

Harmonized Tariff Schedule

Immunological products are currently traded under the following three separate 6-digit subheadings of the Harmonized Tariff Schedule of the United States (HTSUS).⁷ These classifications are used within Harmonized System (HS) as well.⁸

3002.13 – Immunological products, unmixed, not put up in measured doses or in forms or packings for retail sale

3002.14 – Immunological products, mixed, not put up in measured doses or in forms or packings for retail sale

3002.15 – Immunological products, put up in measured doses or in forms or packings for retail sale

The above three breakouts went into effect on January 1, 2017, and they had previously been classified in a larger category that included multiple blood products.⁹ The HTS defines immunological products as peptides and proteins which are directly involved in the regulation of immunological processes, such as mAbs, antibody fragments, antibody conjugates and antibody fragment conjugates. Of note is that a majority of global exports for immunological products for all years studied come from the subheading 3002.15, products put up in measured doses or in forms or packings for retail sale.¹⁰

⁷ Harmonized Tariff Schedule of the United States (2022), Revision 4, USITC Publication 5318, April 2022, Chapter 30.

⁸ The HTSUS refers to the system of codes within the United States, whereas the HS and its codes is used throughout the world. At the first 6-digits, the HTSUS and HS codes are the same. ITA “Understanding HS Codes and the Schedule B,” accessed April 31, 2022; The World Customs Organization, “What is the Harmonized System?” accessed April 31, 2022.

⁹ On August 20, 2014, the Commission instituted Investigation 1205—11, pursuant to section 1205 of the Omnibus Trade and Competitiveness Act of 1988 (the Trade Act of 1988) (19 U.S.C.3005), for purposes of recommending to the President possible modifications of the HTS (79 FR. 50943, Aug. 26, 2014). One of the modifications under consideration concerned the World Customs Organization’s (WCO) Recommendation of June 27, 2014 that Contracting Parties to the International Convention on the Harmonized Commodity Description and Coding System modify their tariff schedules to conform with amendments to the Harmonized System (HS). A WCO HS amendment deleted HS 3002.10 and added HS 3002.11, 3002.12, 3002.13, 3002.14, 3002.15, and 3002.19. U.S. International Trade Commission, “Recommended Modifications in the Harmonized Tariff Schedule to Conform with Amendments to the Harmonized System Recommended by the World Customs Organization, and to Address Other Matters,” Appendix B, pp. 106-107; Appendix E, pp. 249-250 (Appendix E is the WCO document of Harmonized System amendments). Investigation number 1205—11. USITC Publication 4556. Washington, DC: USITC, July 2015.

Subsequent to Investigation 1205—11, the WCO’s HS modifications were implemented into the HTSUS on January 1, 2017. Subheading 3002.10.02 was deleted and new subheadings 3002.11.00 through 3002.19.00 were added. The U.S. International Trade Commission, “Modifications to the Harmonized Tariff Schedule of the United States under Section 1206 of the Omnibus Trade and Competitiveness Act of 1988 and for Other Purposes,” Items 101-102. USITC Publication 4653. Washington, DC: USITC, December 2016.

As the new breakouts in the HTS for immunological products were implemented on January 1, 2017, specific trade data is only available beginning in January of 2017.

¹⁰ Years 2017-20, IHS Markit, Global Trade Atlas, accessed November 15, 2021.

Biologics

Biologics are known for their treatment in many disease areas. They have revolutionized cancer treatment options, transformed treatment for patients suffering from autoimmune conditions, and have served as effective first-in-class treatments for patients with conditions that have lacked effective treatment options thus far.¹¹ Patients suffering from chronic, immune-mediated diseases such as rheumatoid arthritis, plaque psoriasis, multiple sclerosis, ulcerative colitis, and Crohn's disease have seen remarkable slowing in disease progression as well as symptom management when treated with a biologic.¹² Current biologics on the market are also being used to treat cancers such as lung, breast, and blood cancers, non-Hodgkin's lymphoma and chronic lymphocytic leukemia.¹³

Monoclonal Antibody Market

Within the biologics market, the monoclonal antibody segment has seen a remarkable amount of growth from both a scientific development standpoint as well as an economic standpoint. The global market for monoclonal antibodies was valued at roughly \$115.2 billion in 2018 and is estimated to continue growing to roughly \$300 billion by 2025.¹⁴ These numbers are unsurprising considering that 70 percent of the top ten best-selling drugs in 2018 consisted of mAbs, with Humira (adalimumab) topping the list with record breaking revenues of \$19.9 billion. While all of the top ten bestselling monoclonal antibody drugs reached revenues of over \$3 billion in 2018, it is interesting to note that the majority of them actually reached over \$6 billion as well.¹⁵ This can be attributed to the expansion of indications for each molecule.¹⁶ As the years pass by, pharmaceutical companies preform clinical trials for drugs that they already have on the market in order to expand upon previous indications for which their products can be used. Expanding upon indications allows the pharmaceutical company to broaden their consumer base while also providing patients with alternative treatment options. Monoclonal antibodies have seen continual success throughout the years with the most common medical applications targeting the therapeutic areas of oncology and immune system disorders.

Table 1 lists the top 10 best-selling monoclonal antibody drugs. Five of the top ten mAbs are in the oncology space, including Herceptin (trastuzumab), Avastin (bevacizumab), Keytruda (pembrolizumab), Opdivo (nivolumab), and Rituxan (rituximab). Of these, Roche's Herceptin targets human epidermal growth factor receptor 2 (HER2) in breast cancer while Avastin targets vascular endothelial growth factor for the treatment of a variety of cancers. Both of these have shown tremendous sustained commercial success throughout the years. More recently Merck & Co's Keytruda and Bristol-Myers Squibb's Opdivo have entered the mAb oncology market as immune checkpoint inhibitors with a different mechanism of action that inhibits programmed cell death protein 1 (PD-1) receptors.¹⁷ Three of the top 10 best-selling mAbs in 2018 are in the immunology space. AbbVie's Humira and Johnson &

¹¹ Ogbru, "Biologics," October 28, 2019.

¹² Feldman, Bagel, and Namak, "Biosimilars for Immune-Mediated Chronic Diseases in Primary Care," May 2018.

¹³ Stone, "Top 10 Biologics Drugs in the United States," May 18, 2021.

¹⁴ Lu et al., "Development of Therapeutic Antibodies for the Treatment of Diseases," January 2, 2020.

¹⁵ Refer to Table 1 of this paper.

¹⁶ The term indication refers to a condition which makes a particular treatment or procedure advisable. MedicineNet, "Medical Definition of Indication," reviewed March 29, 2021.

¹⁷ Biopharma Dealmakers, "Moving Up with the Monoclonals," September 19, 2019.

Johnson's Remicade target and block tumor necrosis factors (TNFs). Using this mechanism of action, both Humira and Remicade have expanded indications treating numerous immune diseases including Crohn's, psoriasis, and rheumatoid arthritis. Finally, Johnson & Johnson's Stelara treats the same diseases as Humira and Remicade but with a different mechanism of action, instead targeting interleukins IL-12 and IL-23.¹⁸

Table 1 Top 10 best selling monoclonal antibody drugs in 2018, in billion US\$

Drug (mAb)	Indications *	Company	2018 Revenue
Humira (Adalimumab)	Rheumatoid arthritis; Psoriasis; Crohn's disease	AbbVie	\$19.9 bn
Opdivo (Nivolumab)	Melanoma; Non-small cell lung cancer; Lymphoma	Bristol-Myers Squibb	\$7.6 bn
Keytruda (Pembrolizumab)	Melanoma; Head and neck cancer; Lymphoma	Merck & Co	\$7.2 bn
Herceptin (Trastuzumab)	Breast cancer; Gastric cancer	Roche/Genentech	\$7.0 bn
Avastin (Bevacizumab)	Colorectal cancer; Breast ERB2 negative cancer; Glioblastoma	Roche/Genentech	\$6.8 bn
Rituxan (Rituximab)	Non-Hodgkin's lymphoma; Chronic lymphocytic leukemia; Rheumatoid arthritis	Roche/Genentech	\$6.8 bn
Remicade (Infliximab)	Crohn's Disease; Rheumatoid arthritis; Ulcerative colitis	Johnson & Johnson	\$5.9 bn
Stelara (Ustekinumab)	Psoriasis; Psoriatic arthritis; Crohn's Disease	Johnson & Johnson	\$5.2 bn
Soliris (Eculizumab)	Paroxysmal nocturnal hemoglobinuria; Atypical hemolytic uremic syndrome	Alexion	\$3.6 bn
Xolair (Omalizumab)	Asthma; Chronic idiopathic urticaria	Roche/Genentech	\$3.0 bn

Source: Lu et al., "Development of Therapeutic Antibodies for the Treatment of Diseases," January 2, 2020, table 2.

*Not all indications for each drug listed. Sales were reported by biologics or pharmaceutical companies.

Even in such a successful area of biopharmaceuticals, innovation is still thriving, in 2019 there were roughly 570 antibody therapeutics in various phases of development globally, with 79 of those novel antibodies currently in late-stage clinical trials.¹⁹ The monoclonal antibody space is currently dominated by the following seven biopharmaceutical companies: Genentech (a member of the Roche group), AbbVie, Johnson & Johnson, Bristol-Myers Squibb, Merck Sharpe & Dohme, Novartis, and Amgen.²⁰

In comparison to other classes of drugs, 9 monoclonal antibodies are ranked among the top 20 drugs by sales value worldwide (table 2).²¹ The top 2 spots by sales are antibodies, including the world's bestselling drug, Humira. In 2012, Humira became the top-selling drug globally and has remained in first place as of 2020.²²

¹⁸ Biopharma Dealmakers, "Moving Up with the Monoclonals," September 19, 2019.

¹⁹ Kaplon and Reichert, "Antibodies to Watch in 2019," Feb-March 2019; Kaplon et al., "Antibodies to Watch in 2020," Jan-Dec 2020.

²⁰ Lu et al., "Development of Therapeutic Antibodies for the Treatment of Diseases," January 2, 2020.

²¹ Antibodies hold rank number 1, 2, 7, 8, 11, 14, 16, 17, and 20.

²² Sagonowsky, "Top 20 Drugs," May 3, 2021.

Table 2 Top 20 drugs by global sales, 2020, antibody therapies shown in bolded blue, in billion US\$

Rank	Brand	Drug	Pharmaceutical Company	Therapy Area/ Drug Class	2020 Worldwide Drug Sales (US \$billion)
1	Humira	Adalimumab	AbbVie	Rheumatic diseases/TNF alfa inhibitors	20.4
2	Keytruda	Pembrolizumab	Merck & Co.	Cancer chemotherapy/Anti-PD-1 monoclonal antibodies	14.4
3	Revlimid	Lenalidomide	Bristol Myers Squibb	Cancer chemotherapy/Antineoplastic Agent	12.2
4	Eliquis	Apixaban	BMS/Pfizer	Anticoagulant for Heart Arrhythmias/Factor Xa inhibitors	9.2
5	Imbruvica	Ibrutinib	Abbvie / J&J	Leukemia and Lymphoma / BTK inhibitors	8.43
6	Eylea	Aflibercept	Regeneron / Bayer	Wet Macular Degeneration / Anti-angiogenic ophthalmic agents	8.4
7	Stelara	Ustekinumab	Janssen	Immunosuppressant/Interleukin inhibitors	7.9
8	Opdivo	Nivolumab	BMS	Cancer Chemotherapy/Anti-PD-1 monoclonal antibodies	7.9
9	Biktarvy	Bictegravir, emtricitabine, tenofovir alafenamide combination	Gilead	HIV /Antiviral combinations	7.3
10	Xarelto	Rivaroxaban	J&J/Bayer	Anticoagulant / Factor Xa inhibitors	6.9
11	Enbrel	Etanercept	Amgen	Antirheumatics/ TNF alfa inhibitors	6.37
12	Prevenar 13	Pneumococcal 13-valent Conjugate Vaccine	Pfizer	Pneumococcal vaccine	5.95
13	Ibrance	Palbociclib	Pfizer	Breast Cancer; Chemotherapy/CDK 4/6 inhibitors	5.39
14	Avastin	Bevacizumab	Roche	Cancer Chemotherapy/ VEGF/VEGFR inhibitors	5.32
15	Trulicity	Dulaglutide	Eli Lilly	Diabetes / Incretin mimetics	5.07
16	Ocrevus	Ocrelizumab	Roche	Multiple Sclerosis / CD20 monoclonal antibodies	4.61
17	Rituxan	Rituximab	Roche/Pharmstandard	Rheumatic Diseases, Cancer Chemotherapy/Antirheumatics, CD20 monoclonal antibodies	4.52
18	Xtandi	Enzalutamide	Astellas Pharma, Pfizer	Prostate cancer / antiandrogens	4.39
19	Tagrisso	Osimertinib	Astra Zeneca	Non-Small Cell Lung Cancer / EGFR inhibitors	4.33

Rank	Brand	Drug	Pharmaceutical Company	Therapy Area/ Drug Class	2020 Worldwide Drug Sales (US \$billion)
20	Remicade	Infliximab	J&J	Rheumatic Diseases/ antirheumatics	4.195

Source: PharmaDigiCoach, "Biggest Blockbuster Drugs of 2020," September 19, 2021; Sagonowsky, "Top 20 Drugs," May 3, 2021.

Biosimilars

In the biotechnology and biopharmaceutical space, obtaining intellectual property rights to a drug product, its formulation, or manufacturing process is critical to gaining market exclusivity and in turn market success. According to U.S. patent law, a utility patent is viable for 20 years from the earliest filing date submitted to the U.S. Patent and Trademark Office (this excludes provisional applications). As some of the most well-known biologics begin to lose patent protection, there has been a remarkable influx of competitors in the market trying to create medically equivalent treatments, known as biosimilar equivalents or biosimilars. According to the FDA, a biosimilar is designed to be "highly similar" to an already FDA-approved reference product with no clinically meaningful differences in purity, molecular structure, and bioactivity.²³

The exact chemical composition of small molecules is very well known and in turn allows for ease in reproducibility when creating an identical generic once a drug reaches patent expiry. Unlike small molecules, the complex molecular structure of biologics makes them costly to develop, produce, and manufacture. This expense is incurred by physicians, patients, payers, and the healthcare system as a whole. In order to help reduce costs and stimulate competition in biologics manufacturing, the U.S. Congress passed legislation that created the BPCIA (Biologics Price Competition and Innovation Act) in 2009.²⁴ This act encourages companies to develop biosimilars through an abbreviated and cost-effective Food and Drug Administration (FDA) approval pathway. It should be noted that in 2005, the European Union established a similar regulatory pathway for biosimilar approval through its regulatory body, the European Medicines Agency (EMA). The emergence of biosimilars provides greater patient access to cost-effective medical equivalents to biologics. Even with legislative efforts being made toward the development of biosimilars, they are still very difficult to develop because they require a great deal of reverse engineering of the original molecule in order to understand its physiochemical and biological characteristics.

The global market for biosimilars was worth roughly \$11.8 billion in 2020 and is projected to grow by 35.7 percent in 2025.²⁵ Examples of biosimilars are depicted in table 3. The increased growth in the biosimilars market is connected to increases in demand for affordable alternatives to biologics as well as the increased incidence of chronic diseases. It can be noted that within the biosimilars market, the monoclonal antibodies (mAbs) segment is the largest.²⁶ This trend is driven by the imminent patent expiration of some of the most

²³ FDA, "What is a Biosimilar?" accessed May 31, 2021; FDA, "Implementation of the Biologics Price Competition and Innovation Act of 2009," February 12, 2016.

²⁴ Boehringer Ingelheim, "What is the Promise of Biologic Medicines?" 2019. FDA, "Implementation of the Biologics Price Competition and Innovation Act of 2009," February 12, 2016.

²⁵ MarketsandMarkets, "Biosimilars Market," March 2020.

²⁶ MarketsandMarkets, "Biosimilars Market," March 2020.

notable blockbuster mAb biologics including but not limited to Remicade (infliximab), Humira (adalimumab), Herceptin (trastuzumab), Avastin (bevacizumab), and Rituxan (rituximab).²⁷

Table 3 Selected monoclonal antibody biologics for which biosimilars are being produced

Product	Molecule	Biosimilar Late-stage Manufacturers	Originator	U.S. Patent Expiration *	EU Patent Expiration *
Immunology					
Remicade	Infliximab	Merck/Samsung Bioepis, Celltrion/Pfizer (Hospira)	Johnson & Johnson	2018	2015
Humira	Adalimumab	Amgen, Sandoz, Boehringer Ingelheim	AbbVie	2016	2018
Oncology					
Herceptin	Trastuzumab	Pfizer, Amgen/Allergan/Synthon, Mylan/Biocon, Cellitron/Teva	Genentech/Roche	2019	2014
Avastin	Bevacizumab	Amgen, Outlook Therapeutics	Genentech/Roche	2019	2022
Rituxan	Rituximab	Sandoz, Boehringer Ingelheim/Cellitron, Pfizer (Hospira)	Biogen/Genentech/Roche	2018	2013

Source: Creative Biolabs, "Biosimilars of Monoclonal Antibodies," accessed May 31, 2021.

*The date given is based on the expected expiry of patents protecting the original molecule.

Some biosimilars brought to market are not available in the United States due to certain patent extensions on original biologics.²⁸ Europe is estimated by Gherghescu and Delgado-Charro to hold the largest share of the market in biosimilars due to patent expiry as well as having established regulatory policies.²⁹

Global Pharmaceutical Landscape

Total global exports of immunological products showed substantial growth from \$89.3 billion in 2017 to \$118.7 billion in 2018 to \$130.2 billion in 2019 to \$161.1 billion in 2020 (table 4). The top exporting countries in 2020 were Germany, Ireland, the Netherlands, the U.S., Belgium, and Switzerland (figure 1).³⁰ The majority of product (87 percent) exported was the type that was for retail sale, while the minority (13 percent) was not for retail sale (figure 2). Ireland, Switzerland, and Singapore drove the trend for products unmixed and not put up for retail sale (HS 3002.13, figure 3). Ireland, the U.S., and the Netherlands drove the trend for products that were mixed and not put up for retail sale (HS 3002.14, figure 4). Switzerland, Ireland, and Germany drove the trend for product put up for retail sale (HS 3002.15, figure 5). The increase

²⁷Creative Biolabs, "Biosimilars of Monoclonal Antibodies," accessed May 31, 2021; Biosimilars Review and Report, "Biosimilar Approval Status," May 18, 2021.

²⁸Feldman, Bagel, and Namak, "Biosimilars for Immune-Mediated Chronic Diseases in Primary Care," May 2018.

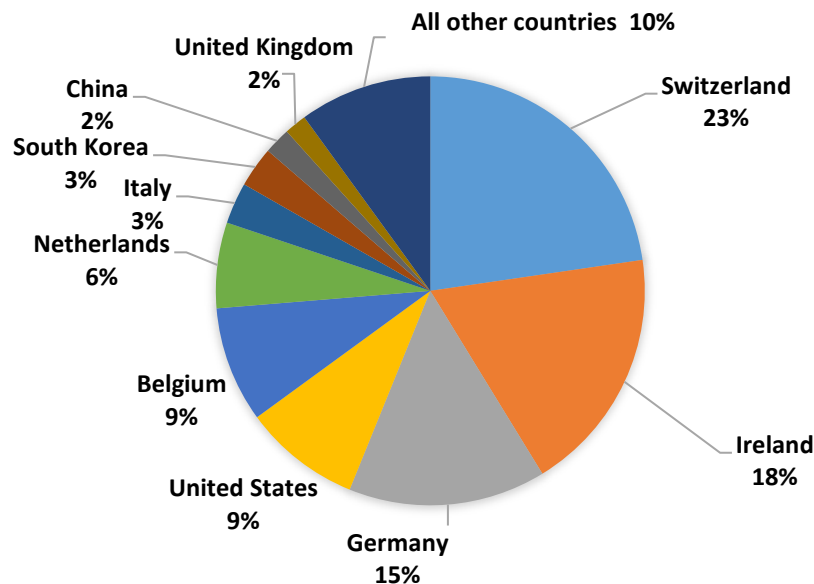
²⁹The EU pioneered the regulatory approval pathway for biosimilars and had its first approval in 2006, whereas the U.S. FDA approved its first biosimilar in 2015. The EU biosimilars market developed faster than the United States. European Medicines Agency and European Commission, "Biosimilars in the EU," 2019; MarketsandMarkets, "Biosimilars Market," March 2020; FDA, "Biosimilar Product Information," 2021; Gherghescu and Delgado-Charro, "The Biosimilar Landscape," 2021. This estimate coincides with data presented in this paper, which shows that seven out of 10 of the top exporting countries are from the EU (see figure 1).

³⁰Immunological products clarified in section entitled "HTS Classification." HTS 3002.13, 3002.14 and 3002.15 are combined.

in global exports from 2017 to 2020 was driven by two major factors: innovation in the ever-expanding biological drugs market as well as the development of biosimilars.³¹

The global top 10 players in the pharmaceutical industry based on pharmaceutical sales include Pfizer, Roche, Johnson & Johnson, Sanofi, Merck, Novartis, AbbVie, Amgen, GlaxoSmithKline, and Bristol-Meyers-Squibb, and these companies export to countries around the world.³² Although they are based in different countries, these multinational companies have holdings around the world that allow them to expand and invest in strategic mergers and acquisitions (M&A) to further their research, development, and manufacturing capabilities. On the other hand, smaller biopharmaceutical companies with much smaller product portfolios often do not have the resources or infrastructure to research, develop, and manufacture their products. These smaller companies out-source certain R&D through partnerships, most commonly with Contract Development & Manufacturing Organizations (CDMOs) or Contract Manufacturing Organizations (CMOs).³³ Smaller companies lower operational costs by allowing CDMOs to complete end-to-end drug development and manufacturing for them.³⁴ Some examples of CMOs include Lonza, AbbVie Contract Manufacturing, and Boehringer Ingelheim Biopharmaceuticals GmbH.³⁵

Figure 1 Immunological products, global export market share, 2020



Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

³¹Refer to Table 3. Biosimilar is the term used for the generic version of a patented biologic.

³²Burke, "Who Are the Top 10 Pharmaceutical Companies in the World?" November 8, 2020.

³³The difference in the two terms is the phase of the pharmaceutical lifecycle. Some companies only perform the manufacturing phase (CMOs) while others offer both manufacturing and development (CDMOs). Another term seen is Contract Research Organizations (CROs) that can perform research functions. Tapemark, "Pharmaceutical CDMOs," accessed December 15, 2021; Hyper Recruitment Solutions, "CRO/CMO," accessed December 15, 2021.

³⁴Quick, "CDMO Trends," June 26, 2019.

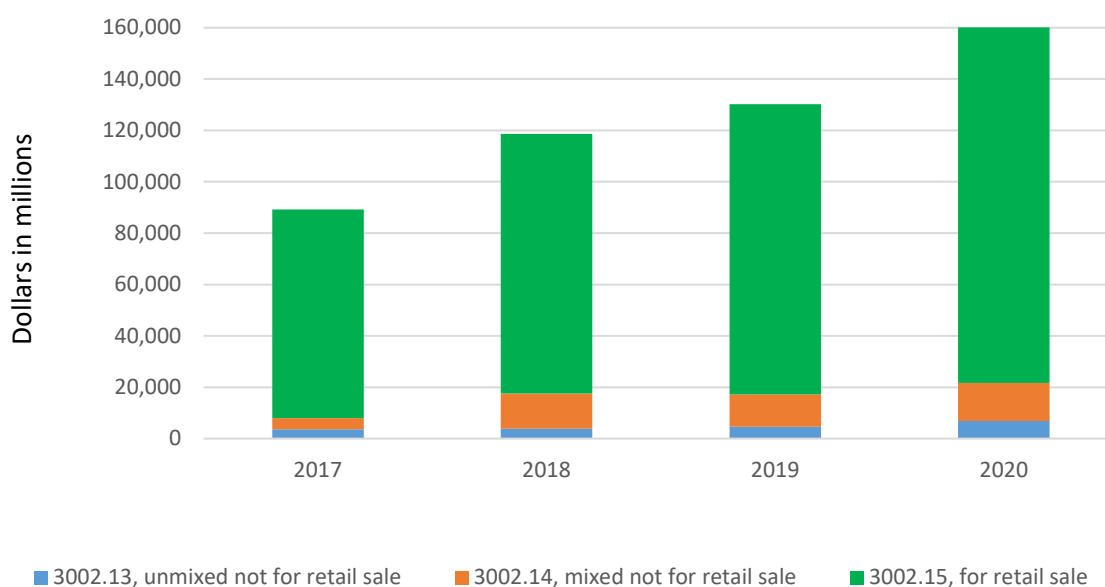
³⁵Grand View Research, "Biopharmaceuticals Contract Manufacturing Market Size," January 2021.

Table 4 Global export statistics of immunological products, (HS 3002.13, 3002.14, and 3002.15 combined), 2017-20, in million US\$

Country	2017	2018	2019	2020	% Change, 2019–20	Share of global exports, 2020
Switzerland	25,463	26,419	31,560	36,553	16%	23%
Ireland	8,302	18,318	21,175	29,889	41%	19%
Germany	18,044	22,398	20,937	23,979	15%	15%
United States	9,788	11,643	13,224	14,233	8%	9%
Belgium	5,898	9,080	10,834	14,053	30%	9%
Netherlands	7,048	10,809	9,309	10,399	12%	6%
Italy	3,746	5,463	6,264	5,023	-20%	3%
South Korea	1,365	1,810	2,144	4,927	130%	3%
China	167	154	195	3,224	1551%	2%
United Kingdom	4,369	3,432	2,621	2,697	3%	2%
All other countries	5,087	9,124	11,892	16,098	35%	10%
Total global exports	89,277	118,650	130,157	161,077	24%	100%

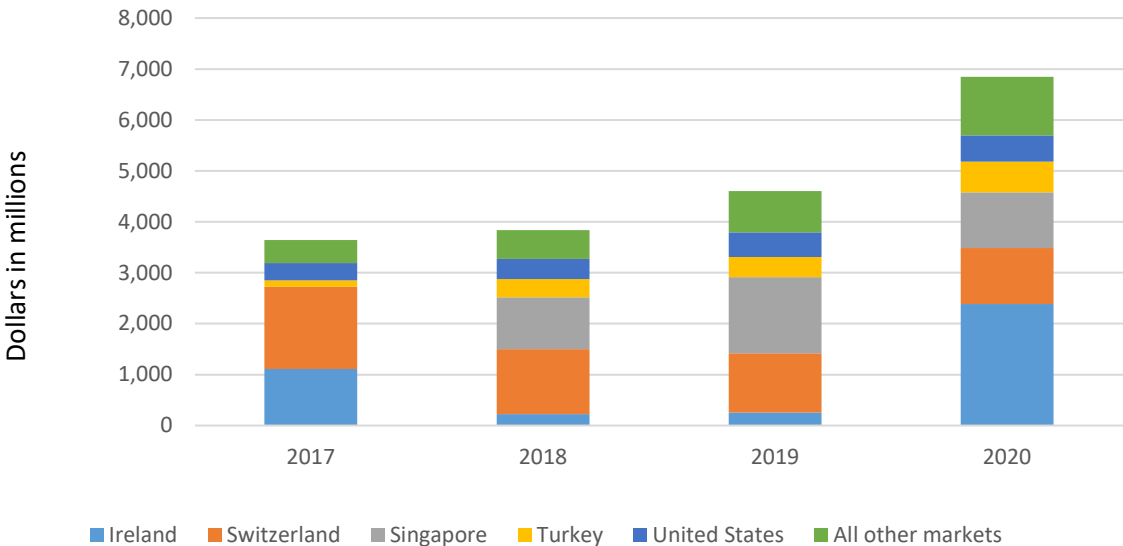
Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

Figure 2 Global exports of immunological products, by type of sale, 2017-20



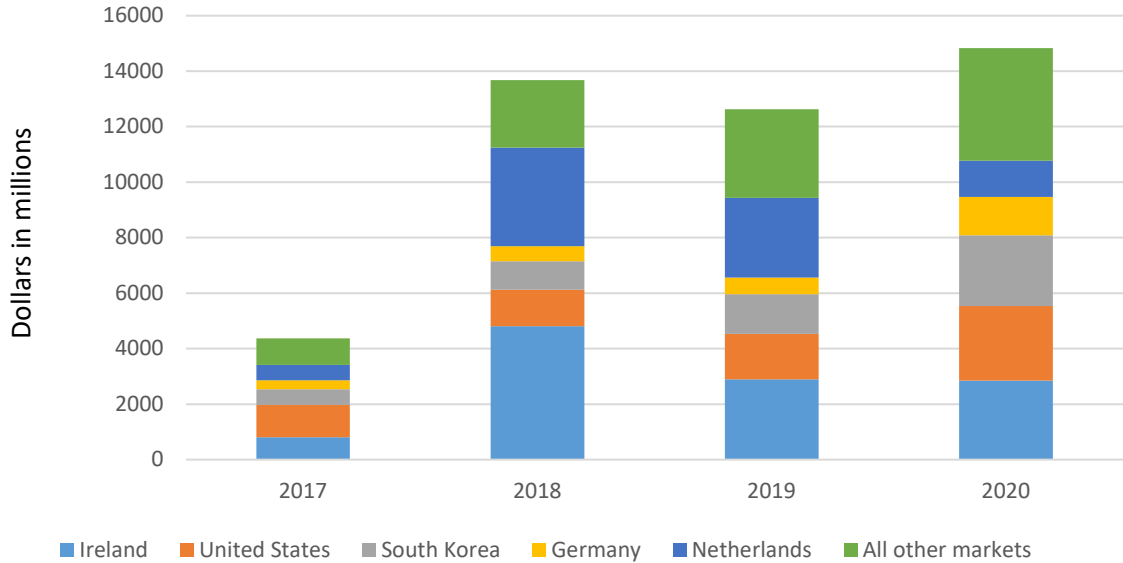
Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

Figure 3 Global exports, HS 3002.13, immunological Products, unmixed, not put up in measured doses or in forms or packings for retail sale, 2017–20, in million US\$



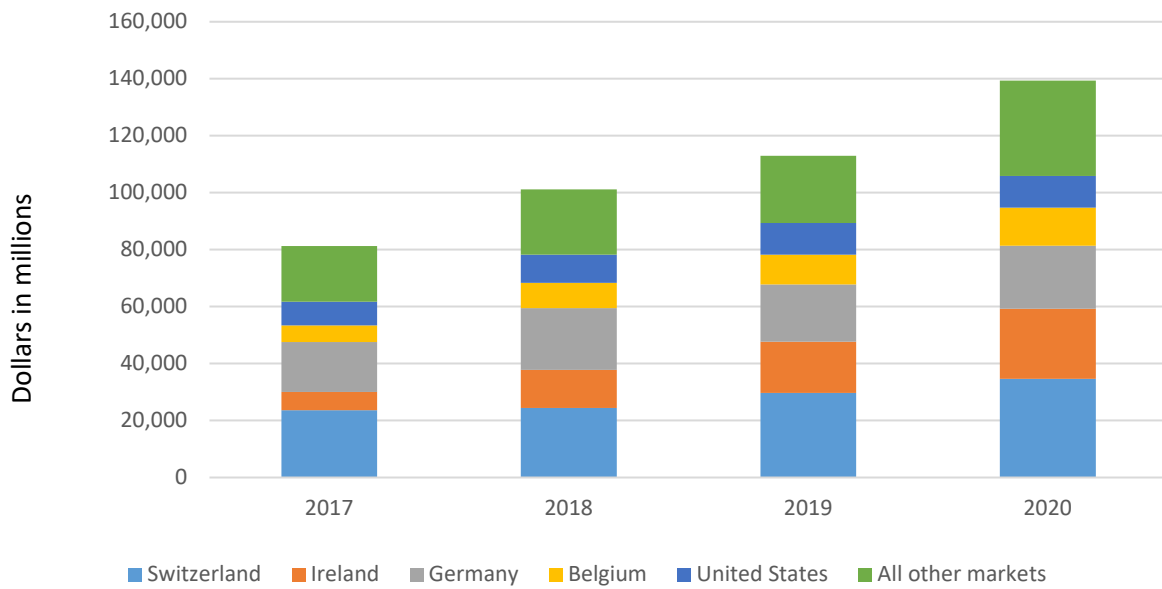
Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

Figure 4 Global exports, HS 3002.14, immunological products, mixed, not put up in measured doses or in forms or packings for retail sale, 2017–20, in million US\$



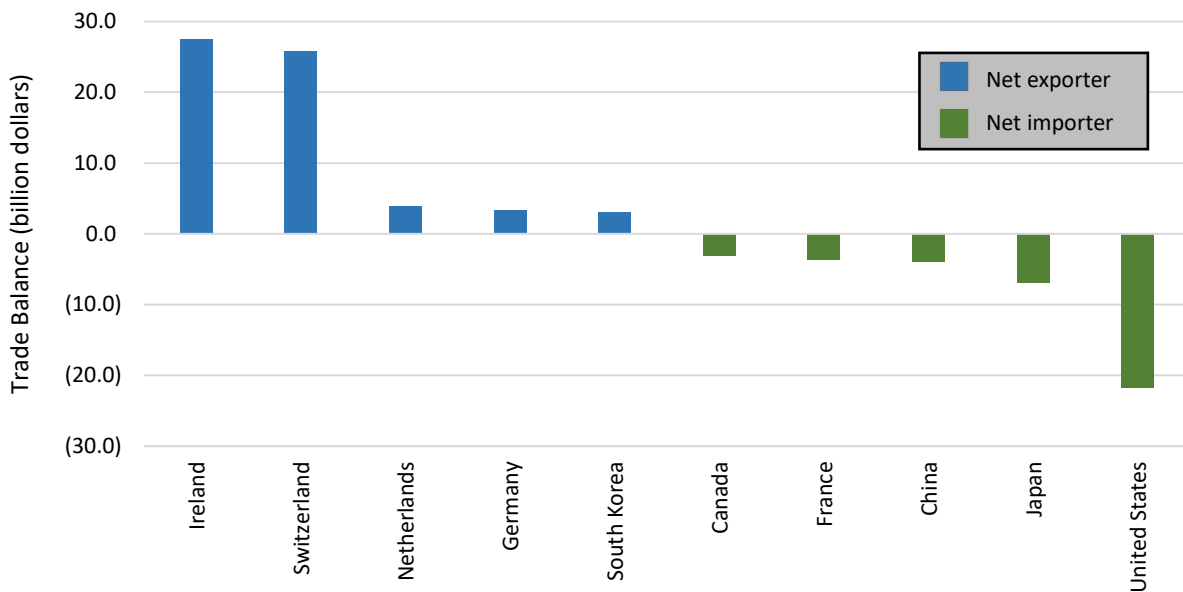
Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

Figure 5 Global exports, HS 3002.15, immunological products, put up in measured doses or in forms or packings for retail sale, 2017–20, in million US\$



Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

Figure 6 Immunological products, trade balance: Top 5 global net exporters and top 5 global net importers, 2020, in billion US\$



Source: IHS Markit, Global Trade Atlas, HS 3002.13, 3002.14, and 3002.15 combined, accessed November 15, 2021.

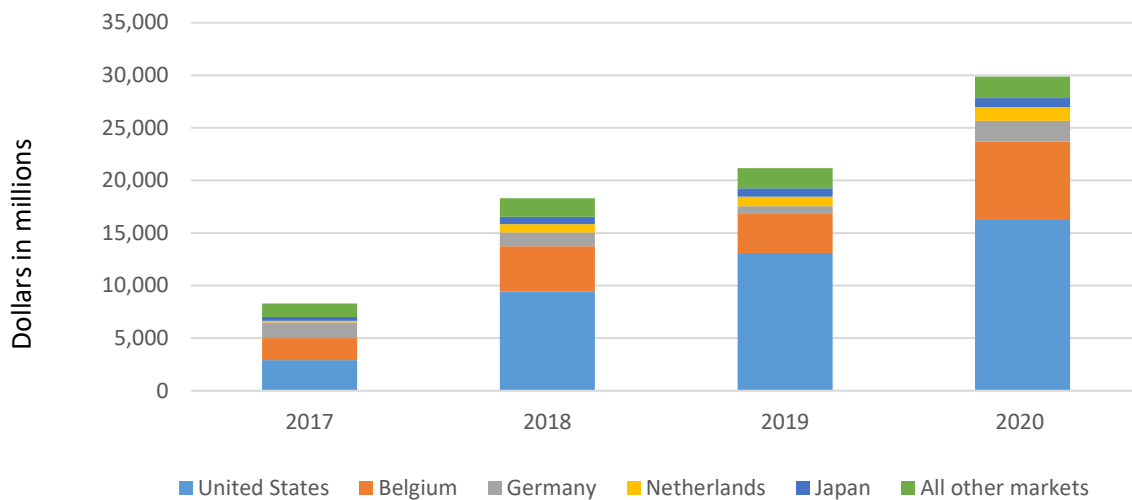
Country Profiles

Ireland

Ireland accounted for 19 percent (\$29.9 billion) of the global export market in 2020, and it is the world’s largest net exporter (table 4, figure 6). Ireland’s top export destinations were the United States (54 percent share of exports) and Belgium (25 percent share) (figure 7). The majority of product exported in 2020 was for retail sale (82 percent), followed by product not for retail sale in mixed form (10 percent), and product not for retail sale unmixed with other substances (8 percent) (figure 8).

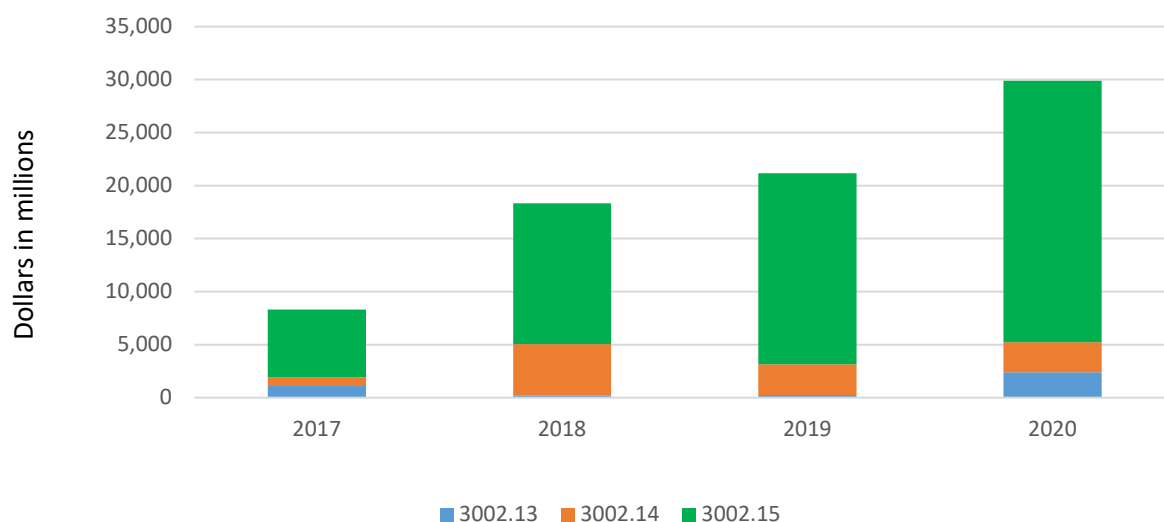
Interestingly, Ireland has seen a remarkable increase in the exports of immunological products from 2017 to 2020. This large jump in exports includes a \$10 billion (120 percent) increase from 2017 to 2018. Ireland is known for being home to 18 of the world’s top 20 pharmaceutical companies. One of the main reasons multi-national pharma and biotech companies have established holdings in Ireland is due to their favorable corporate tax rates coming in at just 12.5 percent. In addition to low tax rates, Ireland also incentivizes the pharma and biotech industry by offering 25 percent tax credit to qualifying pharmaceutical research and development (R&D).³⁶ Tax incentives and relative geographic proximity has led to the establishment of Ireland as the leading world epicenter for the manufacturing and subsequent exports of pharmaceuticals.

Figure 7 Ireland: Total exports of immunological products by destination country, 2017–20, in millions of US\$



Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

³⁶ Innopharma Education, “Why Ireland is Attracting the World’s Top Pharmaceutical Companies,” accessed May 31, 2021.

Figure 8 Ireland: Total exports of immunological products, by type of sale, 2017–20, in millions of US\$

Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

Note: HS 3002.13 is unmixed, not for retail sale, HS 3002.14 is mixed, not for retail sale, and HS 3002.15 is for retail sale.

Of the 90 biopharmaceutical plants in Ireland, fifty are FDA approved.³⁷ Pfizer was the first multinational pharmaceutical business to establish operations in Ireland and has since invested nearly \$8 billion in operations over the last 51 years. Pfizer has built four major manufacturing plants throughout Ireland with its single largest investment going into their Grange Castle Biotech facility in Dublin that boasts high-tech manufacturing capabilities in mammalian cell culture, protein purification, and aseptic syringe filling. Another notable Pfizer manufacturing site is the Ringaskiddy active pharmaceutical ingredient (API) plant in Cork that specializes in the manufacturing and export of bulk active pharmaceutical ingredients.³⁸ In 2014 Pfizer invested \$330 million into its Grange Castle and Ringaskiddy plants in order to expand upon their R&D and manufacturing capabilities.³⁹ Ireland is the leading manufacturing base for Pfizer globally, and the vice-president of Pfizer’s global supply, Dr. Paul Duffy, has remarked that medicines manufactured in Ireland are distributed to more than 100 countries around the world.⁴⁰

In addition to Pfizer, there are a large number of big pharma players in the industry that also have prominent manufacturing facilities in Ireland. Merck Sharp & Dohme (MSD), a subsidiary of Merck & Co., has taken advantage of opportunities in Ireland with manufacturing facilities in Dublin, Cork, Carlow and Tipperary. In February 2018, MSD announced its plans for the expansion of a new biologics manufacturing facility in Swords, Dublin that will be used to produce immune-oncology treatments, such as pembrolizumab.⁴¹ In 2017, Janssen pharmaceuticals, the pharmaceutical subsidiary of Johnson & Johnson announced the \$300 million expansion of their biologics manufacturing facility in Ringaskiddy, Cork. The

³⁷IDA Ireland, “Biopharmaceutical Industry in Ireland,” accessed May 31, 2021.

³⁸Pfizer, “About Pfizer in Ireland: Business Operations,” accessed May 31, 2021.

³⁹Kennedy, “Pfizer Opens Doors on US\$30M Lab in Cork,” May 1, 2014; Palmer, “Pfizer Planning Ireland Biologics Plant Expansion,” July 5, 2016.

⁴⁰The Irish Times, “Pfizer Ireland’s Influence Continues to Grow,” June 18, 2019.

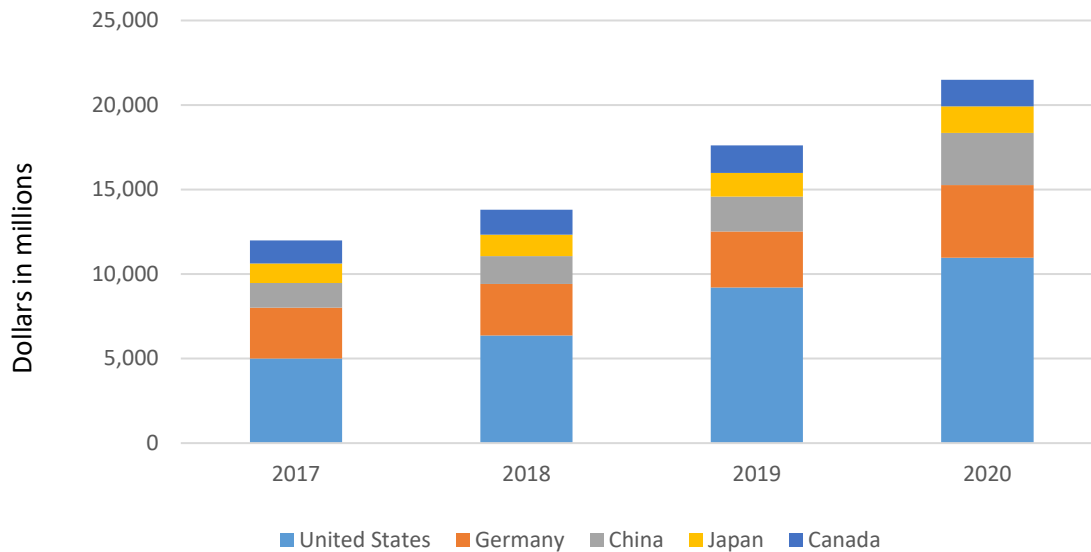
⁴¹Immuno-oncology refers to oncology drugs that are immune in nature, such as monoclonal antibodies. Pharmaceutical Technology, “MSD’s Biologics Manufacturing Facility, Swords, Ireland,” accessed May 31, 2021.

new facility will chiefly serve as site for the production of oncology and immunology treatments and is projected to generate 72 batches of monoclonal antibody products a year.⁴² Other high-profile biopharma companies that have established themselves in Ireland include GlaxoSmithKline (GSK), Allergan, Mylan, Teva Pharmaceuticals, Eli Lilly, and Amgen.⁴³

Switzerland

Switzerland accounted for 23 percent (\$36.6 billion) of the total global exports market in 2020 (table 4, figure 1). This makes Switzerland the country with the largest share of global exports of immunological products. Switzerland is the second largest global net exporter (figure 6). Switzerland’s top export destinations were the United States (30 percent share of exports) and Germany (12 percent share) (figure 9). The majority of products exported from 2017-2020 were for retail sale (figure 10), and the percentage of retail to non-retail products stayed relatively steady throughout that period. If a product is not in retail form, it may have to be shipped to another facility or country to be packaged and manufactured to its final form. In 2020, retail sale products had a share of 95 percent, followed by product not for retail sale in unmixed form (3 percent), and product not for retail sale mixed with other substances (2 percent) (figure 10). Most notably, exports increased by roughly \$5 billion (20 percent) from 2018 to 2019.

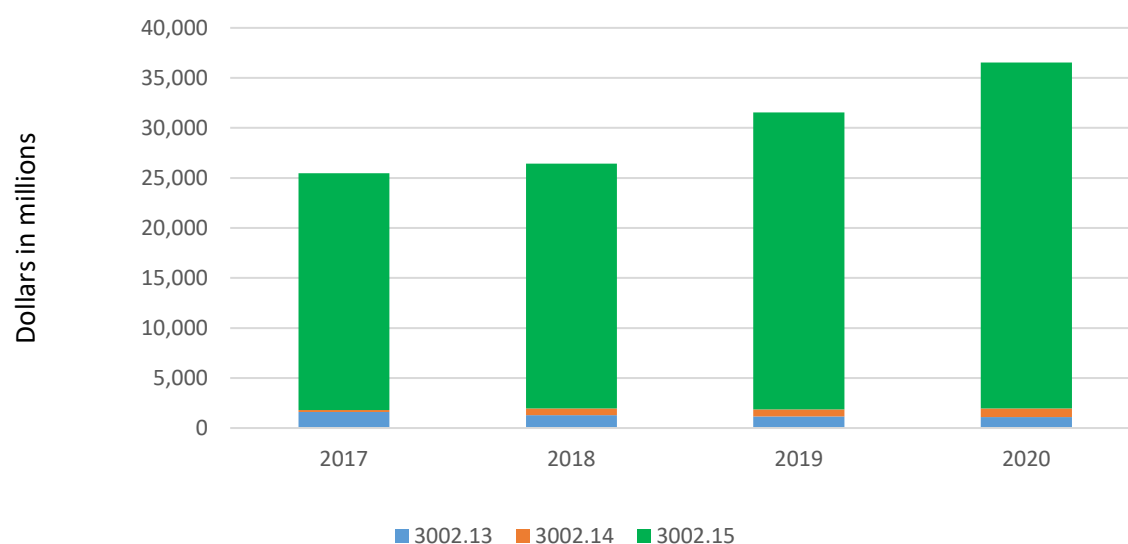
Figure 9 Switzerland: Total exports of immunological products by destination country, 2017–20, in millions of US\$



Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

⁴² Pharmaceutical Technology, “Janssen Sciences’ Biomedicines Manufacturing Facility, Ringaskiddy, Ireland,” accessed May 31, 2021.

⁴³ IDA Ireland, “Biopharmaceutical Industry in Ireland,” accessed May 31, 2021; Innopharma Education, “Why Ireland is Attracting the World’s Top Pharmaceutical Companies,” accessed May 31, 2021.

Figure 10 Switzerland: Total exports of immunological products, by type of sale, 2017–20, in millions of US\$

Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

Note: HS 3002.13 is unmixed, not for retail sale, HS 3002.14 is mixed, not for retail sale, and HS 3002.15 is for retail sale.

Interestingly, 38 percent of Switzerland’s total exports can be attributed to pharmaceuticals.⁴⁴ Switzerland is home to over 250 pharmaceutical companies. Most notably, two of the world’s leading pharmaceutical companies, Roche and Novartis, both have headquarters in Basel, Switzerland. Basel is known in Europe for being a huge life science hub due to its geographic location at the cross borders of Germany, France, and Switzerland. It is surrounded by highly esteemed research institutions including the University of Basel, Friedrich Miescher Institute for Biomedical research, and Eidgenössische Technische Hochschule (ETH) Zurich that collaborate with nearby pharmaceutical companies allowing for the synergistic development of drugs.

In 2018 the Swiss government funded a program known as BaseLaunch that incentivizes therapeutic innovation. BaseLaunch has partnered with local pharmaceutical companies including Johnson & Johnson, Roche, Pfizer, Novartis, and Roviant Sciences to fund and accelerate start-up therapeutic platform ventures.⁴⁵ Switzerland is also home to a number of CDMOs that specialize in biologics process development and manufacturing. One of these CDMOs, Lonza, conducts drug product service activities in its facilities located in Basel and Stücker while it handles fill and finish procedures in its cGMP (Current Good Manufacturing Practice) facilities in Stein.⁴⁶ In 2017 Lonza and French drug maker Sanofi pledged \$285 million in a joint venture to build a large-scale cGMP mammalian cell culture facility in Switzerland for monoclonal antibody production.⁴⁷

⁴⁴Pharmaceutical Technology, “A Formula for Success: Inside Swiss Pharma,” updated January 27, 2020.

⁴⁵BaseLaunch, “About Us,” accessed May 31, 2021.

⁴⁶Lonza, “Parenteral Drug Product Services,” accessed May 31, 2021.

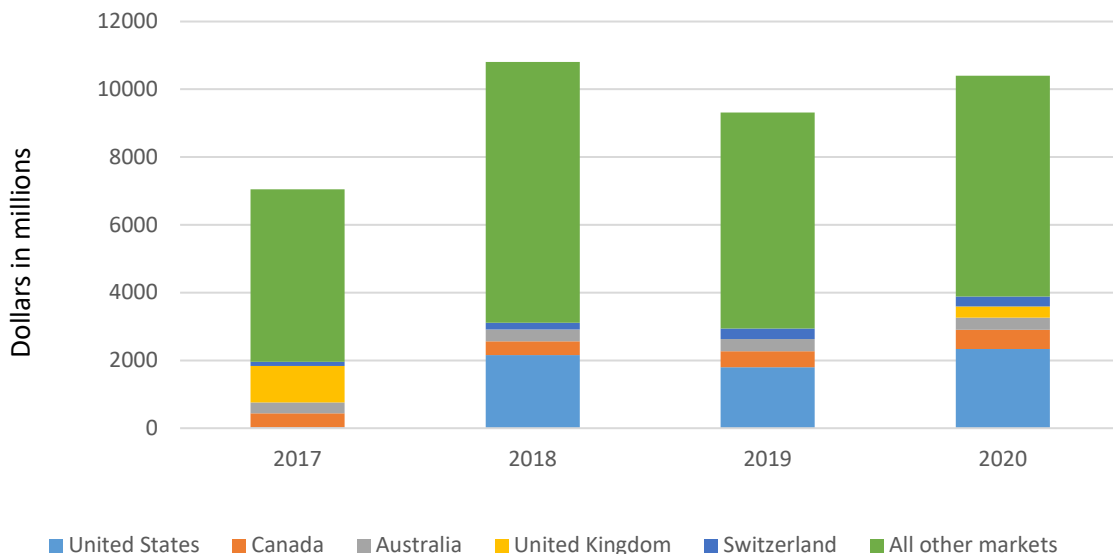
⁴⁷ Genetic Engineering and Biotechnology News, “Lonza, Sanofi Pledge \$288 million to Build Large-scale Biologics Plant in Switzerland,” February 27, 2017.

The Netherlands

The Netherlands accounted for 6 percent (\$10.4 billion) of the global export market in 2020 (figure 1, table 4). It is the world’s third largest net exporter (figure 6). The Netherlands’ top export destinations were the United States (22 percent share of exports) and Canada (5 percent share) (figure 11). The majority of products exported in 2017-2020 were for retail sale; however, the percentage of products for retail sale varied over that period, ranging from 67 percent in 2018 to 92 percent in 2017. If a product is not in retail form, it may have to be shipped to another facility or country to be packaged and manufactured to its final form. In 2020 the majority was for retail sale (87 percent), followed by product not for retail sale in mixed form (13 percent), and product not for retail sale unmixed with other substances (0 percent) (figure 12).

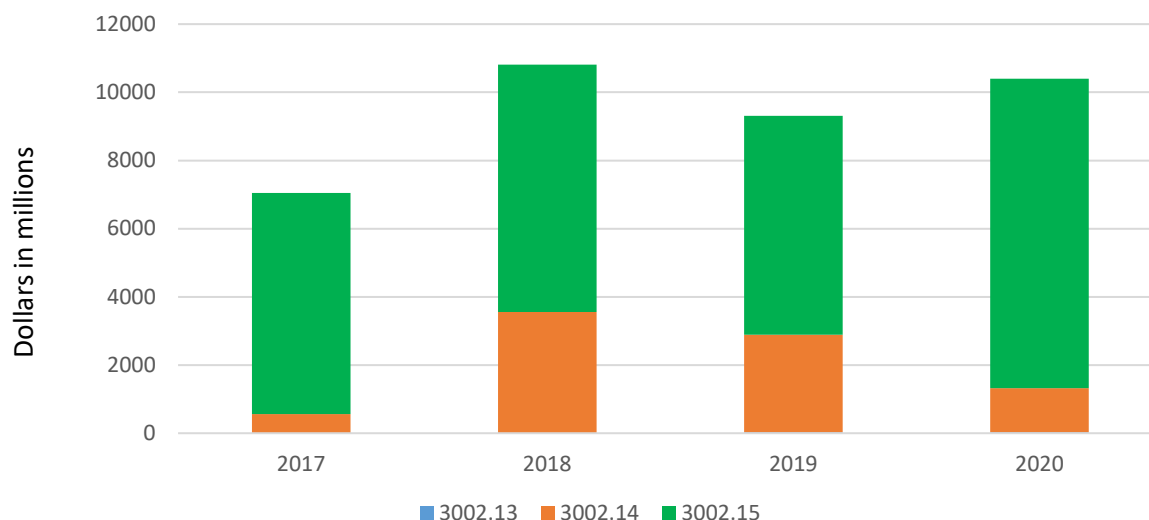
The global export market share that is attributed to the Netherlands seems large when taking into account their population size and the relative size of their pharmaceutical sector. Upon further research, the method of transportation of these traded goods, via ship, in conjunction with the Rotterdam effect may play a role in explaining the Netherlands’ relatively large market share of the global trade. The Rotterdam-Antwerp effect refers to the distortion of trade calculations that occurs when goods flow through ports on the way to their final destination. European regulations require that all traded goods be recorded upon entry and exit of the EU, thus leading to possible inflated trade calculations when goods are simply unloaded and reloaded onto different ships within a short period of time. More specifically, because Rotterdam is one of the leading ports in Europe, the Netherlands market share may be a high since many countries use this port as through-fares for other EU countries.⁴⁸

Figure 11 The Netherlands: Total exports of immunological products, by destination country, 2017–20, in millions of US\$



Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

⁴⁸ Economics Online, “The Rotterdam Effect,” accessed May 31, 2021.

Figure 12 The Netherlands: Total exports of immunological products, by type of sale, 2017–20, in millions of US\$

Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

Note: HS 3002.13 is unmixed, not for retail sale, HS 3002.14 is mixed, not for retail sale, and HS 3002.15 is for retail sale.

Holland is known to be one of the most attractive and inventive life science environments in Europe with roughly 420 biopharmaceutical companies, 12 research universities and 8 medical centers collaborating on R&D initiatives within a compact 120-mile radius.⁴⁹ The Netherlands prides its success in the biopharmaceutical industry to its emphasis on public-private partnerships (PPPs) that allow for joint ventures for the advancement of personalized medical treatments. Some notable Dutch PPPs include Health-RI, Oncode Institute, and RegMed-XB that look to revolutionize the areas of research infrastructure, oncology, and regenerative medicine strategies, respectively.⁵⁰ In addition to the collaborative life science research institutions, the corporate tax system, with rates ranging between 20-25 percent, has made the country a very inviting prospect to multi-national large pharmaceutical companies looking to expand into Europe. Furthermore, specific tax incentives including the WBSO R&D tax credit and the Innovation Box initiatives aim to support companies that look to innovate in the research and development of cutting-edge scientific pursuits.⁵¹ It is for these reasons that multi-national biopharmaceutical companies including Janssen Pharmaceuticals, MSD, Amgen, and AstraZeneca have expanded their operations into the Netherlands.

The Netherlands is also home to two life science hubs, Pivot Park and Leiden BioScience Park. Pivot Park is well known for its expertise in pharmaceutical R&D as well as its high-quality biologics manufacturing facilities.⁵² The Leiden BioScience Park is ranked as one of the top 5 bioscience parks in Europe and is the largest life science cluster in Netherlands.⁵³ It boasts over 100 biomedical life science companies, many

⁴⁹Pearson, "The Netherlands Ups Its Pharmaceutical Game," December 6, 2018.

⁵⁰Health Holland, "Public Private Partnerships," accessed May 31, 2021.

⁵¹Invest in Holland, "Incentives and Taxes in the Netherlands," accessed May 31, 2021.

⁵²Pivot Park, "Facilities and Infrastructure," accessed May 31, 2021.

⁵³FactCards, "Leiden Bio Science Park," accessed May 31, 2021.

start-ups, and quite a few research institutions all of which collaborate to further the discovery, development, and production of cutting-edge medications.⁵⁴

The Netherlands' biopharmaceutical industry is expected to flourish with the relocation of the European Medicines Agency (EMA) headquarters, the EU's regulatory body, from the UK to Amsterdam after the UK Brexit vote in 2017.⁵⁵ The EMA officially began operating in Amsterdam in March of 2019 and its highly anticipated arrival enticed biotech and biopharmaceutical companies to invest in manufacturing facilities. Smaller companies like Halix, a CDMO for biologics manufacturing, completed construction on a state-of-the-art cGMP compliant facility in November 2019 in Leiden in order to increase the manufacture of antibody therapeutic products.⁵⁶ Gilead Sciences' subsidiary, Kite Pharma, has also invested in the expansion of their biopharmaceutical manufacturing capabilities with the estimated completion of their newest facilities in Hoofddorp, Netherlands in 2020. As a leader in the development of immunotherapies in oncology, Kite intends for this plant to be used for the production and manufacturing of their Chimeric antigen receptor T-cell (CAR-T) therapies.⁵⁷

Germany

Germany accounted for 15 percent (\$24.0 billion) of the global exports market in 2020 (table 4, figure 1), and it is the world's fourth largest net exporter (figure 6). Germany's top export destinations were the Netherlands (20 percent share of exports), the United States (19 percent share), and Switzerland (9 percent share) (table 13). Nearly all of products exported from 2017-2020 were for retail sale, and the percentage of product decreased steadily from 97 percent in 2017 to 92 percent in 2020. Nearly all products in 2020 were for retail sale (92 percent), followed by product not for retail sale in mixed form (6 percent), and product not for retail sale unmixed with other substances (2 percent) (table 14).

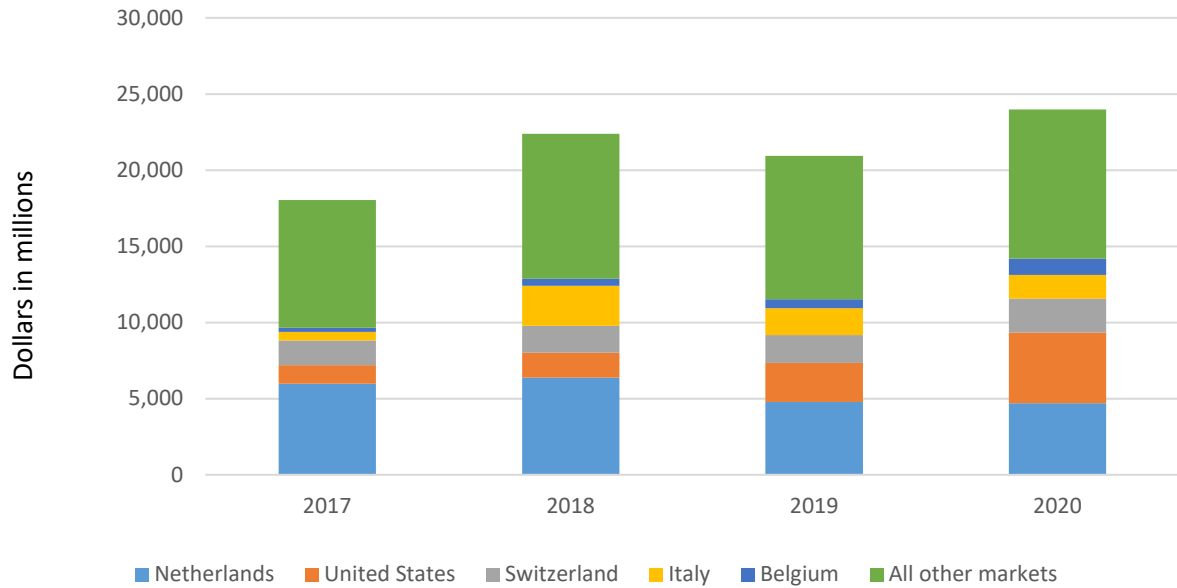
⁵⁴Yumpu, "Brochure on Leiden Bio Science Park," accessed May 31, 2021.

⁵⁵European Medicines Agency, "Relocation to Amsterdam," updated April 30, 2020.

⁵⁶HALIX, "Antibody Manufacturing," accessed May 31, 2021; Pharmaceutical Technology, "HALIX cGMP Biopharmaceutical Facility, Leiden," accessed May 31, 2021.

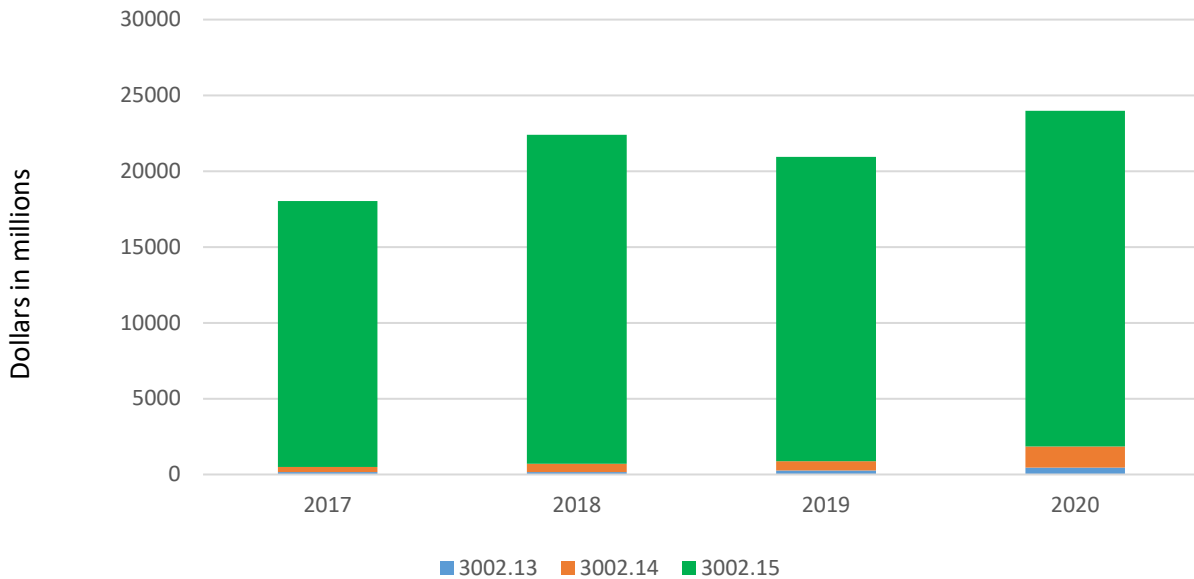
⁵⁷Pharmaceutical Technology, "Kite Pharma's Biopharmaceutical Manufacturing Facility," accessed May 31, 2021.

Figure 13 Germany: Total exports of immunological products by destination country, 2017–20, in millions of US\$



Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

Figure 14 Germany: Total exports of immunological products, by type of sale, 2017–20, in millions of US\$



Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

Note: HS 3002.13 is unmixed, not for retail sale, HS 3002.14 is mixed, not for retail sale, and HS 3002.15 is for retail sale.

Germany is considered a leader in the European pharmaceutical market for its expertise in finished product manufacturing. According to a report produced annually by Convention on Pharmaceutical Ingredients (CPI) Worldwide, in 2019 Germany scored remarkably high in the areas of API manufacturing and innovation, and there was an 11 percent increase in Germany's score from 2018 to 2019.⁵⁸

Germany is a powerhouse in European production locations because of the long standing high-quality standards of operation.⁵⁹ German biomanufacturing facilities capitalize on their efficiency by utilizing high throughput processing and the latest cutting-edge machinery.⁶⁰ One way Germany excels in the biopharmaceutical manufacturing industry is by being home to a great number of CMOs that enable pharmaceutical companies around the world to engage in partnerships.⁶¹ These international partnerships allow companies to select specific services ranging from product development to mammalian cell culture to sterile-fill-finish expertise from German CMOs at a lower cost than if they were to manufacture a drug product on their own.⁶² Germany Trade & Invest is a federal economic development agency that implements branding initiatives like "Health – Made in Germany" that assist in facilitating partnerships between foreign businesses and German contract research organizations (CROs). In an effort to promote foreign business collaboration they have made the "German Biomanufacturing Guide" filled with active German biomanufacturing businesses within Germany that aids pharmaceutical companies in finding the most ideal facilities to manufacture from. In regard to physical location, Germany is very centrally located within Europe which allows for ease of production and subsequent distribution of products.

The German market is very open to foreign direct investment.⁶³ The German government does not impose regulations to trade or barriers to entry which is very appealing to companies looking to establish holdings. In regard to corporate tax, the tax burden ranges from roughly 30 percent to as low as 22.3 percent.⁶⁴ Although this is not as low as Ireland, Germany has provided double taxation agreements that are put into place to ensure foreign parent companies are not taxed twice when relocating dividends from their German holdings.⁶⁵

Examples of German pharmaceutical companies include Boehringer Ingelheim, which is one of the largest privately owned pharmaceutical companies in the world. They are highly regarded for having over 35 years of experience and cultivated expertise in R&D, production, and manufacturing of biologics. All of their

⁵⁸Hargreaves, "Germany Seen as the Leader of European Pharma Industry," October 31, 2019.

⁵⁹ Germany has had a history of quality production of different products. Proch, "'Made in Germany' is World's Favorite Brand," March 27, 2017; Ideas2IT, "Why Germany is Synonymous with Quality," March 18, 2020; Expatrio, "German Business Culture," accessed April 31, 2022; Germany Trade and Invest, "The Pharmaceutical Industry in Germany," 2017-2018.

⁶⁰Germany Trade and Invest, "The Pharmaceutical Industry in Germany," 2017-2018.

⁶¹ BusinessWire, "European Pharmaceutical Contract Manufacturing Market Growth," December 3, 2021; Research and Markets, "European Pharmaceutical Contract Manufacturing Market Forecast, 2018-23," January 2019; Boehringer Ingelheim, "Global Biopharma Contract Manufacturing," accessed April 31, 2022.

⁶²Boehringer Ingelheim, "About Boehringer Ingelheim BioXcellence," accessed April 31, 2022; AbbVie, "Contract Manufacturing: Biologics," accessed April 30, 2021.

⁶³Trading Economics, "Germany Foreign Direct Investment," accessed April 31, 2022; Krause, "Foreign Direct Investment Screening in Germany," June 19, 2020.

⁶⁴The 22.3 percent are for certain German municipalities in some cases. Germany Trade and Invest, "The Pharmaceutical Industry in Germany," 2017-2018; Trading Economics, "Germany Corporate Tax Rate," accessed April 31, 2022; Bray, "Corporate Tax Rates Around the World," December 9, 2021.

⁶⁵Trading Economics, "United Kingdom Indicators," accessed April 31, 2022; Germany Trade and Invest, "The Pharmaceutical Industry in Germany," 2017-2018; Bray, "Corporate Tax Rates Around the World," December 9, 2021.

plants worldwide operate under cGMP standard regulations enforced by the FDA which is one of the reasons they are trusted to manufacture biologics from 15 of the top 20 pharmaceutical companies around the world.⁶⁶ They also created their very own CMO, BioXcellence, which allowed them to expand their operations further. With a shift in their product pipeline to roughly 40 percent biologics in 2018, they invested \$268 million in the expansion of their biologics site in Biberach, Germany, which was already the largest multi-product plant for the use of mammalian cell culture while boasting large-scale bioreactors with cGMP capacities up to 15,000 liters.⁶⁷

Sandoz is the German division of Novartis that has been known as the global leader in biosimilars for the past 2 decades.⁶⁸ Two of the key disease areas with drugs in late-stage development include immunology and oncology. AbbVie is also known for having their largest research and development facilities outside of the United States in Ludwigshafen, Germany, where they produce all of the biologic therapies used in AbbVie's clinical trials around the world.⁶⁹ Merck KGaA which is also known as Merck Serono, is the German division of Merck that focuses on the development of biopharmaceuticals with headquarters in Darmstadt. In 2015, they invested \$73 million in the expansion of research laboratories on their Darmstadt campus headquarters to enhance R&D collaboration on their biopharmaceutical pipeline portfolio.⁷⁰ Merck KGaA further built upon this investment by pledging \$1.13 billion from 2019-2025 to further expand upon the manufacturing capabilities at their headquarters.⁷¹ These companies may have seen their manufacturing capabilities becoming stagnant and in turn decided to expand upon their facilities in recent years to hopefully regain dominance in the coming years. This thinking could account for the lower export values in 2019. With these new biologic focused facilities coming into the market, it is expected that there will be an increase in the export of immunological products.

Singapore

Singapore is actively developing its immunological products industry. The country only began exporting immunological products under the statistical reporting numbers previously listed starting in 2018 but surprisingly accounted for 2 percent (\$2 billion) of the total global exports market in 2019, and it is a net exporter.⁷² Singapore's top export destinations in 2020 were the United States (34 percent share of exports), Belgium (16 percent share) and Switzerland (10 percent share) (figure 15). The majority of product exported was not for retail sale in unmixed form (56 percent), followed by product not for retail sale in mixed form (19 percent), and product for retail sale (24 percent) (figure 16). Singapore is one of the world's top exporters of product not for retail in unmixed form (figure 3).

⁶⁶Boehringer Ingelheim, "What is the Promise of Biologic Medicines?" 2019.

⁶⁷Boehringer Ingelheim, "The Origin of Our Success Story," accessed May 31, 2021; Taylor, "Boehringer Commits €230M to Build Biologics Sector," June 25, 2018.

⁶⁸Sandoz Biopharmaceuticals, "Sandoz Biosimilars," July 2017.

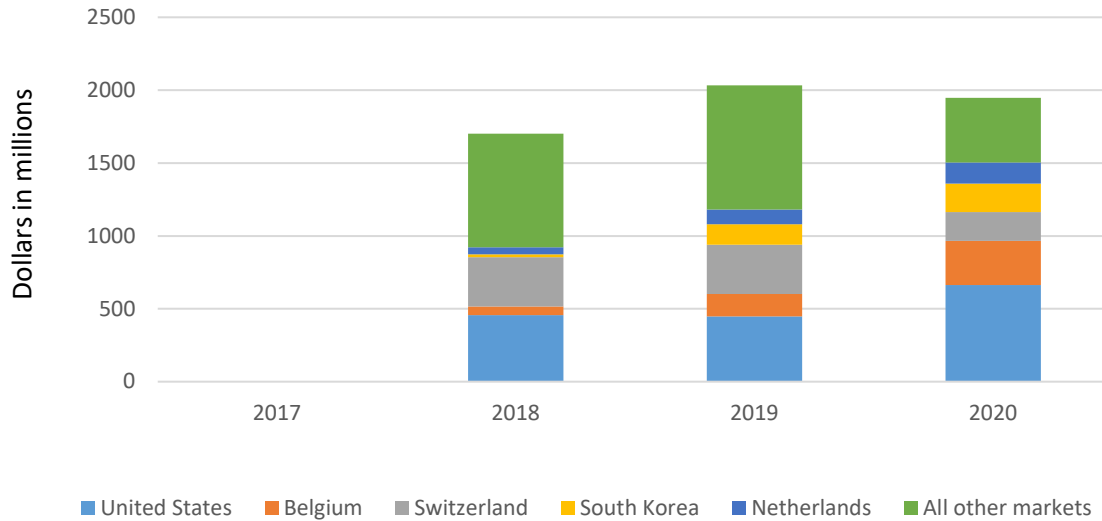
⁶⁹AbbVie, "Inside the Labs at AbbVie Ludwigshafen," November 27, 2018.

⁷⁰ Pharmaceutical Technology, "Merck Serono Biopharmaceutical R&D Facility Expansion, Darmstadt," accessed May 31, 2021.

⁷¹Hargreaves, "Merck KGaA Invests €1bn in Darmstadt HQ," March 25, 2019.

⁷²Global Trade Atlas, accessed June 1, 2020.

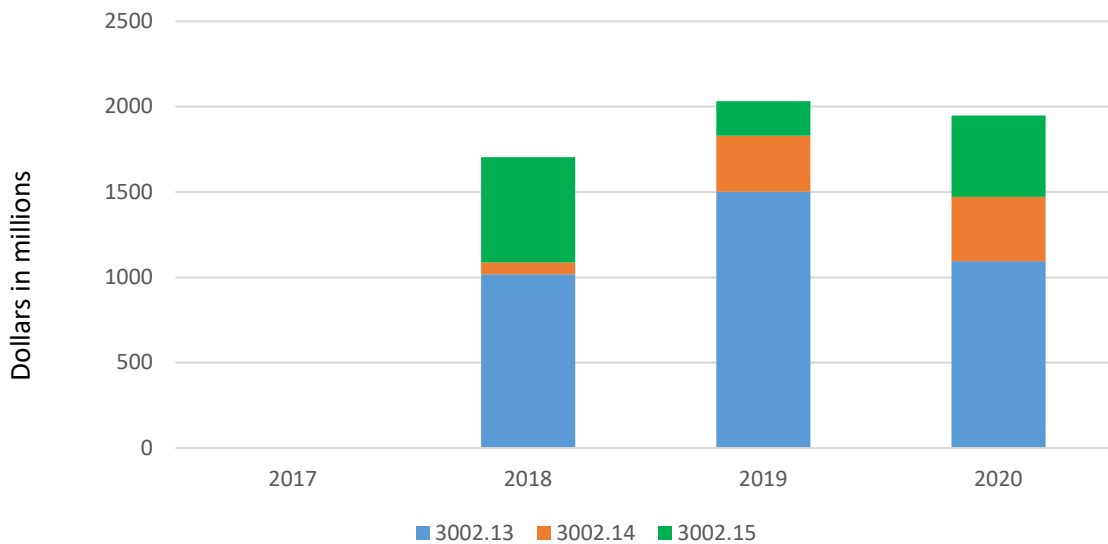
Figure 15 Singapore: Total exports of immunological products by destination country, 2017–20, in millions of US\$



Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

Note: GTA reports zero for Singapore in 2017. As mentioned in the HTS classification section, the new breakouts for immunological products went into effect in 2017, and it is possible exports were not reported.

Figure 16 Singapore: Total exports of immunological products, by type of sale, 2017–20, in millions of US\$



Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

Note: HS 3002.13 is unmixed, not for retail sale, HS 3002.14 is mixed, not for retail sale, and HS 3002.15 is for retail sale.

Note: GTA reports zero for Singapore in 2017. As mentioned in the HTS classification section, the new breakouts for immunological products went into effect in 2017, and it is possible exports were not reported.

In the past couple of decades Singapore has undergone rapid growth in the pharmaceutical sector and has become the Asian hub for biopharmaceutical manufacturing with roughly 3–5 percent of the nation’s gross

domestic product (GDP) being attributed to the pharmaceutical manufacturing industry.⁷³ Singapore achieved such growth by developing a skilled workforce through government initiatives such as the Professional Conversion Program for the biologics manufacturing industry. That program was implemented in 2014 and aimed to train graduating students on necessary skills to join the workforce.

Singapore is also well known for its ability to engage in strategic partnerships with public research institutions as well as with foreign pharmaceutical companies. In 2017, Pharma Innovation Programme Singapore (PIPS) was created as a platform for the synergistic collaboration and innovation of research institutions like the National University of Singapore and Agency for Science, Technology and Research with larger biopharmaceutical companies including Pfizer, Amgen, GlaxoSmithKline (GSK), and Lonza on biologics manufacturing technologies.⁷⁴

Over the years, Singapore has lowered its corporate tax rate; in 1980 it had a 40 percent rate, in 1990 it had a 32 percent rate, in 2000 it had a 26 percent rate, and in 2010, it changed to a 17 percent rate.⁷⁵ Singapore has attracted foreign pharmaceutical and biotech investments in manufacturing by offering low corporate tax rates of 17 percent, including tax exemptions for new companies on the first \$100,000 of annual profits for the first 3 years.⁷⁶ The country is currently home to roughly 55 pharmaceutical manufacturing plants with the majority of them built with investments from collaborative partnerships with major pharmaceutical businesses.⁷⁷

The United States

The United States accounted for 9 percent (\$14.2 billion) of the market share of the global exports of immunological products in 2020 (figure 1, table 4). The top export destinations of U.S. products were the Netherlands (17 percent share of exports), Italy (11 percent share), and Germany (10 percent share) (figure 17). The majority of product exported from 2017-20 was for retail sale. In 2020, the majority was for retail sale (78 percent), followed by product not for retail sale in mixed form (19 percent), and product not for retail sale unmixed with other substances (4 percent) (figure 18). The United States, a net importer, runs a trade deficit in this area for various reasons, chiefly driven by the shift in the U.S. pharmaceutical culture toward the increased investment in research and innovation through various legislative efforts.⁷⁸

⁷³Si, "Overview of the Singapore Pharmbio Sector," 2019/2020: Yee, "Overview of the Singapore Pharmbio Sector," accessed May 31, 2021.

⁷⁴Leitch and Richter, "Future-proofed Pharma," December 7, 2018.

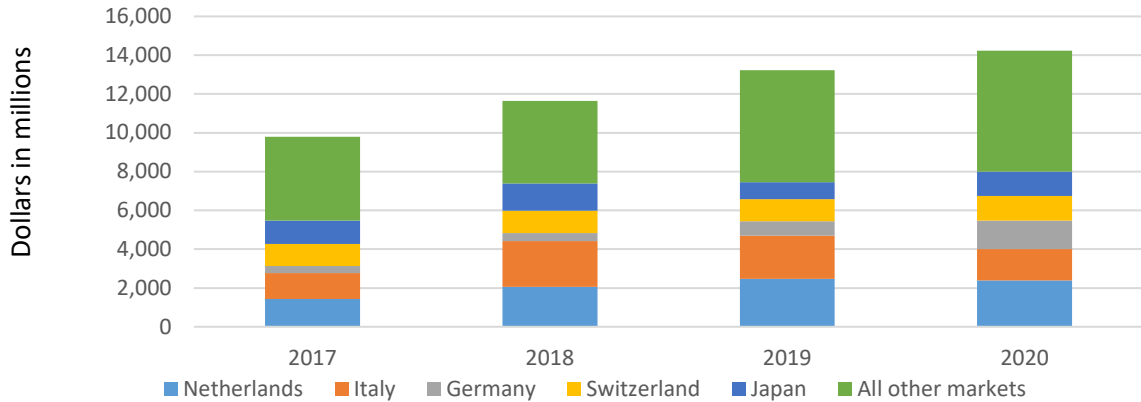
⁷⁵Bray, "Corporate Tax Rates Around the World," December 9, 2021.

⁷⁶PricewaterhouseCoopers, "Pharma 2020: Taxing Times Ahead," accessed May 31, 2021.

⁷⁷The Straits Times, "Singapore Pharma Sector an Increasingly Important Part of Manufacturing," updated July 25, 2019.

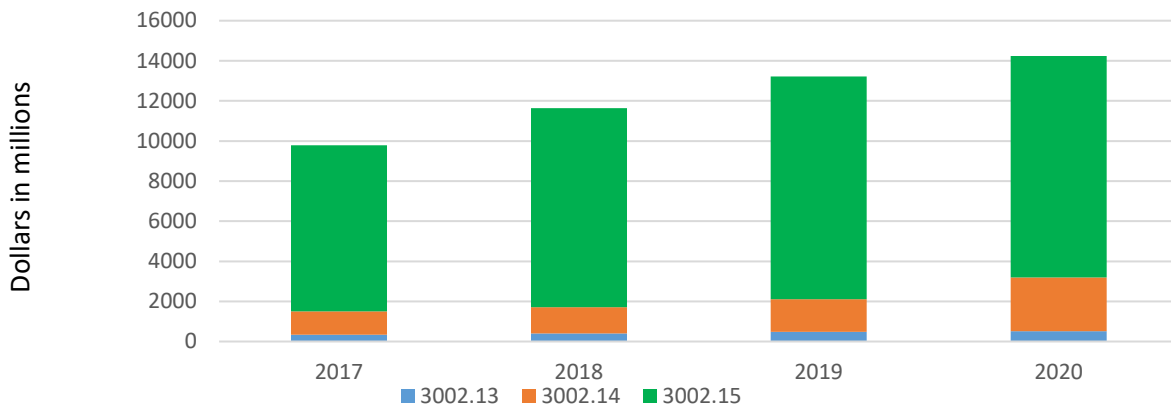
⁷⁸The U.S. imported roughly \$26.7 billion in 2019, which made it the global top net importing country of immunological products (figure 6). The majority of product imported from 2017-20 was for retail sale. In 2020, the majority imported was for retail sale (83 percent), followed by product not for retail sale in mixed form (15 percent), and product not for retail sale unmixed with other substances (2 percent) (figure 19).

Figure 17 The United States: Total exports of immunological products by destination country, 2017–20, in millions of US\$



Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021. All three HS categories (HS 3002.13, 3002.14, and 3002.15 are combined).

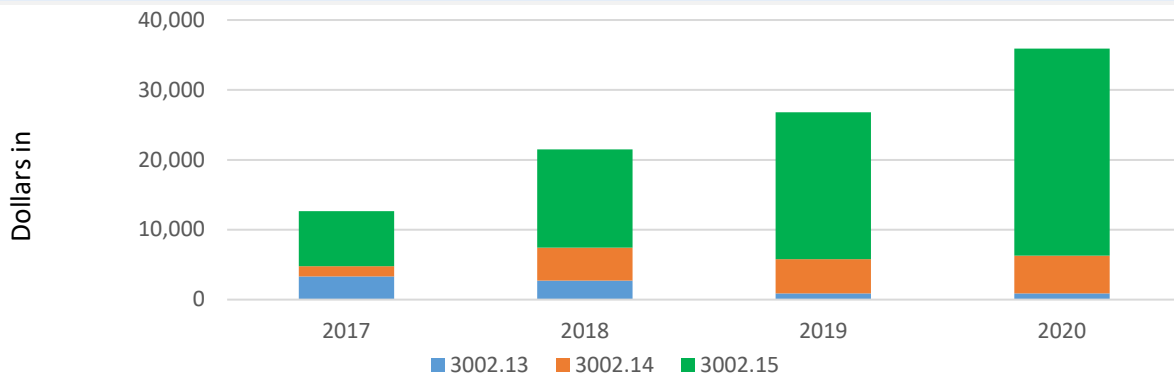
Figure 18 The United States: Total exports of immunological products, by type of sale, 2017–20, in millions of US\$



Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

Note: HS 3002.13 is unmixed, not for retail sale, HS 3002.14 is mixed, not for retail sale, and HS 3002.15 is for retail sale.

Figure 19 The United States: Total imports of immunological products, by type of sale, 2017–20, in millions of US\$



Source: IHS Markit, Global Trade Atlas, retrieved November 15, 2021.

Note: HS 3002.13 is unmixed, not for retail sale, HS 3002.14 is mixed, not for retail sale, and HS 3002.15 is for retail sale.

The United States has proved itself as the world leader in biopharmaceutical R&D innovation by increasing medical R&D investments in an effort to develop cutting edge treatments and cures. In a report produced by the White House in February of 2020, the Council of Economic Advisors estimated that the United States is responsible for funding roughly half of all global medical research while investing in 75 percent of global medical venture capital. It is for this reason that intellectual property rights for the majority of new medicines are held by U.S.-based firms.⁷⁹ This increase in R&D efforts has led to inherent decrease of domestic manufacturing and subsequent shift toward the outsourcing of biopharmaceutical manufacturing overseas. According to a report produced by the FDA in October 2019, 72 percent of API manufacturers that supply the U.S. market are overseas with 26 percent coming from the EU.⁸⁰ The United States has shifted its manufacturing capabilities overseas due to decreased labor costs and fewer environmental regulations, among other cost benefits that ultimately allow U.S. firms the ability to increase productivity while still keeping costs low.

Drug products that are imported into the United States must comply with the FDA's standards and regulatory requirements. In regard to biomanufacturing, drug products that are imported into the US are required to have been manufactured in a cGMP certified facility. The FDA conducts inspections of overseas manufacturing facilities that produce drug components to be imported into the U.S. in order to ensure that cGMP regulations are followed. This is done in order to maintain the integrity and standardization of procedures that are followed in the United States. Furthermore, the FDA has the authority to put companies on import alert, ceasing imports of certain products from a company, due to inconsistencies in manufacturing and or violations of inspections among other reasons.⁸¹

There has been a great push toward global regulatory harmonization with the formation of the International Council for Harmonisation that aims to present countries with standard guidelines regarding technical and manufacturing processes for pharmaceuticals.⁸² The FDA continuously devises and implements updated policies and regulations that aim to stay relevant and consistent with the advancements in medicine and manufacturing. For instance, Biomedical Advanced Research and Development Authority (BARDA) partnered with the FDA's Center for Drug Evaluation and Research (CDER) to create advanced regulatory framework to allow for the development of mobile advanced manufacturing facilities that will aim to produce drugs near critical points of care.⁸³ It is interesting to note that with advancements in medicine and biologics come advancements in biological manufacturing capabilities.⁸⁴

Conclusion

The global trade of immunological products has seen tremendous growth in recent years due to biotechnological advances and capabilities in the way companies innovate, develop, and manufacture biologic therapeutics. Total global export value of immunological products has grown from \$89.3 billion in 2017 to \$161.1 billion in 2020, and various countries have innovated to build the industry. Major global net exporting countries included Ireland, Switzerland, the Netherlands (possibly due to the Rotterdam Effect),

⁷⁹The White House, "Funding the Global Benefits to Biopharmaceutical Innovation," February 2020, 9.

⁸⁰FDA, "Safeguarding Pharmaceutical Supply Chains in a Global Economy," October 30, 2019.

⁸¹FDA, "Import Alerts," current May 14, 2019.

⁸²International Council for Harmonisation, "Mission," accessed May 31, 2021.

⁸³FDA, "Safeguarding Pharmaceutical Supply Chains in a Global Economy," October 30, 2019.

⁸⁴Deloitte, "Advanced Biopharmaceutical Manufacturing: An Evolution Underway," 2015; Kim, "Technologies and Tactics for Accelerating End-to-end Biologic Drug Development," November 29, 2021.

and Germany. Other countries, such as Singapore, encouraged a skilled workforce and tax incentives for future growth. Even though the United States exported \$14.2 billion worth of immunological products in 2020, it is a net importer in the global industry. For five of the six countries analyzed, the main export category was in the form put up for retail sale. Singapore was the exception to the trend, as its major form of product was unmixed and not put up in doses in forms or packings for retail sale. Key themes that emerged in successful exporting countries include low corporate tax rates, increased investor backing, incentivizing legislation, advantageous partnerships, as well as the establishment of specialized manufacturing facilities.

Bibliography

AbbVie, "Contract Manufacturing: Biologics."

<https://www.abbviecontractmfg.com/services/manufacturing/biologics-contract-manufacturing.html> (accessed May 30, 2021).

AbbVie. "Inside the Labs at AbbVie Ludwigshafen." AbbVie News Center, November 27, 2018.

<https://news.abbvie.com/news/abbvie-news-briefs/inside-labs-abbvie-ludwigshafen.htm>.

BaseLaunch. "About Us." <https://baselaunch.ch/baselaunch-about-us/> (accessed May 31, 2021).

Biopharma Dealmakers. "Moving Up with the Monoclonals." *Nature Portfolio*, September 19, 2019.

<https://www.nature.com/articles/d43747-020-00765-2>.

Biosimilars Review and Report. "Biosimilar Approval Status," updated May 18, 2021.

<https://biosimilarsrr.com/us-biosimilar-filings/>.

Boehringer Ingelheim, "About Boehringer Ingelheim BioXcellence." <https://www.bioxcellence.com/about-us> (accessed April 31, 2022).

Boehringer Ingelheim. "Global Biopharma Contract Manufacturing." <https://www.boehringer-ingelheim.com/bioxcellence> (accessed April 31, 2022).

Boehringer Ingelheim. "The Origin of Our Success Story." <https://www.bioxcellence.com/global-network/biberach> (accessed May 31, 2021).

Boehringer Ingelheim, "What is the Promise of Biologic Medicines?" 2019.

https://www.boehringer-ingelheim.us/sites/us/files/files/bi_ta_leavebehind_0.pdf

Bray, Sean. "Corporate Tax Rates Around the World, 2021." The Tax Foundation, Download Data: 1980-2021 Rates, December 9, 2021. <https://taxfoundation.org/publications/corporate-tax-rates-around-the-world/>.

Burke, Hannah. "Who Are the Top 10 Pharmaceutical Companies in the World?" Proclinical. November 8, 2020. <https://www.proclinical.com/blogs/2019-3/the-top-10-pharmaceutical-companies-in-the-world-2019>.

BusinessWire. "European Pharmaceutical Contract Manufacturing Market Growth Trends, 2021-2026: Increasing Outsourcing Volume by Pharmaceutical Companies." December 3, 2021.

<https://www.yahoo.com/now/european-pharmaceutical-contract-manufacturing-market-110900380.html>.

Chhabra, Munish. "Biologic Therapeutic Modalities," *Translational Biotechnology: A Journey from Laboratory to Clinics*. Academic Press, 2021, 137-164.

Creative Biolabs. "Biosimilars of Monoclonal Antibodies." <https://www.creativebiolabs.net/biosimilars-of-mono-clonal-antibodies.htm> (accessed May 31, 2021).

