

# Chemical and Biological Contract Manufacturing Services: Potential Proliferation Concerns and Impacts on Strategic Trade Controls

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## Abstract

The use of contract manufacturing services in the chemical, pharmaceutical, and biotechnology industries has grown significantly in recent years, but the potential for such service providers to be exploited for chemical or biological weapons proliferation has garnered little attention, despite the role of contract manufacturers in the A.Q. Khan nuclear proliferation network. This article examines the dual-use potential and global spread of chemical and biological contract manufacturing and their ramifications for related strategic trade controls (STCs). Hundreds of providers of dual-use contract services were found worldwide, but they were primarily located in jurisdictions with comprehensive or partial STC regulations. This provides some degree of protection against their misuse. However, the results outlined below also suggest that chemical and biological contract manufacturers are a critical community to target for STC outreach activities and efforts to increase industry compliance. Targeted outreach would help prevent contract manufacturing service providers from unwittingly contributing to the production and proliferation of chemical and biological weapons.

## Keywords

Australia Group, Chemical Weapons Convention, contract manufacturing, CW precursors, dual-use chemical technology, dual-use biotechnology, pathogens, toxins, strategic trade controls, export controls

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## Introduction

Contract manufacturing —i.e., contractual engagement of a third-party provider to generate a product— has become an increasingly attractive option over the last decade for chemical, pharmaceutical, and biotechnology companies seeking to reduce costs and operate competitively in a business environment characterized by increasing regulation, dwindling product approval, and rapidly advancing technology. In the chemical sector, contract manufacturers enable increased manufacturing capacity and flexibility without large capital investments by those requiring the service, as well as access to synthetic and process expertise that may not be available in-house and management of safety and regulatory issues. For the pharmaceutical and biotechnology sectors, contract manufacturing lowers drug discovery risks for larger companies and provides flexible, immediate access to highly trained technical expertise. Significant cost efficiencies can be realized through many dimensions of contract manufacturing, including greater control by tertiary pharmaceutical companies over how they concentrate or offload their investment in expertise and equipment. Current estimates place the number of chemical contract manufacturers in the thousands<sup>4</sup>, and pharmaceutical and biotech contract manufacturers at over 500 worldwide<sup>5</sup>—and rapidly growing.

Contract manufacturing firms and service providers have thus far received relatively little attention in the context of chemical weapons (CW) and biological weapons (BW) proliferation and related strategic trade controls (STCs), despite exploitation of contract manufacturing by A.Q. Khan's nuclear proliferation network<sup>6,7</sup>. One notable article from 2012<sup>8</sup> addressed the importance of STC awareness for the pharmaceuticals contracting industry, but focused primarily on the legal and regulatory framework with which companies needed familiarity. A 2014 United States National Academy of Sciences report on chemical manufacturing equipment highlighted shifts to contract manufacturing in the pharmaceutical industry as a potential source of concern, but only in the context of trade controls over the surplus dual-use equipment generated by outsourcing rather than how the contract services provided by these companies could be exploited for proliferation.<sup>9</sup>

This article explores the CW or BW proliferation potential posed by contract manufacturing service providers and possible ramifications for STC implementation. This is accomplished through an illustrative survey of companies providing “*dual-use*” chemical or biological contract services—i.e., a service that has legitimate commercial applications but that could also be exploited toward producing a CW or BW agent. Services for both production of materials and their

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<sup>4</sup> Chemical Information Services' ContractMFG database alone has 2,000 custom manufacturers. See <https://chemicalinfo.com/services/contractmfg/>.

<sup>5</sup> Roots Analysis. 2015. *Contract Manufacturing in Pharmaceutical Industry, 2015–2025*. p. 22. Vancouver: Roots Analysis.

<sup>6</sup> Charles D. Lutes. 2008. “New Players on the Scene: A.Q. Khan and the Nuclear Black Market.” Accessed September 14, 2016. <http://iipdigital.usembassy.gov/st/english/publication/2008/08/20080815121848xjyrrep0.1191522.html#axzz4KFVWTxgx>.

<sup>7</sup> U.S. Department of State. 2009. “Designation of A.Q. Khan and Associates for Nuclear Proliferation Activities.” Accessed September 14, 2016. <http://www.state.gov/t/isn/115913.htm>.

<sup>8</sup> McClafferty, Eric, and Brooke Ringel. 2012. “Export Controls and the Biotech Industry: Are You in Compliance?” *Contract Pharma* May 4: 98–103.

<sup>9</sup> Kathryn Hughes and Joe Alper, rapporteurs. 2014. *The Global Movement and Tracking of Chemical Manufacturing Equipment: A Workshop Summary*. Washington, DC: The National Academies Press. <http://www.nap.edu/catalog/18820/the-global-movement-and-tracking-of-chemical-manufacturing-equipment-a>

refinement are investigated, since a proliferator may seek to split the overall process among providers to conceal their activities. The distribution of these companies across countries according to their Australia Group (AG) membership status and the comprehensiveness of their national control lists are used to assess a basic level of proliferation risk. These findings are analyzed, in turn, to determine potential adverse consequences for STCs and how they might be mitigated.

For the purposes of this article, the term “contract manufacturing” or “contract services” will be used to describe any arrangement in which a third-party company is engaged in producing or processing chemical or biological materials on demand via some type of contract. In sectors that use these types of arrangements, a broader array of terminology is used to distinguish the terms of a given agreement. For example, a “toll manufacturing” arrangement typically involves a company (the customer) supplying raw materials and paying a toll (fee) to have another company manufacture a product; the toll manufacturer effectively rents its facility and equipment, and the customer is responsible for materials and process specifications.<sup>10</sup> In contrast, a contract manufacturer may source raw materials as well as provide facilities and equipment, creating a custom-made product for an individual customer. A “contract manufacturer” may be referred to as a “custom manufacturer,” and both terms are sometimes used interchangeably with the term “toll manufacturer.”<sup>11</sup> Of further note, competition and additional market forces on the pharmaceutical/biotech sectors have been pushing contract manufacturers to operate as umbrella service companies, offering all services from initial research and development to production and manufacturing under one roof. Thus, the terms “contract development and manufacturing organization” and “contract research and manufacturing services” are increasingly becoming part of the contract manufacturing lexicon<sup>12</sup>. While differences in contractual arrangements and number of services offered could have ramifications for the level of proliferation risk, such differentiation is beyond the scope of this article. To avoid confusion regarding these nuances in terminology, all companies in this article are referred to as contract manufacturing service providers.

## Results and Discussion

### *Chemical Contract Services*

The primary contract services of potential CW proliferation concern are those involving chemical synthesis, particularly for key precursors that would be subject to STCs and scrutiny by responsible suppliers. In addition, contract distillation or other purification-related services, which are sometimes offered independently of custom synthesis, may be of interest. Therefore, a survey was conducted of companies capable of custom synthesis using CW-relevant chemistries, as well as those providing contract distillation or purification services.

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<sup>10</sup> Sierra Coating Technologies, LLC. 2015. “Toll Manufacturing versus Contract Manufacturing.” <http://www.sierracoating.com/toll-manufacturing-versus-contract-manufacturing/>.

<sup>11</sup> SOCMA. 2016. “Types of Specialty Chemical Manufacturers.” <http://specialtymanufacturing.socma.com/specialty-manufacturers>.

<sup>12</sup> Roots Analysis. 2015. *Contract Manufacturing in Pharmaceutical Industry, 2015-2025*. p. 23. Vancouver: Roots Analysis.

## Custom Synthesis

Providers of organophosphorus chemistries and chlorination and fluorination reactions were investigated for this study. Such reactions are relevant to the synthesis of advanced precursors for nerve and blister agents found in Schedule 2 of the Chemical Weapons Convention (CWC)<sup>13</sup> and on the AG Common Control List (CCL) of CW Precursors.<sup>14</sup> Denying proliferators access to Schedule 2 chemicals can be an effective chokepoint given their relatively moderate commercial availability and their chemical similarity to CW agents. A database of custom manufacturers<sup>15</sup> covering 2,000 companies in over 55 countries was searched for companies providing related reactions, and search results were visualized in Tableau. The database was used to achieve a representative sampling of contract service providers, such that the results reported herein should be considered illustrative—not exhaustive—of the overall provider landscape. Companies were analyzed according to specific reactions of greatest dual-use concern, as well as whether they are located in a country which is a member of the AG. In addition, it was assessed whether the country or economy in which the company is located has an export control list that adheres to the AG CCL of CW Precursors; for those locations outside of AG membership, adoption of an EU-style dual-use list or a national list matching the AG CW precursor list as of 2014<sup>16</sup> was considered as a proxy for adherence to the list. It is important to note, however, that all locations identified in this study are States Parties to the CWC except for Israel and Taiwan. States Parties to the CWC are bound to never “assist, encourage or induce, in any way, anyone to engage in any activity prohibited to a State Party”<sup>17</sup> under the treaty. Further, the CWC’s definition of chemicals weapons includes precursors for toxic chemicals.<sup>18</sup> As such, no State Party should assist the development or production of chemical weapons through supply of CW precursors. However, national implementing legislation for the CWC varies among States Parties, and an analysis of the status of such legislation in each country was not undertaken for this study. Therefore, the establishment of a comprehensive dual-use export control list that includes AG-listed chemicals, rather than CWC membership, was taken as a benchmark.

Figure 1 displays search results summarizing companies offering organophosphorus chemistries of potential relevance to CW precursor production, grouped by location and AG membership status. Company numbers represent distinct counts by company name in a given country or economy; some companies have multiple locations, and some provide multiple relevant reaction types of concern, but these were not distinguished for the purpose of this analysis. Results indicate that a strong majority of organophosphorus chemistry providers are located in AG member

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<sup>13</sup> Organisation for the Prohibition of Chemical Weapons. “Annex on Chemicals.” Chemical Weapons Convention. Accessed April 22, 2016. <https://www.opcw.org/chemical-weapons-convention/annexes/annex-on-chemicals/>.

<sup>14</sup> The Australia Group. 2015. “Export Control List: Chemical Weapons Precursors.” Accessed April 21, 2016. <http://www.australiagroup.net/en/precursors.html>.

<sup>15</sup> Chemical Information Services. “ContractMFG.” <https://chemicalinfo.com/services/contractmfg/>.

<sup>16</sup> That is, prior to the 2015 addition of diethylamine (DEA) to the AG list, to account for reasonable lags in the legislative process to update national control lists. The most recent addition of chemicals to the list prior to DEA was 2009, giving adequate time for the regulatory process to catch up by 2014 in those countries committed to following the AG list.

<sup>17</sup> Organisation for the Prohibition of Chemical Weapons. “Article I. General Obligations.” Chemical Weapons Convention. Accessed May 27, 2016. <https://www.opcw.org/chemical-weapons-convention/articles/article-i-general-obligations/>.

<sup>18</sup> Organisation for the Prohibition of Chemical Weapons. “Article II. Definitions and Criteria.” Chemical Weapons Convention. Accessed May 27, 2016. <https://www.opcw.org/chemical-weapons-convention/articles/article-ii-definitions-and-criteria/>.

countries: 150 compared to 56 in non-member locations, or 73%. The United States has the largest number of providers, exceeding the country with the next largest count, India, by more than a factor of two.

Examining the distribution of companies by fidelity to the AG CCL of CW Precursors (Figure 2) shows an even greater percentage of companies whose exports of listed precursors likely would be subject to national trade controls. Only one company out of the 206 found is in a country whose national control list does not adhere in part or in full to the AG list. Furthermore, while India's and China's national export control lists only partially cover the AG CW precursor control list, they are comprehensive with respect to CWC scheduled chemicals. Therefore, any CWC scheduled organophosphorus compound synthesized by a company on their soil would be subject to national STCs.

Similar analyses were conducted for chlorination and fluorination services. Figure 3 shows distinct company counts grouped by location and AG membership status. There is a substantially larger number of companies offering these reactions compared with organophosphorus chemistries: 526 distinct companies vs. 206 companies. In the case of chlorination and fluorination, the majority of providers are still in AG member countries, but only 56%. The balance changes somewhat when the individual reaction types are analyzed separately. The three reactions considered were fluorination, chlorination, and thionyl chloride ( $\text{SOCl}_2$ ) reactions, the last being a method of chlorination. As shown in Table 1, fluorination is less commonly provided than chlorination (204 vs. 475 companies) and is more concentrated in AG member countries (67% for fluorination vs. 56% for chlorination).  $\text{SOCl}_2$  reactions are provided by few companies in the database used for this investigation, and those companies show a nearly even split between AG members and non-members. Figure 4 shows the distribution of companies by adherence to the AG CCL of CW Precursors. Again, only one company is in a country that does not adhere in part or in full, but the proportion of companies in partially adherent countries is substantially larger than for organophosphorus chemistry providers. India's and China's controls over CWC scheduled chemicals would again provide regulatory control over any scheduled chemicals resulting from custom chlorination or fluorination, although there are some AG-listed compounds that would not have been covered by those countries' lists at the time of the research conducted for this article.<sup>19</sup>

#### Distillation and Purification-Related Services

A survey was also conducted of companies providing custom or toll distillation; custom purification; or other purification, separation, or filtration services. The website of each company, when available, was reviewed to assess the potential for the company's services to be used for isolating significant quantities of dual-use chemicals of CW concern. Companies separating only laboratory-scale amounts and/or processing benign chemicals were considered of limited relevance for dual-use activities, while companies with corrosion-resistant equipment and/or citing work with harsh (and/or explicitly dual-use) chemicals were considered likely to be relevant. Companies reporting use of all-stainless-steel equipment that provided little detail about chemicals processed were considered potentially relevant, while some companies published insufficient information to determine the extent of their capabilities. While stainless steel is not considered

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<sup>19</sup> Namely, 2-chloroethanol (107-07-3), dimethylamine hydrochloride (506-59-2), and triethanolamine hydrochloride (637-39-8). Other unscheduled, AG-listed compounds containing chlorine or fluorine are basic chemicals unlikely to be provided by contract synthesis providers (e.g., sodium fluoride).

sufficiently corrosion-resistant to be a specified material of construction in the AG CCL of Dual-Use Chemical Equipment, it could be exploited for a one-time purification operation.

A total of 52 distinct company locations providing contract distillation or purification services were identified. Of these, 32 were assessed to be capable or potentially capable of being used to purify significant quantities of CW-related, controlled chemicals. Figure 5 displays the AG membership status of those companies. Once again, the majority of companies are located in AG member countries. Likewise, as shown in Figure 6, all are located in countries that either fully or partially incorporate the AG CCL of CW Precursors into their regulations. However, as previously noted, India and China impose STCs on all CWC scheduled chemicals, such that only purified chemicals listed by the AG but not the CWC potentially would fall outside of control.

### ***Biological Contract Services***

Contract services of greatest concern for potential BW production include fermentation (cultivation) of pathogens and toxins that would be subject to STCs. Further, contract lyophilization or other stabilization services such as spray drying are also of interest. Both of these are rate-limiting steps in the BW production process. Therefore, a survey was conducted of companies offering contract fermentation and contract stabilization services.

#### **Fermentation Services**

An investigation was conducted of providers offering contract fermentation services for both microbial and mammalian cells. These services are relevant for the cultivation of pathogens (viruses, bacteria, and fungi) and production of toxins listed on the AG CCL of Human and Animal Pathogens and Toxins<sup>20</sup> and the AG CCL of Plant Pathogens<sup>21</sup>. A proliferator's inability to access fermentation expertise and equipment can serve as a choke point in the high quantity and high quality production of BW agents. Listed bacteria and fungi can be cultivated directly, while listed viruses are produced by cultivating mammalian host cells infected with the virus. Several AG-listed toxins can be produced by cultivating the toxin-producing microbial or mammalian producer cells<sup>22</sup>. The same database of custom manufacturers<sup>23</sup> used for chemical contract service searches was queried for companies providing contract fermentation services. This information was supplemented with companies listed as providing contract fermentation services from an independent database in a 2015 pharmaceutical contract manufacturing industry report<sup>24</sup>. The website of each company was reviewed to assess the company's ability to provide contract fermentation services, the types of cells they could cultivate, and the company's approximate total fermentation capacity.

Companies whose websites clearly indicated that they only fermented food products (e.g., beer, wine, cheese, and yogurt) were eliminated, but all other companies were included in analyses

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<sup>20</sup> The Australia Group. 2015. "List of Human and Animal Pathogens and Toxins for Export Control." [http://www.australiagroup.net/en/human\\_animal\\_pathogens.html](http://www.australiagroup.net/en/human_animal_pathogens.html).

<sup>21</sup> The Australia Group. 2012. "List of Plant Pathogens for Export Control." <http://www.australiagroup.net/en/plants.html>.

<sup>22</sup> Contract providers of peptide synthesis were not considered because the majority of AG-listed toxins are large, complex macromolecules and likely outside the present capability of such a contract service provider.

<sup>23</sup> Chemical Information Services. "ContractMFG." <https://chemicalinfo.com/services/contractmfg/>.

<sup>24</sup> Roots Analysis. 2015. *Contract Manufacturing in Pharmaceutical Industry, 2015-2025*. Vancouver: Roots Analysis.

irrespective of their ability to provide biological containment required for safe handling of most AG-listed pathogens (Biosafety Level 3 [BSL3] or Biosafety Level 4 [BSL4]). The data were considered this way for two reasons. First, there are at least 32 AG-listed pathogens that are harmful to animals or plants, but are not harmful to humans. Second, several AG-listed toxins are proteins which can be expressed in cultured microbial or mammalian cells that do not normally produce toxins. Given limitations in available data, delving into issues of compliance and biosafety protocols for individual companies is beyond the scope of this paper. Of 123 contract fermentation company locations thus identified, two companies explicitly mentioned their “containment facilities,” two additional companies referenced their ability to cultivate “infectious diseases,” and a further two companies specifically mentioned their BSL3 biocontainment capabilities. All six companies were located in AG member countries.

Figure 7 displays the number of locations offering contract fermentation services, grouped by AG membership status. Similarly to the chemical contract services analyses, the majority of companies are located in AG member countries (104 of 123 companies, or 84%), with the exception of India, China, and Taiwan (19 companies). Further, as shown in Figure 8, all companies are located in countries or jurisdictions that either fully or partially adhered to the AG CCL of Human and Animal Pathogens and Toxins and the AG CCL of Plant Pathogens at the time of research conducted for this article. The Indian national control list and the Chinese national control list contain roughly 75% of the pathogens and toxins on the AG CCLs. Similarly to our chemical services analysis, adoption of an EU-style dual-use list or a national list matching the AG CCL of Human and Animal Pathogens and Toxins and the AG CCL of Plant Pathogens as of 2014 were considered as proxies for adherence to the list<sup>25</sup>.

Table 2 and Table 3 further break down the cell cultivation services offered by each identified company location, grouped by AG member status. While information provided on company websites varied, companies in both AG member and non-member countries/jurisdictions indicated their ability to cultivate bacteria, yeast, and mammalian cells. Table 4 displays the approximate cultivation capacity offered by each identified company location, grouped by AG member status. The majority of companies identified offered fermentation scales of between 101 and 10,000 L. All companies identified as a result of this analysis are likely to possess fermenters with cultivation capacities greater than the AG threshold for control (20 L), but delving deeper into specific company equipment holdings or service offerings was beyond the scope of this analysis.

### Stabilization Services

Companies offering contract lyophilization (freeze-drying) or spray-drying services were also investigated. These services are relevant for the preservation of pathogens and toxins listed on the AG CCL of Human and Animal Pathogens and Toxins and the AG CCL of Plant Pathogens. Preservation or stabilization is a critical step for a proliferator. Incorrect preservation of a pathogen or toxin likely results in its destruction shortly after production, but proper preservation means it can retain viability for weeks or months. The same databases used for identifying fermentation providers were queried for companies providing contract stabilization services. The website of

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<sup>25</sup> This includes an assumption that these countries or jurisdictions will, at a legislatively appropriate time, update their control lists to reflect changes made by the EU or the AG—including the addition of severe acute respiratory syndrome-related coronavirus (SARS-related coronavirus) and reconstructed 1918 influenza virus as well as approximately 25 nomenclature changes since 2014.

each company was reviewed to assess the company's ability to provide contract stabilization services, whether it provided lyophilization or spray drying. On the basis of their target clients' general desire to produce large batches of pharmaceutical products, companies identified as providing contract stabilization services likely possess lyophilizers with condenser capacities of > 10 kg ice/24 hours and < 1000 kg ice/24 hours, which are the thresholds for control on the AG CCL of Dual-Use Biological Equipment<sup>26</sup>. The lyophilizers were also likely steam-sterilizable, given their repeated application in preservation of pharmaceutical products.

Figure 9 displays the AG membership status of 64 company locations identified as offering contract stabilization services. Similarly to all prior analyses, the vast majority of companies (56 of 64, or 87%) are located in AG member countries; the exceptions are India and China. Further, as shown in Figure 10, all companies are located in countries that either fully or partially adopt both the AG CCL of Human and Animal Pathogens and Toxins and the AG CCL of Plant Pathogens.

### **Conclusion: Proliferation Potential of Contract Manufacturing and Implications for Strategic Trade Controls**

The results of this survey indicate that there are hundreds of contract manufacturers potentially capable of synthesizing CWC Schedule 2 precursors that pose a significant proliferation risk. However, that the vast majority of those companies are located in AG member countries or places where control lists include—in whole or in part—chemicals on the AG CCL of CW Precursors and integrate the CWC Schedules of Chemicals. In the case of contract distillation and purification service providers, this survey indicates that the vast majority of companies providing relevant or potentially relevant contract purification services are located in jurisdictions that have STC regulations in line with the AG and/or are CWC States Parties.

The survey of companies offering custom fermentation services found at least 123 worldwide locations providing this service, after excluding food producers. The survey of companies offering custom lyophilization or spray-drying services identified at least 64 worldwide locations engaged in this type of business with equipment that likely met AG specifications for control. While it is important to emphasize that this count is not exhaustive, analysis of these representative data in both cases indicates that the vast majority of companies identified are located in AG member countries or jurisdictions whose national control lists incorporate—in whole or in part—pathogens and toxins listed on both the AG CCL of Human and Animal Pathogens and Toxins and the AG CCL of Plant Pathogens.

These results indicate that the majority of providers of dual-use chemical and biological contract services would be subject to laws and regulations that would prohibit contributing those services to CW or BW proliferant activities. Preventing the exploitation of these providers by proliferators therefore becomes primarily an issue of increasing company awareness of—and incentivizing them to comply with—existing STCs. Although there is a sizeable community of such companies, lack of literature on related outreach implies a need to engage them on STC compliance. Service

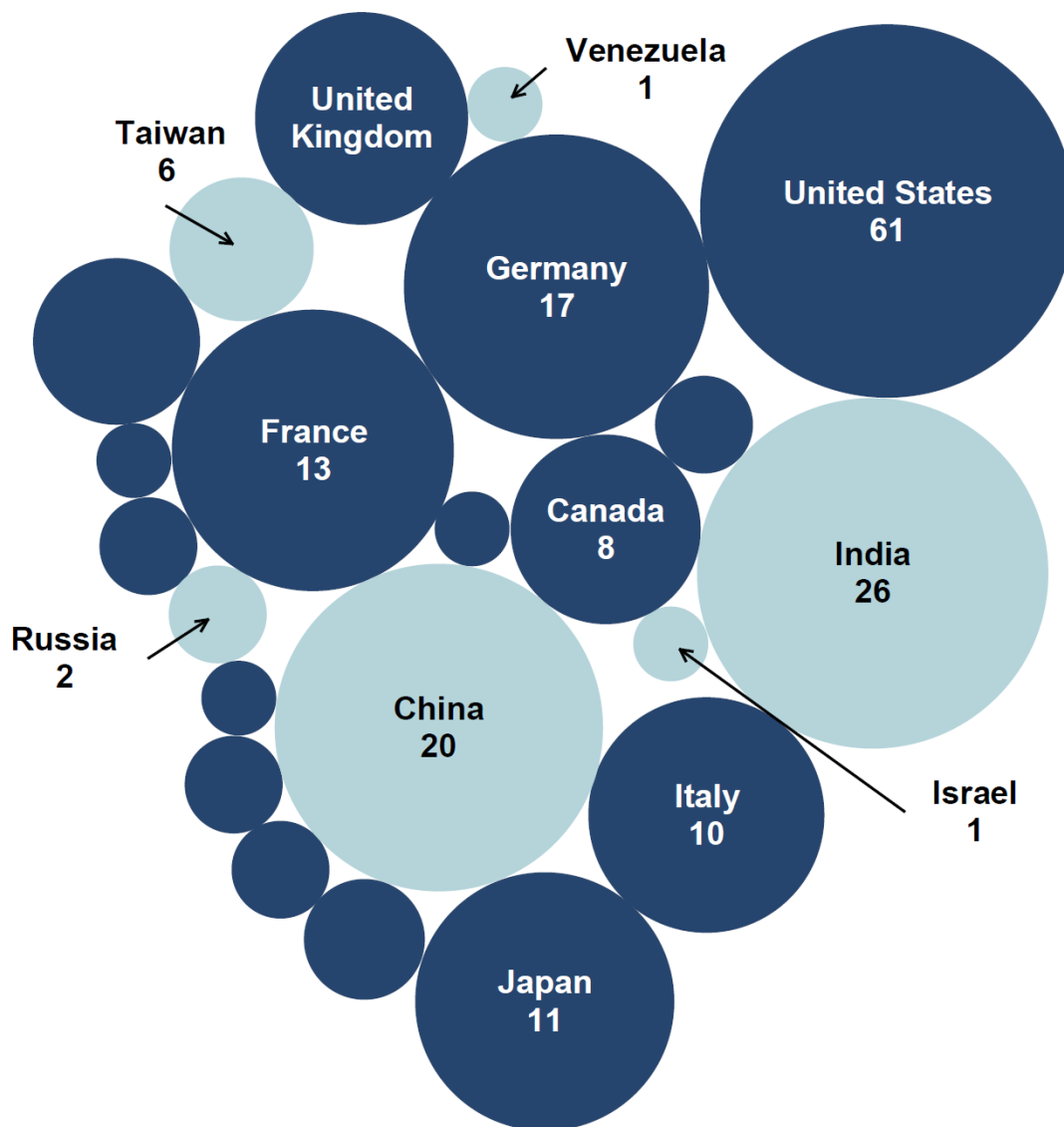
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<sup>26</sup> The Australia Group. 2015. "Control List of Dual-use Biological Equipment and Related Technology and Software. [http://www.australiagroup.net/en/dual\\_biological.html](http://www.australiagroup.net/en/dual_biological.html).



providers of organophosphorus chemistry, fluorination, and fermentation could be prioritized as outreach targets based on the enhanced dual-use risk posed by those activities. Organizations tasked with such outreach to the chemical and biotechnology industries should ensure that contract manufacturing service providers are not overlooked. Outreach efforts should focus on corporate due diligence, vetting of customers, and the internal compliance programs of the contract service provider. Potential avenues for engagement include visits to individual contract service providers, contract manufacturing expos, related conferences, and professional organizations. Tools such as subscription-based databases of contract manufacturers could be utilized to identify outreach targets and ensure they are invited to outreach events. Increasing STC-related outreach to contract manufacturing service providers and using this outreach to inform these companies about how they may be exploited will be especially important as advances in technology (e.g., synthetic biology) shift potential CW and BW concerns away from materials and commodities currently listed for export control and towards CW and BW concerns that are not listed and are increasingly harder to document on export control lists.

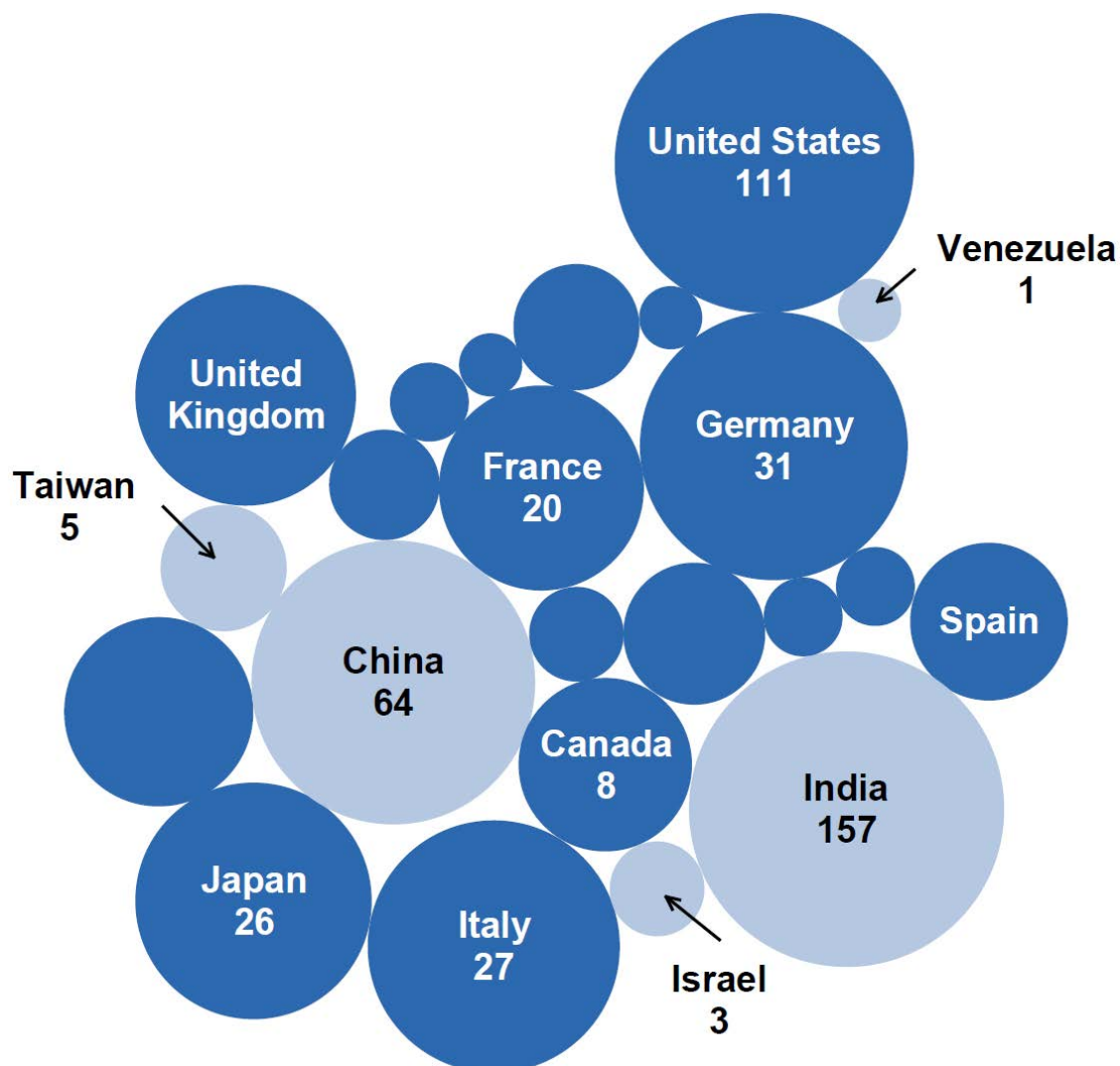
## Figures and Tables



**Figure 1.** Number of companies offering CW-relevant organophosphorus chemistries, grouped by location and AG membership status. Circle diameter qualitatively represents the count of distinct company names in each location. AG members are indicated by dark blue, with non-members in light blue. A complete listing of countries and number of resident companies is provided in the Appendix (Table A1).



**Figure 2.** Number of companies offering CW-relevant organophosphorus chemistries, grouped by location and adherence to the AG CW precursor control list. Rectangle size represents the count of distinct company names in each location. Full adherence is indicated by dark blue. Partial adherence is indicated by medium blue. Non-adherence is indicated by light blue and includes only one country (Venezuela). A complete listing of countries and number of resident companies is provided in the Appendix (Table A2).



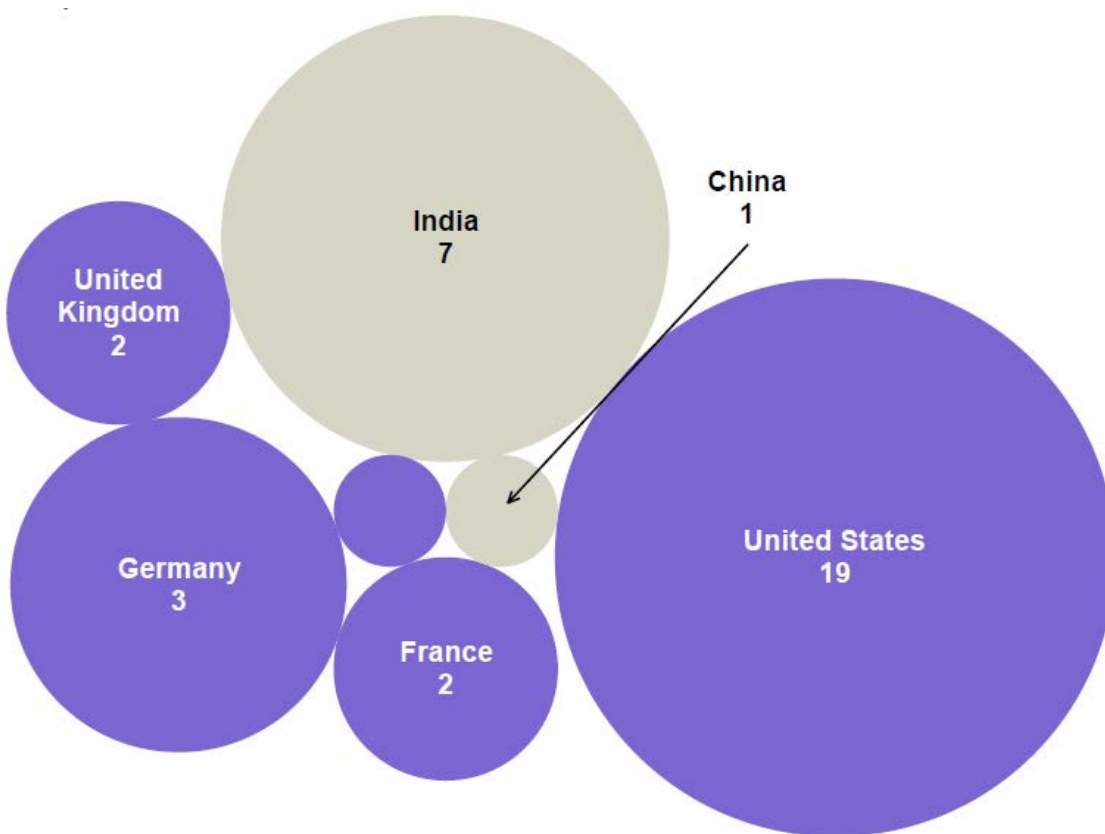
**Figure 3.** Number of companies offering CW-relevant chlorination and fluorination chemistries, grouped by location and AG membership status. Circle diameter qualitatively represents the count of distinct company names in each location. AG members are indicated by dark blue, with non-members in light blue. A complete listing of locations and number of resident companies is provided in the Appendix (Table A3).

AG Member	Location	Chlorination	Fluorination	SOCI2 Reactions
Yes	Austria	3		
	Belgium	5	3	
	Canada	8	4	
	France	19	9	1
	Germany	27	15	1
	Hungary	2		
	Italy	27	7	
	Japan	23	13	
	Mexico	4	1	
	Netherlands	2	1	
	Norway	1		
	Poland	5		1
	Portugal	1	1	
	South Korea	2	1	
	Spain	7	1	
	Switzerland	15	7	1
	United Kingdom	22	10	1
	United States	94	63	
No	China	50	40	
	India	149	23	6
	Israel	3	1	
	Taiwan	5	3	
	Venezuela	1	1	

**Table 1.** Number of companies offering CW-relevant chlorination and fluorination chemistries, grouped by AG membership status, location, and reaction.



**Figure 4.** Number of companies offering CW-relevant chlorination and fluorination chemistries, grouped by location and adherence to the AG CW precursor control list. Rectangle size represents the count of distinct company names in each location. Full adherence is indicated by dark blue. Partial adherence is indicated by light blue. Non-adherence is indicated by gray and includes only one country (Venezuela). A complete listing of locations and number of resident companies is provided in the Appendix (Table A4).

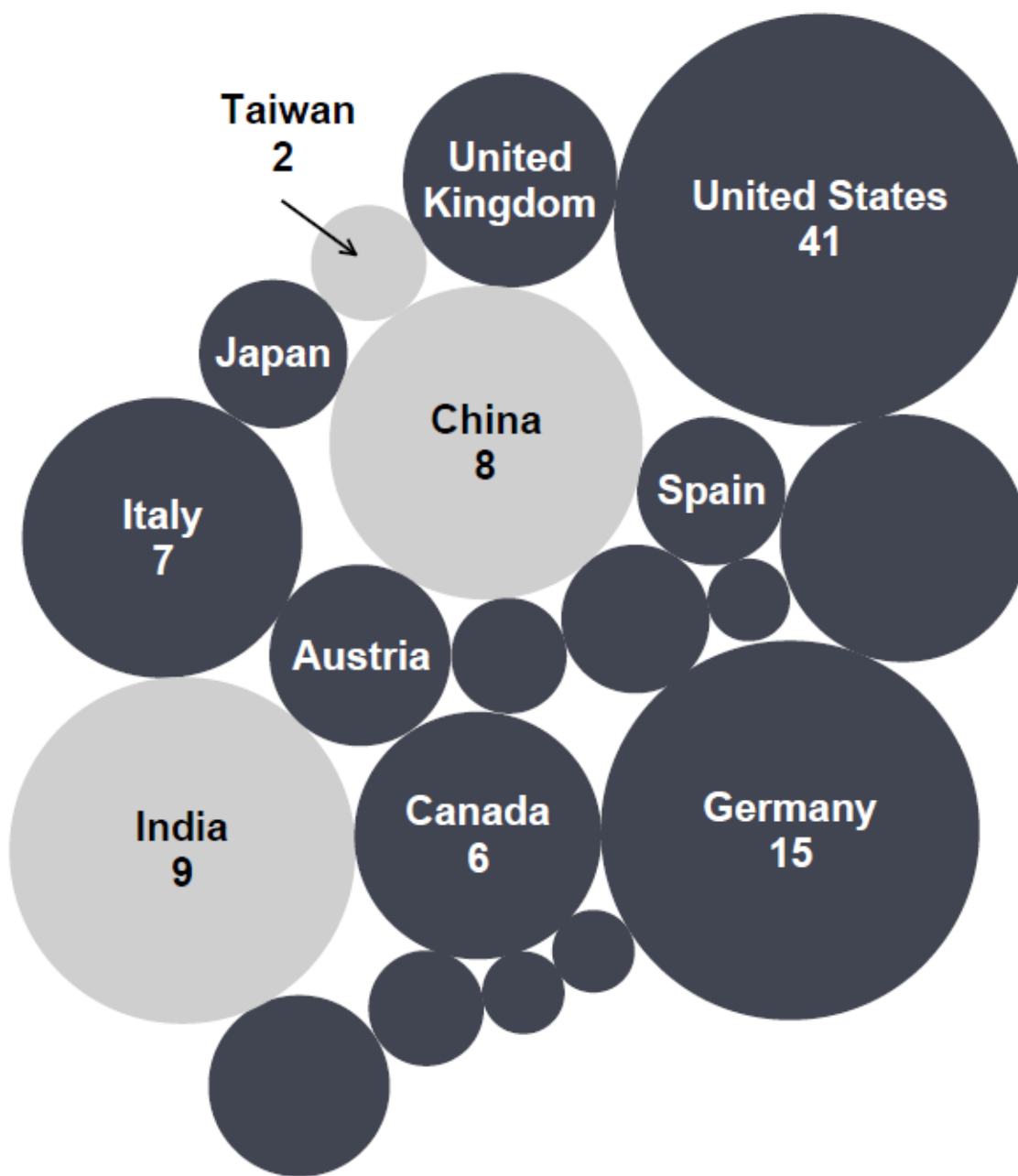


**Figure 5.** Number of companies offering CW-relevant distillation and purification services, grouped by location and AG membership status. Circle diameter qualitatively represents the count of distinct company names in each location. AG members are indicated by purple, with non-members in gray. A complete listing of locations and number of resident companies may be found in the Appendix (Table A5).

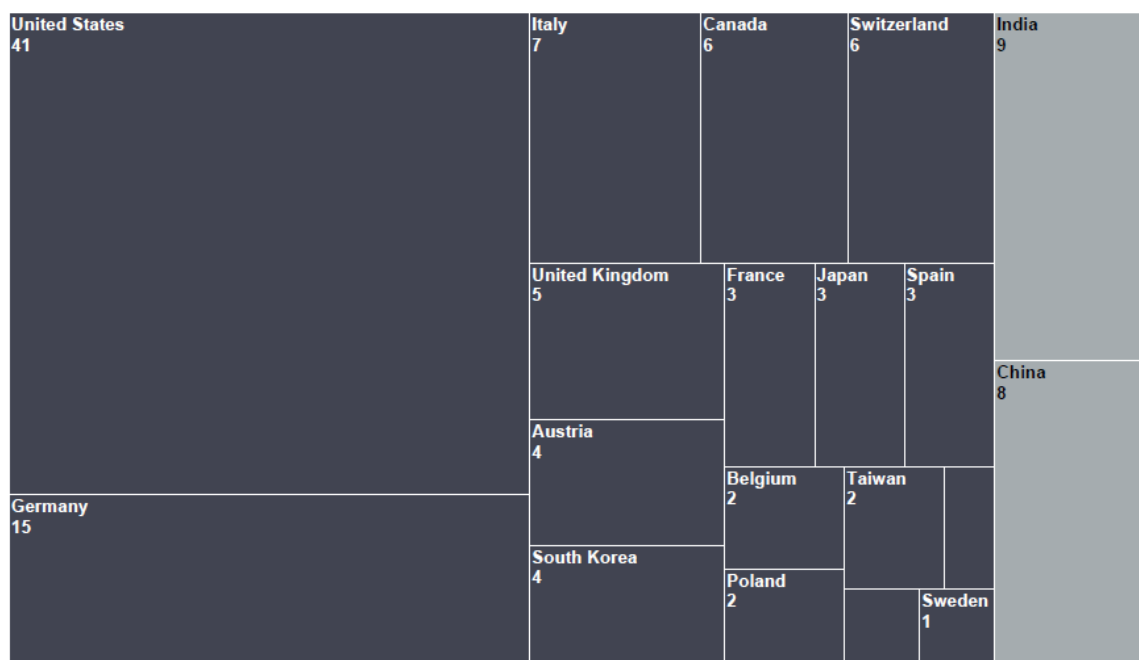


**Figure 6.** Number of companies offering CW-relevant distillation and purification services, grouped by location and adherence to the AG CW precursor control list. Rectangle size represents the count of distinct company names in each country. Full adherence is indicated in purple. Partial adherence is indicated in gray. A complete listing of locations and number of resident companies is provided in the Appendix (Table A6).





**Figure 7.** Number of companies offering BW-relevant fermentation services, grouped by location and AG membership status. Circle diameter qualitatively represents the count of distinct company names in each location. AG members are indicated by black, with non-members in gray. A complete listing of locations and number of resident companies may be found in the Appendix (Table A7).



**Figure 8.** Number of companies offering BW-relevant fermentation services, grouped by location and adherence to the AG BW pathogens and toxins control lists. Rectangle size represents the count of distinct company names in each location. Full adherence is indicated in black. Partial adherence is indicated in gray. A complete listing of locations and number of resident companies is provided in the Appendix (Table A8).

AG Member	Location	Yes	Not provided
Yes	Austria	3	1
	Belgium	2	
	Canada	4	1
	France	2	1
	Germany	7	7
	Italy	4	3
	Japan	2	1
	Mexico	1	
	Netherlands		1
	Poland	1	1
	South Korea	1	3
	Spain	1	2
	Sweden		1
	Switzerland	3	3
	United Kingdom	1	4
	United States	20	21
No	China	1	7
	India	2	7
	Taiwan	1	1

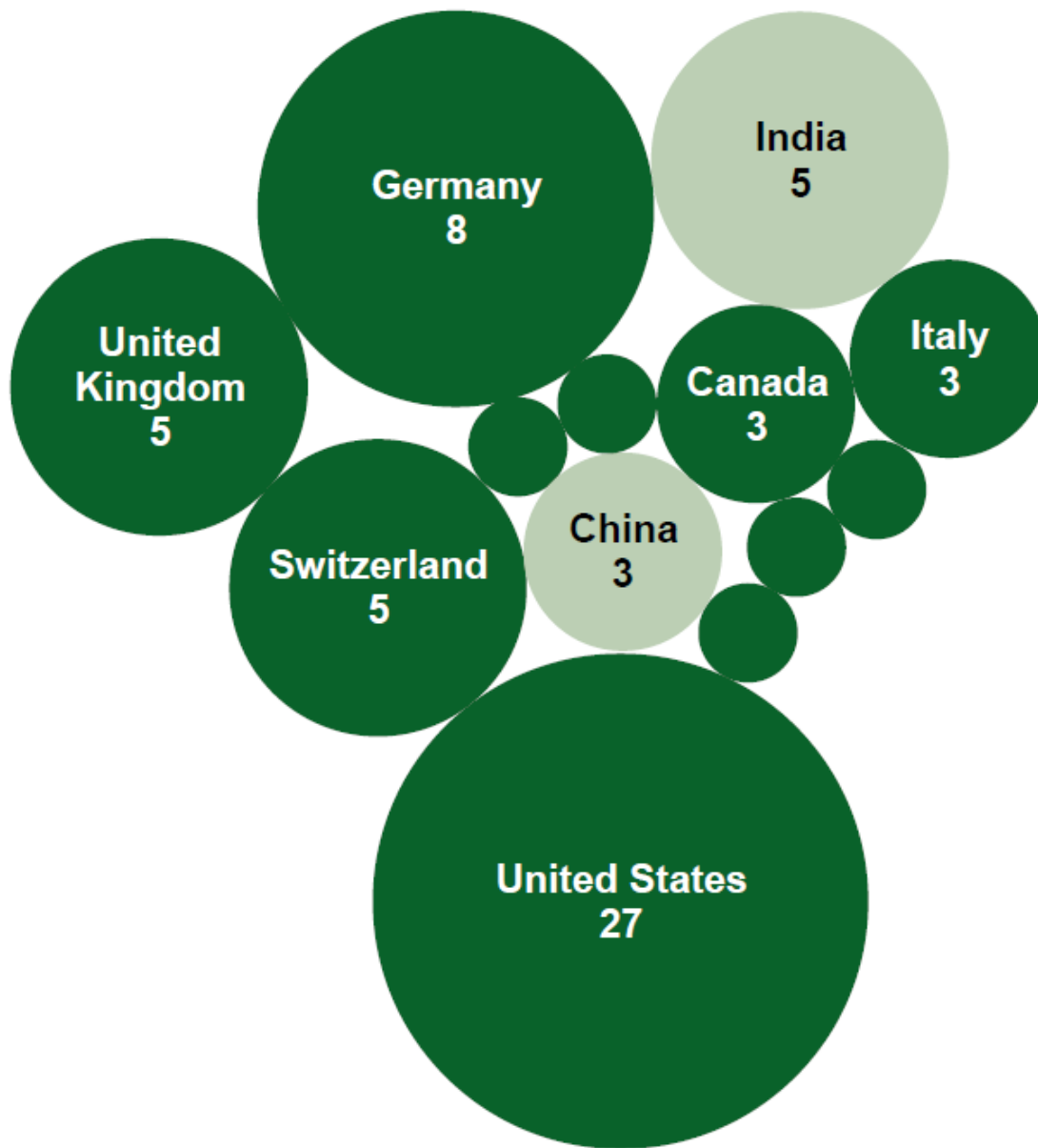
**Table 2.** Number of companies offering BW-relevant fermentation services, grouped by AG membership status, location, and companies' stated ability to cultivate microbial (bacterial and yeast) cells. "Yes" indicates that the company provided this information on its website. "Not provided" indicates that the company provided no information on its website.

AG Member	Location	Yes	Not provided
Yes	Austria	2	2
	Belgium	1	1
	Canada	1	4
	France	3	
	Germany	8	6
	Italy	1	6
	Japan	2	1
	Mexico	1	
	Netherlands		1
	Poland	1	1
	South Korea	3	1
	Spain	2	1
	Sweden		1
	Switzerland	4	2
	United Kingdom	2	3
	United States	33	8
No	China	4	4
	India	1	8
	Taiwan	2	

**Table 3.** Number of companies offering BW-relevant fermentation services, grouped by AG membership status, location, and companies' stated ability to cultivate mammalian cells. "Yes" indicates the company provided this information on its website. "Not provided" indicates that the company provided no information on its website.

AG Member	Location	1-100	101-1000	1001-10,000	>10,001	Not provided
Yes	Austria	1		2	1	
	Belgium		2			
	Canada			1	3	2
	France	1	1	1		
	Germany	1	5	3	2	4
	Italy				1	6
	Japan			2		1
	Mexico				1	
	Netherlands					1
	Poland		1			1
	South Korea		1	1	1	1
	Spain		1	1		1
	Sweden					1
	Switzerland		1	2	2	1
	United Kingdom			2	1	2
	United States	4	13	9	7	11
No	China		2	1	1	4
	India		1			8
	Taiwan			1	1	

**Table 4.** Number of companies offering BW-relevant fermentation services, grouped by AG membership status, location, and the maximum fermentation capacity (in liters) provided by individual companies. “Not provided” indicates that the company provided no information on its website.



**Figure 9.** Number of companies offering BW-relevant stabilization services, grouped by country location and AG member status. Circle qualitatively diameter represents the count of distinct company names in each location. AG members are indicated by dark green, with non-members in light green. A complete listing of locations and number of resident companies may be found in the Appendix (Table A9).



**Figure 10.** Number of companies offering BW-relevant stabilization services, grouped by location and adherence to the AG BW pathogens and toxins control lists. Rectangle size represents the count of distinct company names in each location. Full adherence is indicated by dark green. Partial adherence is indicated by light green. A complete listing of locations and number of resident companies may be found in the Appendix (Table A10).

## Appendix

AG Member	Location	
Yes	Austria	1
	Canada	8
	France	13
	Germany	17
	Hungary	2
	Italy	10
	Japan	11
	Mexico	3
	Netherlands	2
	Norway	2
	Poland	1
	Spain	2
	Sweden	1
	Switzerland	7
	United Kingdom	9
	United States	61
No	China	20
	India	26
	Israel	1
	Russia	2
	Taiwan	6
	Venezuela	1

**Table A1.** Complete listing of locations and number of resident companies offering CW-relevant organophosphorus chemistries, grouped by location and AG membership status.



<b>Adheres to AG Control Lists</b>	<b>Location</b>	
<b>Yes</b>	Austria	1
	Canada	8
	France	13
	Germany	17
	Hungary	2
	Italy	10
	Japan	11
	Mexico	3
	Netherlands	2
	Norway	2
	Poland	1
	Russia	2
	Spain	2
	Sweden	1
	Switzerland	7
	Taiwan	6
	United Kingdom	9
	United States	61
<b>Partial</b>	China	20
	India	26
	Israel	1
<b>No</b>	Venezuela	1

**Table A2.** Complete listing of countries and number of resident companies offering CW-relevant organophosphorus chemistries, grouped by location and adherence to the AG CW precursor control list.

<b>AG Member</b>	<b>Location</b>	
<b>Yes</b>	Austria	3
	Belgium	6
	Canada	8
	France	20
	Germany	31
	Hungary	2
	Italy	27
	Japan	26
	Mexico	4
	Netherlands	2
	Norway	1
	Poland	5
	Portugal	1
	South Korea	2
	Spain	7
	Switzerland	15
	United Kingdom	25
	United States	111
<b>No</b>	China	64
	India	157
	Israel	3
	Taiwan	5
	Venezuela	1

**Table A3.** Complete listing of locations and number of resident companies offering chlorination and fluorination chemistries, grouped by location and AG membership status.

Adheres to AG Control Lists	Location	
<b>Yes</b>	Austria	3
	Belgium	6
	Canada	8
	France	20
	Germany	31
	Hungary	2
	Italy	27
	Japan	26
	Mexico	4
	Netherlands	2
	Norway	1
	Poland	5
	Portugal	1
	South Korea	2
	Spain	7
	Switzerland	15
	Taiwan	5
	United Kingdom	25
	United States	111
<b>Partial</b>	China	64
	India	157
	Israel	3
<b>No</b>	Venezuela	1

**Table A4.** Complete listing of countries and number of resident companies offering chlorination and/or fluorination reactions, grouped by location and adherence to the AG CW precursor control list.

AG Member	Location	Likely	Maybe	Unknown	Unlikely
Yes	Belgium		1		
	France	1	1		1
	Germany	2	1		2
	Switzerland				2
	United Kingdom	2	1		1
	United States	8	11		7
No	China			1	2
	India	2	3	2	1
	Venezuela				1

**Table A5.** Complete listing of countries and number of resident companies offering CW-relevant distillation and purification services, grouped by location and AG membership status. “Unknown” and “Unlikely” were not included in Figure 5.

Adheres to AG Control Lists	Location	Likely	Maybe	Unknown	Unlikely
<b>Yes</b>	Belgium		1		
	France	1	1		1
	Germany	2	1		2
	Switzerland				2
	United Kingdom	2	1		1
	United States	8	11		7
<b>Partial</b>	China			1	2
	India	2	3	2	1
<b>No</b>	Venezuela				1

**Table A6.** Complete listing of countries and number of resident companies offering CW-relevant distillation and purification services, grouped by location and adherence to the AG CW precursor control list. “Unknown” and “Unlikely” were not included in Figure 6.

<b>AG Member</b>	<b>Location</b>	
<b>Yes</b>	Austria	4
	Belgium	2
	Canada	6
	France	3
	Germany	15
	Italy	7
	Japan	3
	Mexico	1
	Netherlands	1
	Poland	2
	South Korea	4
	Spain	3
	Sweden	1
	Switzerland	6
	United Kingdom	5
	United States	41
<b>No</b>	China	8
	India	9
	Taiwan	2

**Table A7.** Complete listing of countries and number of resident companies offering BW-relevant fermentation services, grouped by location and AG membership status.

<b>Adheres to AG Control Lists</b>	<b>Location</b>	
<b>Yes</b>	Austria	4
	Belgium	2
	Canada	6
	France	3
	Germany	15
	Italy	7
	Japan	3
	Mexico	1
	Netherlands	1
	Poland	2
	South Korea	4
	Spain	3
	Sweden	1
	Switzerland	6
	Taiwan	2
	United Kingdom	5
	United States	41
<b>Partial</b>	China	8
	India	9

**Table A8.** Complete listing of countries and number of resident companies offering BW-relevant fermentation services, grouped by location and adherence to the AG BW pathogens and toxins control lists.

<b>AG Member</b>	<b>Location</b>	
<b>Yes</b>	Austria	1
	Canada	3
	France	1
	Germany	8
	Italy	3
	Japan	1
	South Korea	1
	Sweden	1
	Switzerland	5
	United Kingdom	5
	United States	27
<b>No</b>	China	3
	India	5

**Table A9.** Complete listing of countries and number of resident companies offering BW-relevant stabilization services, grouped by location and AG member status.



Adheres to AG Control Lists	Location	
Yes	Austria	1
	Canada	3
	France	1
	Germany	8
	Italy	3
	Japan	1
	South Korea	1
	Sweden	1
	Switzerland	5
	United Kingdom	5
	United States	27
Partial	China	3
	India	5

**Table A10.** Complete listing of countries and number of resident companies offering BW-relevant stabilization services, grouped by location and adherence to the AG BW pathogens and toxins control lists.