birth defects, while the revision removes this limitation. Importantly, amended TSCA also includes a new section that requires EPA to reduce and replace vertebrate animal testing when this can be scientifically justified and to develop and implement a strategic plan to promote the use of alternative test methods that are not based on vertebrate animals. The development of these new test methods and their application to microorganisms will have a significant impact on industrial biotechnology stakeholders, particularly innovators.

Whether EPA's new testing authority will significantly impact the preparation and qualitative review of notifications and exemption requests submitted on microorganisms is unclear. Current EPA regulations specify to a high degree of precision as to what information must be provided in a Microbial Commercial Activity Notification (MCAN) or exemption request, and EPA guidance provides further detail and a suggested data submission format. Submitters must, for example, submit information on microorganism identity, byproducts resulting from the manufacture, processing, use, and disposal of the microorganism, production volume, use information, and worker exposure and environmental release information. An MCAN submission must include this information ''to the extent such information is known to or reasonably ascertainable by the submitter.''

Despite the detailed information requested under current law, under new TSCA Section 4, EPA is authorized to use a rule, order, or consent agreement to require the development of more information to enable it to make a risk determination or to meet other allowed needs, including for the purpose of reviewing a notice under Section 5. How this expanded authority plays out with respect to possibly expanded requirements to be met by submitters in preparing and by EPA in reviewing MCANs and other notifications remains to be seem. Conceptually, the impact could be considerable.

TSCA Section 5 Manufacture and Processing Notices

Under EPA regulations, either a Section 5(h)(4) exemption or an MCAN under TSCA Section 5(a)(1)(A) is required for ''new'' microorganisms that are ''intergeneric''[8] at least 90 days prior to the manufacture, import, or processing of a ''new microorganism'' for a commercial purpose[9] or for a significant new use (SNU).[10] ''New'' microorganisms, like new conventional chemical substances, are those not included in the TSCA Inventory.[11]

The regulations define ''microorganism'' as an ''organism classified, using the 5-kingdom classification system of Whittacker, in the kingdoms Monera (or Procaryotae), Protista, Fungi, and the Chlorophyta and the Rhodophyta of the Plantae, and a virus or virus-like particle.''[12] An ''intergeneric microorganism'' is a microorganism formed by ''the deliberate combination of genetic material originally isolated from organisms of different taxonomic genera.''[13] EPA has clarified that microorganisms created through synthetic biology (chemically synthesized genes) can be considered intergeneric. The regulations are codified at 40 C.F.R. Part 725.

Exemptions from MCAN requirements include: the R&D exemption, which includes a TSCA Environmental Release Application (TERA) for R&D activities conducted outside a structure; the Tier I or Tier II exemption for manufacture and use in contained systems; and a Test Marketing Exemption Application (TMEA). If a notifier can satisfy the criteria and requirements for any of these exemptions, it may, depending on the particular exemption, commence manufacture or importation without notifying EPA (in the case of R&D activities conducted ''inside a structure,'' as discussed further below) or may obtain expedited EPA review (e.g., a 45-day review) for a TMEA rather than a 90-day MCAN review.

TSCA Section 5(h)(4)[14] and EPA's regulations provide that an MCAN exemption application will not be granted unless EPA can determine that the microorganism ''will not present an unreasonable risk of injury to health or the environment.''[15] New TSCA Section 5(h)(4) retains this ''will not present'' determination and, importantly, expands it to ''includ[e] an unreasonable risk to a potentially exposed or susceptible subpopulation identified by the Administrator under the conditions of use.'' Again, the inclusion of the potentially exposed or susceptible subpopulation language and the conditions of use identified in the notification could impose new challenges on submitters. At a minimum, this means submitters must be mindful of the relevance of sensitive subpopulations and to be extremely focused on knowing as much as possible about exposure and potential risk scenarios associated with all use conditions set forth in the application.

Amended TSCA retains much of old TSCA Section 5 but makes significant changes that could prove challenging unless MCANs are prepared strategically, thoughtfully, and comprehensively. Under revised Section 5(a)(3), EPA is required to review all new chemical notifications (both Premanufacture Notifications (PMN) for conventional chemicals and MCANs for microorganisms) and SNU notifications, and make one of three affirmative determinations and take required actions as outlined below depending upon the determination. In evaluating whether an ''unreasonable risk'' is presented by such cases, EPA is required to consider potentially exposed or susceptible populations identified as relevant and, in some cases, this includes the concept of ''under the conditions of use.'' EPA is required to undertake a staged review focusing initially on the determination and then on the action required given the determination

made. As is true generally under new TSCA, as part of this staged process, EPA is disallowed to consider cost or other non-risk factors in determining whether a chemical presents an unreasonable risk.

This approach to new chemical review represents a fundamental departure from old TSCA. Previously, new chemical innovators submitted a notice under Section 5 and if 90 days passed without EPA action, the submitter could commence chemical production or import upon the submission of a Notice of Commencement. Under new TSCA, this passive approach has been replaced by an active one and an affirmative EPA determination and any needed actions are required as a predicate to chemical production.

In satisfying the requirement that EPA make a determination and take required actions on all new chemicals and SNUs, there are three alternative determinations available to EPA under new TSCA. First, EPA can determine that the new chemical or SNU presents an unreasonable risk of injury to health or the environment, in which case, EPA is required to regulate under Section 5(f) and must then also promulgate a Significant New Use Rule (SNUR) or explain why not.

The second alternative consists of a series of ''or'' statements. EPA can determine the information available on the chemical is insufficient to permit a reasoned evaluation of the health or environmental effects of the chemical, **or** in the absence of sufficient information, the substance may present an unreasonable risk, **or** that the substance will be produced in substantial quantities and it either enters or may be anticipated to enter the environment in substantial quantities or there is or may be significant or substantial human exposure. If any of these determinations is satisfied, EPA is required to issue an order under Section 5(e) and either to implement a SNUR or explain why it is not taking this step.

The language for the second alternative is similar to that in old TSCA Section 5(e) except that in old TSCA, the first italicized ''or'' is an ''and'' (also non-risk factors or potentially exposed or susceptible subpopulations are not discussed in old TSCA). The effect of the change from ''and'' to ''or'' is to broaden substantially the scope and effect of the provision and allow EPA regulatory action based merely on a lack of hazard information. This new hazard-based authority can be expected to be of significant interest and potential concern to industrial biotech innovators.

The third determination EPA can make is that the new chemical or SNU is not likely to present an unreasonable risk, in which case, the notice submitter can commence manufacture/processing forthwith once the determination has been made, notwithstanding any remaining portion of the applicable review period. EPA is also required to publish a statement of its finding. This determination and its statement are not legally reviewable. EPA has stated that it intends to make all such notices available on its website and to publish them in the Federal Register.

New TSCA tightens the SNUR requirements for articles such that EPA must find that the potential for exposure to the chemical subject to a SNUR through the article justifies the notification. This requirement is expected to narrow the number and the scope of notifications required for articles.

Whether the new affirmative determination requirement under TSCA Section 5 can be expected to impose new challenges for microorganism innovators is unclear. On the one hand, historically, EPA has not been required to process a large number of MCANs or other biotech submissions and those that have been processed reportedly have not been found lacking critical information.

On the other hand, EPA has already gone on record in acknowledging that its Points to Consider document was developed ''to accommodate the development of new information relevant to risk assessment of biotechnology products regulated under TSCA.''[16] According to EPA, the Points to Consider document does not currently provide specific support for those using the emerging technologies of algae production and biotechnology. EPA stated that to keep its risk assessment process for biotechnology algae open and transparent, it intends ''to develop a separate document on the scientific and technological issues it currently understands to be key and unique for evaluating risks from the production and use of biotechnology algae.'' EPA convened an expert workshop in September 2015 and focused on the technical questions that EPA believes are important to its development of a biotechnology algae considerations document. EPA will develop its ''Considerations for Biotechnology Algae'' document in parallel with updating the Points to Consider.[17]

EPA notes that the number of TSCA biotechnology submissions is increasing rapidly. For 2015, EPA's website indicates that EPA received 34 MCANs. Through March 31, 2016, EPA's website shows that six MCANs have been submitted, a slower rate than last year.[18] According to EPA, most newer cases employ some form of biotechnology, such as the use of chemically synthesized, codon optimized genes. Importantly, EPA notes its recognition that some of the algae submissions are from companies that ''have had little or no experience with new substance review under TSCA.'' EPA expects that for these companies in particular, it will be useful to have focused guidance on how to submit an MCAN or TERA that includes information to help answer the questions that EPA will ask in its evaluation of their submissions. Consolidating information on emerging technologies will make it easier for interested parties to understand both what information is needed to support risk assessments, as well as why such information is needed. Presumably, EPA's evolving guidance will provide useful information on the sufficiency of information for Section 5 determination purposes, and how to identify and protect sensitive subpopulations.

Given the relatively modest (but growing) number of MCAN and TERA submissions, the generally richer data and information content found in Section 5 notices for intergeneric microorganisms, the impact of the new Section 5 determination requirement on grounds that EPA lacks ''sufficient information,'' however this phase is interpreted and applied, or that the new microorganism is not expected to present an unreasonable risk, including an unreasonable risk to potentially exposed or susceptible subpopulations, may not be as consequential as this requirement is expected to be on EPA's review of conventional PMNs (where the typical notice contains little if any test data). That said, at this early stage of new TSCA implementation, submitters need to be keenly aware of what these new legal requirements are, redouble efforts to prepare notifications as comprehensively as possible, and recognize that EPA has considerably more authority now under new TSCA than under old TSCA.

To achieve prompt commercialization without triggering regulation under Section 5(e), EPA must be in a position to determine that the new microorganism ''is not likely to present an unreasonable risk.'' To reach this determination, EPA must also be in the position of believing that it has sufficient information ''to permit a reasoned evaluation of the health and environmental effects'' (and thus avoiding triggering of the insufficient information determination). If EPA is not able to support the ''not likely to present'' determination, it will be required to impose restrictions, as needed, to abate any such risk, or to require the development of information needed to support a reasoned determination, or to deny the application entirely.

TSCA Section 6 Prioritization, Risk Evaluation, and Regulation

New TSCA significantly revises Section 6 by adding prioritization and risk evaluation steps to the process, deleting the problematic ''least burdensome'' language in old TSCA Section 6(a), and including ambitious timelines for completion of the key steps in the process, including prioritizations, risk evaluations, and risk management actions. The law also simplifies the procedural requirements in TSCA for promulgation of risk management rules while adding new requirements and providing for certain exemptions from such rules.

New TSCA includes numeric goals, preferences, and deadlines for completion of prioritizations. It requires that EPA implement a risk-based screening process that includes considerations such as hazard and exposure potential, persistence and bioaccumulation, and storage near significant sources of drinking water. The screening process applies criteria (to be developed by rule) for designating high- and low-priority chemicals for the risk evaluation step and the process period for prioritizing a given chemical is limited to a maximum of 12 months, including opportunities for submission of information and comments by the public.

Under the process:

- EPA must designate chemicals as ''high-priority'' if it concludes without consideration of costs or other non-risk factors that the substance *may present* an unreasonable risk because of a *potential hazard and a potential route of exposure* under the conditions of use, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant by EPA. EPA is required to conduct risk evaluations on all high-priority chemicals. Chemicals that do not meet the high-priority standard are designated as ''low-priority.'' Low-priority designations are subject to legal challenge.
- EPA must provide at least 90 days for interested persons to submit relevant information on a substance for which EPA has initiated the prioritization process. This period can be extended for no more than three months to allow for receipt or evaluation of prioritization testing conducted under Section 4(a)(2)(B). The default decision at the end of the 12-month period, if the available information is insufficient to support a low-priority designation, is to designate a chemical as high-priority.

In addition to requiring that EPA initiate risk evaluations on all high-priority chemicals, new TSCA also specifies certain timing requirements and goals for risk evaluations. The risk evaluation standard is to determine whether a chemical presents an unreasonable risk under the conditions of use, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified by EPA as relevant. EPA is required to publish the intended scope of the risk evaluation according to ambitious timelines and then to complete the risk evaluation not later than three and a half years after its initiation.

Certain requirements must be met in conducting risk evaluations, including integrating and assessing the available hazard and exposure information, describing the weight of the scientific evidence, and describing whether aggregate or sentinel exposures to a chemical were considered and the basis for that consideration. Chemicals that are determined to meet the risk evaluation standard must be moved into the risk management process.

EPA has a maximum of four years to complete the risk management rulemaking. The action taken must be ''to the extent necessary so that the chemical substance no longer presents'' an unreasonable risk. As noted above, EPA must meet certain requirements in promulgating Section 6 rules, certain exemptions and limitations are available generally, and exemptions can be granted from ban and phase-out actions if certain conditions can be met.[19]

On the whole, the Section 6 revisions are not likely to have a significant impact on existing microorganisms. Notified intergeneric microorganisms that have entered commerce have been through a more recent and comprehensive premarket review by EPA, and are not expected to pose the types of potential risks that more conventional industrial chemical substances that were grandfathered under TSCA years ago are more likely to present. Additionally, microorganisms are not expected to be prioritized for review unless storage sites are located near significant drinking water sources, which is unlikely.

TSCA Section 8 Reporting and Retention of Information

New TSCA substantially amends TSCA Section 8 having to do with recordkeeping and reporting obligations. The changes include provisions concerning a TSCA ''Inventory reset'' process, requiring that EPA continue to use certain Class 2 chemical nomenclatures, treating individual members of TSCA Section 8(b)(2) statutory mixture categories as being included in the Inventory, and requiring that EPA enter into a negotiated rulemaking leading to development of a rule limiting reporting requirements for inorganic byproducts that are recycled, reused, or reprocessed.

Small businesses involved in industrial biotechnology may also be interested in following or participating in activities relating to a new provision at TSCA Section 8(a)(3)(C) that requires EPA to consult with the Small Business Administration (SBA) regarding the adequacy of the current standards for small manufacturers, provide for notice and comment, and make a determination as to whether revision of the standards is warranted no later than 180 days after enactment.[20] One issue worth noting is the definition of ''small manufacturer,'' which has not been revised since it was originally incorporated into

the 1986 Inventory Update Rule guidance. Using the Bureau of Labor Statistics inflation calculation, $4,000,000 in 1986 is equivalent to $8,767,000 in 2016. Given the significant differential between these monetary thresholds, it seems reasonable to conclude that the initial consultation between EPA and SBA will result in a decision to revise the small manufacturer standard.

Another important issue to monitor is the Inventory reset process required under new TSCA. This includes development of a reporting rule to inform EPA's designation of chemicals as active or inactive in commerce. The status of inactive chemicals can subsequently be changed to active by notifying EPA prior to manufacture or processing. EPA is expected to issue a proposed rule in December 2016 and a final rule in June 2017 implementing this requirement, which will involve reporting on chemicals manufactured, imported, or processed at any time and in any amount during the ten years preceding enactment of the new law.

Given the relatively discrete number of microorganisms listed on the TSCA Inventory, most can be expected to be active substances. It will be important, however, for manufacturers, importers, and processors of microorganisms to participate in the rulemaking EPA intends to propose in December, and ensure all active TSCA microorganisms are identified and reported as such after the final rule is issued next June. The industrial biotechnology industry will also need to be alert to the Inventory reset for all chemicals that are used, for example, in bioreactors, to grow out and commercially produce conventional as well as intergeneric microorganisms. Use of such chemicals as nutrients or for other purposes in manufacturing such microorganisms can be considered processing under TSCA and companies will want to ensure these chemicals are designated as active in the Inventory reset. While chemicals can be easily activated as described above, there could be enforcement sensitivities if a company, for example, inadvertently processes a long-standing but infrequently used chemical (perhaps one held in a storage room) that has not been reported for the active Inventory. Industrial biotechnology companies should engage with their suppliers to ensure that all nutrients and other processing aids are reported as active.

Section 9 Relationship to Other Federal Laws

New TSCA amends TSCA Section 9 in ways that substantially expand the scope and operation of the section with the result that, whereas actions or referrals under Section 9 were rare over TSCA's history, the situation seems likely to change. For example, new TSCA Section 9(a) is potentially significant in that, while it does require an EPA conclusion of presents an unreasonable risk to trigger the referral, the receiving agency or EPA office must appropriately respond within the time period specified by EPA, or EPA can be compelled to act against the unreasonable risk.

Another provision under new TSCA Section 9(e) requires that EPA shall make information on exposures and releases of chemical substances available to another agency or EPA office if these exposures and releases ''may be prevented or reduced under another Federal law.''

Section 14 Confidential Business Information

Amended TSCA revises and replaces TSCA Section 14 concerning Confidential Business Information (CBI). It includes several new sections concerning information not protected from disclosure. A critical aspect in this regard is information from health and safety studies. While new TSCA does not prohibit the disclosure of such information on chemicals offered for commercial distribution or for which testing or notification is required per Sections 4 or 5, the law makes careful edits to a key passage from old TSCA. New TSCA makes clear that the release of certain types of general information is not prohibited, including, for example, aggregated production volumes.

Amended TSCA requires that companies meet certain requirements in asserting CBI claims, including substantiation, and providing additional substantiation in the case of confidential chemical identity. Such claims, when and to the extent approved by EPA, receive protection from disclosure for a period of ten years, which can be renewed if requirements are met. At the same time, new TSCA also includes a provision stating that certain types of information are essentially presumed to be CBI (for example, marketing and sales information) and are not subject to substantiation requirements. Amended TSCA specifies certain Duties of Administrator in reviewing and acting on CBI claims, and gives EPA discretion to review claims in certain circumstances, such as when chemicals are designated as high-priority.

In an important shift, amended TSCA allows certain exceptions to protections from disclosure if various requirements can be met. Under these exceptions, disclosure is allowed, for example, to a state or tribal government for the purpose of administration or enforcement of a law, to a federal, state, or tribal health or environmental professional, or to a treating physician or nurse.

On the whole, changes in Section 14 are not expected to impose new or extraordinary requirements on industrial biotechnology stakeholders, and likely will not have a significant practical impact on the community.

Section 18 State-Federal Relationship

Preemption is one of the most debated aspects of TSCA reform, and new TSCA significantly changes when states cannot establish new laws or continue to enforce existing laws. Specifically, while states' actions taken before April 22, 2016, or any action taken pursuant to a state law that was in effect on August 31, 2003, are grandfathered and remain in effect regardless of any EPA action, states are prohibited from establishing or continuing to enforce statutes, administrative actions, or in some cases criminal penalties that would:

- Require information already required under a TSCA Section 4, 5, or 6 rule, consent agreement, or order;
- Prohibit or restrict a chemical after EPA has made a Section 6(i)(1) determination or issued a final Section 6(a) rule; or
- Subject a chemical to the same notification of use already established in a Section 5 SNUR.

There are additional provisions allowing states to seek from EPA a waiver from preemption restrictions and ensuring that

preemption does not affect state or federal common law rights and private remedies (e.g., tort actions).

As the regulation of microorganisms has by and large been left to EPA under TSCA, the preemption provisions are not expected to impose new or different requirements on biotech stakeholders.

Section 26 Administration of the Act

New TSCA significantly revises and expands this section relative to old TSCA, including expanding the fee authority, establishing a fund to hold the fees that are then to be used (subject to appropriations) to defray the costs of certain EPA activities under Sections 4, 5, and 6, requiring the use by EPA of the best available science in making scientific decisions, requiring EPA to develop and periodically review any policies, procedures, and guidance (PP&G) necessary to carry out the amendments to the Act, and requiring EPA to establish a Science Advisory Committee on Chemicals (SACC).

As noted above, EPA initiated a process in 2015 to update its Points to Consider document and presumably EPA is continuing to work on this document. While new PP&Gs are unlikely to be considered early on in the implementation process, it is questionable whether EPA will need to incorporate, at least to some degree, the effect of the changes to the new TSCA Section 5 into its Points to Consider document. If so, this is required to be completed within the next two years. Whether the SACC can be expected to address issues unique to industrial biotechnology is unclear. It is unlikely, however, given the more pressing need to address other issues pertinent to more conventional chemical substances. At the same time, to the extent EPA decides it needs to reflect the new TSCA changes in it Points to Consider document, or if, as discussed above under Section 4, EPA considers possibly expanded requirements for testing to be met by MCAN submitters, the need for involvement by the SACC could increase and, if so, the industrial biotechnology community will want to engage with the SACC to ensure pertinent developments are scientifically sound and managed appropriately.

The fees component of Section 26 will also have an impact on the industrial biotechnology community as the fee EPA is required to assess in connection with a notification is expected to increase, potentially by quite a bit. EPA has indicated that it intends to tackle the new fee provisions early and to get a final rule out by June 2017. More immediately, EPA convened a stakeholders meeting in August to discuss how to go about setting fees and implement the new provisions.

Conclusion

New TSCA is now a muscular federal law, the implications of which will continue to unfold as EPA systematically implements its new authorities. The statutory provisions alone, however, are sufficiently robust and extensive to compel the attention of industrial biotechnology stakeholders. All are encouraged to read, understand, and carefully analyze how new TSCA and EPA's ongoing implementation efforts will materially impact the review and consideration of MCANs and other notifications. Engagement in the rulemakings that EPA is already preparing is essential, and will help to ensure that the benefits of products of industrial biotechnology are an important element in the regulatory equation.

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REFERENCES

1. Pub. L. No. 114-182, 130 Stat. 448; and Pub. L. No. 94-469, 90 Stat. (2003) Available at: www.gpo.gov/fdsys.
2. TSCA § 2(b), 15 U.S.C. § 2601(b).
3. TSCA § 3(2)(A), 15 U.S.C. § 2602(2)(A); see also 40 C.F.R. §§ 710.3(d), 720.3(e).
4. 62 Fed. Reg. 17910 (Apr. 11, 1997). More recently EPA has stated that "chemically synthesized genes" can be considered "intergeneric," thus clarifying that microorganisms created via synthetic biology can fall within the scope of these regulations.
5. TSCA § 2(b), 15 U.S.C. § 2601(b). In remarks expressed in the Senate on June 7, 2016, Senator David Vitter reinforced TSCA's policy and stated, "We also needed to ensure that American companies, which are world leaders today in science, research, and innovation remain so and do not get put behind a regulatory system which is overly burdensome and unavailable." 114 Cong. Rec. S3511-3513 (daily ed. June 7, 2016).
6. TSCA § 2(b)(3), 15 U.S.C. § 2601(b)(3).
7. TSCA § 2(c), 15 U.S.C. § 2601(c).
8. 40 C.F.R. § 725.1(a). "Microorganisms that are not intergeneric are automatically included on the Inventory." 40 C.F.R. § 725.8(b). Further, manufacturers, importers, or processors required to file an MCAN for research and development (R&D) activities may instead file a TSCA Experimental Release Application (TERA) for a specific test under certain situations. 40 C.F.R. § 725.1(c).
9. 40 C.F.R. § 725.150. If an MCAN is submitted and not needed, EPA will notify the submitter. 40 C.F.R. § 725.28.
10. 40 C.F.R. § 725.1(b).
11. 40 C.F.R. § 725.3. If it is not possible to determine if a microorganism or use is listed on the Inventory, the regulations outline procedures that persons intending to conduct activities involving microorganisms should use to determine their obligations. See 40 C.F.R. § 725.15; EPA, Points to Consider in the Preparation of TSCA Biotechnology Submissions for Microorganisms (Points to Consider) (June 1997) at 8. Available at www.epa.gov/sites/production/files/2015-08/documents/biotech_points_to_consider.pdf. The review process for a "bona fide" submission generally takes 30 days after submission. Points to Consider at 8.
12. 40 C.F.R. § 725.3.
13. *Id*.. An "intergeneric microorganism" includes "a microorganism which contains a mobile genetic element which was first identified in a microorganism in a genus different from the recipient microorganism." It "does not include a microorganism which contains introduced genetic material consisting of only well-characterized, non-coding regulatory regions from another genus." *Id.* The regulations provide further guidance on the types of microorganisms subject to the requirements, and we would be pleased to provide a more detailed analysis upon your request.

14. TSCA § 5(h)(4), 15 U.S.C. § 2604(h)(4). New TSCA Section 26(p)(1) makes clear that the Section 5(h)(4) exemptions promulgated under old TSCA remain available to notifiers under the new law.
15. 40 C.F.R. § 725.67(a), (b).
16. EPA Biotechnology Algae Project (2015) at 1. Available at: www.epa.gov/sites/production/files/2015-09/documents/biotechnology_algae_project.pdf (Last accessed July 2016).
17. We note also that the Obama Administration in July 2015 commenced a multi-phase process to modernize the Coordinated Framework for the Regulation of Biotechnology (Coordinated Framework) by directing EPA, the U.S. Food and Drug Administration, and the U.S. Department of Agriculture to update the Coordinated Framework. Last updated in 1992 (57 Fed. Reg. 6753 (Feb. 27, 1992)) and first rolled out in 1986, the Coordinated Framework outlines a comprehensive federal regulatory policy for products of biotechnology. The memorandum directs the federal agencies to develop a long-term strategy to ensure that the regulatory system for biotechnology products is prepared for future products, and commissions an expert analysis of the future landscape of biotechnology products. The Administration readily admitted that the complexity of the regulatory system can make it difficult for the public to understand how the safety of biotechnology products is evaluated, and navigating the regulatory process for these products can be unduly challenging, especially for small companies. Per the Administration's Memorandum Modernizing the Regulatory System for Biotechnology Products (July 2, 2015), the objectives of the updating process "are to ensure public confidence in the regulatory system and to prevent unnecessary barriers to future innovation and competitiveness by improving the transparency, coordination, predictability, and efficiency of the regulation of biotechnology products while continuing to protect health and the environment." As the Coordinated Framework document addresses EPA's role in the regulation of products of biotechnology under TSCA, the modernizing process could indirectly identify areas where EPA might discharge its new authorities under TSCA to fulfill the goals of the modernization exercise.
18. EPA Biotechnology Algae Project at 1.
19. EPA. TSCA Biotechnology Notifications Status (2016). Available at: www.epa.gov/regulation-biotechnology-under-tsca-and-fifra/tsca-biotechnology-notifications-status (Last accessed July 2016).
20. As currently defined in 40 C.F.R. § 704.3, a small manufacturer or importer must meet either of the following standards: (1) *First standard.* A manufacturer or importer of a substance is small if its total annual sales, when combined with those of its parent company (if any), are less than $40 million. However, if the annual production or importation volume of a particular substance at any individual site owned or controlled by the manufacturer or importer is greater than 45,400 kilograms (100,000 pounds), the manufacturer or importer shall not qualify as small for purposes of reporting on the production or importation of that substance at that site, unless the manufacturer or importer qualifies as small under standard (2) of this definition. (2) *Second standard.* A manufacturer or importer of a substance is small if its total annual sales, when combined with those of its parent company (if any), are less than $4 million, regardless of the quantity of substances produced or imported by that manufacturer or importer.