ORGANIC PROCESS RESEARCH & DEVELOPMENT
OPR&D

pubs.acs.org/OPRD Perspective

The Fine Chemical Industry, 2000−2024

Rosaria Ciriminna,* Cristina Della Pina,* Rafael Luque,* and Mario Pagliaro*

Cite This: https://doi.org/10.1021/acs.oprd.5c00010 Read Online

ACCESS | Metrics & More | Article Recommendations

ABSTRACT: The fine chemical industry manufactures products that are used by many major industrial sectors, including the food and beverage, cosmetics, nutraceutical, pharmaceutical, electronics, paper, automotive, painting, and water industries. The industry saw significant changes in the first quarter of the current century, including the uptake of new "greener" production technology, digitalization, and changes in the structure and geographical distribution. Despite its relevance and significant annual growth rates lasting for decades, knowledge of this industry among chemistry and chemical engineering scholars, including graduate and undergraduate students, is often limited. Providing an updated critical insight into industry and the main changes that have occurred in the past 25 years, this study identifies the technology and policy drivers of change. The conclusions of the study may inform further practice-oriented education on industrial aspects of the chemical enterprise.

KEYWORDS: *fine chemical industry, fine chemicals, green chemistry, green industrial chemistry, continuous manufacturing*

■ INTRODUCTION

The fine chemical industry produces high-value compounds, today generally priced at no less than $15/kg, manufactured with a high degree of purity and in relatively small amounts (from a few tens to several thousand tonnes per year) when compared to basic chemicals.[1] The industry supplies virtually all major industrial sectors, including the food and beverage, cosmetics, nutraceutical, pharmaceutical, electronics, paper, automotive, and painting industries, and many others.

According to Pollak,[2] its emergence as a distinct entity dates back to the second half of the 1970s, when a large pharmaceutical company was forced by insufficient internal production capacity to outsource the procurement of the precursors of the highly successful active pharmaceutical ingredient (API) cimetidine to a fine chemical company based in Switzerland. Actually, the industry is even older than the oil-based petrochemical industry (created "suddenly" between the 1880s and the late 1920s, simultaneously in Europe, the USA, and Japan),[3] having started in the mid-1800s using as raw materials numerous different natural products.

Evidence that the term "fine chemicals" was used already in the early 1900s can be found, for example, in volume 27 of *The Journal of the Society of Chemical Industry*. Published in London by the Society of Chemical Industry, the journal at that time was a collection of issues devoted to inform readers on novelties from the scientific and patent literature. Section XX of the journal's volume 27 (issue 18), published in 1908, opening on page 956, was entitled "Fine Chemicals, Alkaloids and Terpenes".[4]

In 1993, the industry had revenues of $42 billion, with the pharmaceutical industry absorbing 50% of the output in terms of value.[5] Twenty years later, in 2014, the industry's market had grown to $128 billion, with pharmaceutical customers now absorbing about 70% of production.[6] After another decade, the market size of the industry exceeded $185 billion,[7] and the overall market was projected to expand at a compound annual growth rate of nearly 7% (to exceed $340 billion by the end of 2033).[7]

Despite its industrial and economic relevance, however, this key industry is not widely recognized by undergraduate and academic research chemists. It is enough, for instance, to ask a research chemist (or even a young chemical engineer) the difference between "fine" and "specialty" chemicals—one would probably get mixed answers. A similar conundrum (see below) is reflected in the scholarly literature and even in chemical trade magazines, where fine and specialty chemicals are often confused.

In the year 2000, Rajagopal published the "Fine Chemicals: Technology and Products" chapter in the *Kirk-Othmer Encyclopedia of Chemical Technology*.[8] In 2018, the same encyclopedia published the fourth updated version of the chapter. In 2013, Pollak and Vouillamoz published a chapter on fine chemicals in *Ullmann's Encyclopedia of Industrial Chemistry*.[2]

In early 2011, Pollak published the book *Fine Chemicals: The Industry and the Business* (the second edition of which was published three months later).[1] The book remains a key reference for anyone interested in learning the history, structure, and scope of this fascinating industry. Besides Pollak's seminal book, another important book, focusing on fine chemicals manufacture, was written in 2001 by one industry practitioner (Cybulski) and three academics (Moulijn, Sharma, and Sheldon), one of whom (Sheldon) had worked in the industry for nearly two decades.[5]

Received: January 7, 2025
Revised: February 6, 2025
Accepted: February 10, 2025

A search within "Article title" carried out in the research database Scopus with the query "fine chemical industry" at the end of 2024 returned only 77 documents.[9] None of these, however, focused on the fine chemical industry *per se*. Aiming to provide an updated insight to inform practice-oriented education on the industrial aspects of the fine chemical enterprise, in this study we outline the structure of the industry and the technology and policy drivers of change in the first 25 years of the 21st century.

STRUCTURE OF THE INDUSTRY

Table 1 illustrates the main differences between bulk (commodity) and fine chemicals in terms of production volume, mode (plant type), and sales channel. Specialty chemicals (specialties) are mixtures of different compounds, and not pure chemical substances, obtained by chemical companies by "formulation" (dissolution and mixing). They are chiefly sold to consumers and to a lesser extent also to other manufacturing companies.

Table 1. Main Features of Bulk and Fine Chemicals[a]

	Bulk (commodity) chemicals	Fine chemicals
Production volume per product	>1000 t/a[b]	<1000 t/a
Plant type	dedicated, continuous	multipurpose, batch
Sales channel	business to business	business to business, captive (or internal) use

[a]Adapted from ref 2 with kind permission. Copyright: 2013, John Wiley and Sons. [b]t/a = tons per annum.

The main customers of the fine chemical industry in 2014 (pharmaceutical with 69% market share, agrochemical with 10%, flavor and fragrances representing 7%, food additives 4%, dyes and pigments 3%, other 7%)[10] were the same a decade later, with slight variations in the end market share of the industry's products.

Fine chemical companies sell their highly pure products ("ingredients") to specialty chemical companies. The latter, including drug manufacturers, formulate the purchased "ingredients" with other chemical product(s) and sell the formulations to consumers and to other companies at prices that are substantially higher than those paid to the suppliers of the "ingredients". In order to incorporate the added economic value, many fine chemical companies are actually divisions incorporated into larger, specialty chemical and pharmaceutical companies.[1]

Production of fine chemicals traditionally takes place in multipurpose and multiproduct plants (MPPs) typically consisting of stirred stainless-steel reactors of 1−6 m^3 volume and glass-lined batch reactors with reflux condensers.[1] Further components of MPP plants are the feed systems for gaseous, liquid, and solid reactants and facilities for recovery of solvents, storage of product, and effluent treatment.

In 2014, a state-of-the-art MPP equipped with a stirring tank, centrifuge, dryer, and (corrosion-resistant) rectification unit installed in Switzerland, a leading country in fine chemical production, cost 32 million CHF.[11] The unit cost for a fully installed reactor in a MPP in 2010 was \$1 million/m^3 for a reactor installed at a fine chemical company based in Europe, North America, or Japan and \$0.1 million/m^3 in a plant based in China or in India.[12]

These figures alone explain the changes that occurred in the manufacturing base of the industry, once an old "European and North American business".[12]

Speaking with a chemical industry magazine in 2011, Pollak noted the following:[12]

> *Globally, there are 2,000−3,000 fine chemical companies, extending from small, "garage-type" outfits in China making just one product, all the way to the big, diversified companies. Among the top 20, 17 are divisions of large chemical or pharmaceutical companies like Albemarle; BASF; and Boehringer-Ingelheim, and there are only three pure players. In terms of geography, nine of the top 20 are located in Europe, which is recognized as the cradle of the fine chemical industry. ... The second largest geographic area is Asia, housing seven of the top 20. With four large companies, the U.S. ranks last. The combined revenues of the top 20 reached about \$10 billion in 2009.*

In brief, the industry comprises very large companies (the top ten individually having sales of \$0.5−1.5 billion per year) followed by a number of midsized companies with sales in the range of \$100−500 million per year, and hundreds of small companies with sales below \$100 million per year.[2] The latter are chiefly located in India and China and originally (when outsourcing started) specialized in niche manufacturing reactions with hazardous gases (e.g., ammonia, diazomethane, ethylene oxide, halogens, hydrogen cyanide, hydrogen sulfide, mercaptans, ozone, phosgens, etc.).[2]

Until the mid-1990s, pharmaceutical and fine chemical companies based in western Europe, the USA, and Japan produced 90% of the global API market demand.[13] In 2017, however, China was producing about 40% of the global API output.[13] Since the early 1990s, indeed, with the start of the second Great Globalization (after the first between 1870 and 1914),[14] European and North American countries (and partly also Japan) outsourced ("offshored") the whole production of off-patent APIs to companies based in China, India, and Taiwan.

With the introduction of ever more stringent environmental regulations in Europe, Japan, and North America, production of fine chemicals was becoming uneconomical, as the cost of disposing of the waste obtained in the manufacture of a pharmaceutical intermediate was rapidly approaching the selling price of the product, due to the "antiquated technologies involving the use of stoichiometric quantities of mainly inorganic reagents in the form of oxidants, reductants, and acids and bases".[15] Coupled to the aforementioned low capital cost,[12] significantly lower operating (labor, environmental, and taxation) expenditures resulted in the accelerated offshoring of fine chemical and generic API production to companies in China and India.

As a result, Europe, North America, Japan, and all former USSR countries became dependent on imports of said APIs as well as many other fine chemicals. In 2010, European companies comprised 7 of the top 10 fine chemical companies.[16] Not surprisingly, in 2019, the top 10 ranking of fine chemical companies now included two companies from China,[17] with several India-based companies close to entering the ranking. Furthermore, even though they are headquartered in Europe or North America, nearly all of the largest fine chemical companies had opened one or more plants in China.

TECHNOLOGY DRIVERS OF CHANGE

In the two decades (2000−2020) during which most fine chemical productions were offshored to companies based in

China and India, three major changes occurred in the manufacturing technology employed by the industry.

First, the industrial use of biocatalysis and of advanced chemical catalysis, such as asymmetric hydrogenation using chiral catalysts and Pd-catalyzed cross-coupling reactions, became common. Biocatalysis in combination with process (separation) technology was uptaken for manufacturing not only antibiotics such as penicillins and cephalosphorins or organic acids such as citric acid but also a wide variety of food and pharmaceutical ingredients.[18] Asymmetric hydrogenation is used, for example, for the synthesis of single-isomer vitamin E, involving the ruthenium-catalyzed asymmetric hydrogenation of allyl alcohols.[19] Cross-coupling reactions, in turn, became widely used across the industry for the synthesis of a wide number of fine chemicals for the agrochemical, pharmaceutical, cosmetics, and electronics industries.[20] The uptake of new biocatalytic (enzymatic or microbial) or catalytic reactions, however, did not require changes in the fermentators or MPPs that remained the manufacturing core of the industry.

Second, toward the end of the first decade of the 2000s, the first continuous manufacturing (CM) production units became commercially available. Given that they had not to face the substantial costs of replacement of already amortized MPP costs, these new manufacturing plants were adopted by the fine chemical and pharmaceutical industries to manufacture "on-patent" APIs in Europe, Japan, and the U.S. Coupled with significantly reduced space ("footprint") requirements, the reduction in waste and energy consumption of CM results in dramatically lower capital and operating expenditure costs when compared to batch production[21]—namely, the *main* barrier to the chemical industry's expansion in terms of competition, as identified by Chandler studying the evolution of the chemical and pharmaceutical industries.[3]

Indeed, in the early 2020s, manufacturers of "generics" (off-patent APIs) in India and China started to resort to CM to manufacture APIs and agrochemicals used to formulate generic drugs.[22] Showing evidence of this major shift occurring in the industry, today chemical engineering companies in India advertise their "vertically integrated end-to-end CM platform"[23] as a service for small and medium-sized companies not willing to face the upfront cost of purchasing new CM fluidic reactors.[23]

The third major technical change in the manufacturing of fine chemicals has been the introduction of digital process design and process control technology such as a "digital twin" (a digital model of a process that serves as its digital counterpart for simulation, testing, monitoring, and maintenance),[24] routinely used in the petrochemical and basic chemical industries to assist in the design and optimization of chemical production processes.[25]

As a result, fine chemical processes are becoming much more robust, with process analytical technology supporting real-time release testing ("the ability to evaluate and ensure the quality of in-process and/or final product based on process data, which typically include a valid combination of measured material attributes and process controls").[26] This allows manufacturers to dramatically reduce product quality fluctuation, for example, in continuous biomanufacturing,[27] reducing failure rates and shortening the shut-down times typical of batch processes.

Obviously, digitalization based on the digital twin approach achieves far better outcomes when applied to "lean" CM processes, and thus *not* to the material-inefficient processes typical of the fine chemical industry having an E(nvironmental) Factor (the ratio between the mass of waste and that of the desired industrial product) typically approaching 50 when producing fine chemicals and exceeding 100 when producing APIs.[28]

Finally, a major technology advance currently still unfolding (promoting, in turn, further uptake of CM) is the recent introduction of several new generation leach-proof heterogeneous catalysts. Their optimal shape and textural properties (minimizing pressure drop and maximizing heat transfer and accessibility to the catalytic species) eliminate the need for catalyst separation from the product, allowing use in the multistep continuous synthesis of fine chemicals via a broad range of different conversions.[29−31]

■ POLICY DRIVERS OF CHANGE

The prolonged disruption of supply chains following the COVID-19 crisis in 2020 substantially worsened the shortage of essential APIs in many European, American, and Asian countries,[32] leading many of their governments to incentivize reshoring of critical API manufacturing.

The political instability in the Red Sea region further contributed to API shortages in Europe, as ships from India and China were forced to reroute around the Horn of Africa, adding 4,000 miles and 30% longer transit time, resulting in more than a doubling of shipping costs.[33]

Suddenly, substantial incentives were made available to pharmaceutical and chemical companies to repatriate production capacity. The U.S. government alone aims to reshore 25% of "small molecule" APIs in five years.[34] Similarly, in Germany, the government in 2023 enforced new legislation that increased prices up to 50% for generic drugs for pediatric use and certain antibiotics, requiring also that in bids for purchasing antibiotics preference is given to APIs manufactured in Germany and other EU countries, enhancing the stockpiling period to 6 months.[35] A similar initiative was taken by Japan, where the government announced in mid-2024 that in order to support the domestic production of antibiotics and reduce the "heavy exposure on China",[36] both subsidies to Japanese chemical companies and preference to domestic producers would be granted in all drug purchasing public tenders.[36] All this will result in incumbent (and new) fine chemical companies starting API production in the countries from which they were offshored during the second Grand Globalization era. Due to the substantially lower capital and operating expenditure costs of CM, however, these companies will adopt it as manufacturing technology.[22]

Evidence that substantial manufacturing innovation is taking place in the fine chemical industry can be indirectly found in the topics discussed in recent exhibits involving the industry. For example, during the 37th International Exhibition for Fine and Specialty Chemicals (Chemspec Europe) held in Germany in June 2024, a symposium included sessions in which industry experts presented the cases of specialty[37] or oleochemical[38] chemical companies transforming their manufacturing processes from batch to continuous. The latter process, now running at commercial scale at a oleochemical plant in Great Britain, allowed a doubling of manufacturing capacity without building expansion and with a significant reduction in the amount of water and energy required.[38] Similarly, a German manufacturer of advanced mixing plants and equipment regularly organizes a seminar held directly at chemical companies, presenting successful case studies of companies modernizing existing mixing and drying equipment used in the production of fine chemicals and APIs.[39]

https://doi.org/10.1021/acs.oprd.5c00010
Org. Process Res. Dev. XXXX, XXX, XXX−XXX

Concomitantly, fine chemical and pharmaceutical companies across the world regularly hire young undergraduates and graduates in chemistry and chemical engineering skilled in flow chemistry, while they advertise tens of job vacancies in these areas on the main online job platforms.[40]

Aware that profound changes are taking place in the industry, governments in China and India are taking the initiative to support innovation and expand their national fine chemical industries. In China, nine government agencies recently issued the "Implementation Plan for Innovative Development of Fine Chemical Industry (2024–2027)".[41] One of the three key areas for the further development of China's $536 billion industry is new manufacturing technology.

In India, awareness of the importance of CM for the manufacture of fine chemicals and APIs is so widespread that the government of the Telangana State on August 2024 signed an agreement with a large U.S.-based manufacturer of CM systems to "collaborate on designing and implementing programs focused on skilling the local workforce in advanced manufacturing and chemical engineering technologies",[42] starting from the company's flow reactors technology.

■ CONCLUSIONS

Providing an updated critical insight into the fine chemical industry and the main changes that occurred in the first 25 years of the 21st century, this study (a preprint of which was published in late 2024)[43] reaches three main conclusions:

First, the industry is a large and rapidly growing segment of the chemical industry, whose revenues exceeding $185 billion in 2022 are expected to expand at a compound annual growth rate of nearly 7% to exceed $340 billion by the end of 2033.[7]

Second, three major changes in manufacturing technology occurred between 2000 and 2024, during which most fine chemical productions were offshored to companies based in China and India, namely, the uptake of biocatalysis and advanced chemical catalysis, the advent of continuous manufacturing, and the adoption of digital process design and process control technology.

Third, the sudden and prolonged disruption of supply chains following the COVID-19 crisis in 2020 led governments in Europe, North America, and Japan to deploy large financial incentives to reshore manufacturing of critical pharmaceuticals.[22]

Concluding an editorial entitled "National aspects of the fine chemical industry",[44] the editor of *Nature* wrote in 1921 that "our future position depends upon our chemical ability, and hence upon the employment of skilled workers directed by trained chemists engaged in a successful organic chemical industry."[44] More than a century later, the relevance of the "organic chemical industry" for every economically developed (or developing) nation has further increased.

The disruption of global supply chains in 2020–2022, followed by the Red Sea crisis, made it clear to governments in Europe, North America, and Japan that reliance on imports for critically important APIs was (and is) a threat to public health. Massive subsidies and incentives were suddenly made available to chemical companies to reshore productions in their home countries. Reshoring started in Europe[22] and is about to further accelerate with new incentives lately deployed in Japan[36] and in the U.S.[34] This will shortly lead to a renaissance of fine chemical production in all countries from where they were outsourced. Due to dramatically lower capital and operating expenses associated with continuous manufacturing of APIs,[37,38,22] most productions reshored will employ CM.

However, we argue, in conclusion, that manufacturing of fine chemicals based on new, advanced technology (CM coupled to digital process design and process control) will expand also to countries and regions of the world—such as Latin America, the Middle East, former USSR republics, Central Asia, and Africa—where the production of fine chemicals was hitherto limited to relatively few countries (Brazil, the former USSR, and South Africa).

Setting up for such advanced production obviously will require skilled labor and access to infrastructure and institutions. Seen from this perspective, significant investments in advanced education in chemistry and chemical engineering will be necessary to provide the fine chemical industry with the highly educated workforce required. Changes to chemical education in light of this paper's conclusions include both changes in existing curricula in catalysis and continuous manufacturing. Education in catalysis needs to be unified, including all its subdisciplines basing its teaching on chemical reaction mechanisms.[45] Teaching CM needs to effectively merge numerous subfields of chemistry (organic chemistry, catalysis, analytical chemistry, materials and polymer chemistry) with chemical engineering to expose undergraduate students to flow chemistry early in their education.[46] Efforts should be devoted to present students with practically useful knowledge and skills, showing them, for instance, how experiments and computation tools such as multiobjective optimization algorithms can be used to identify optimum reaction conditions to simultaneously maximize yield and minimize cost (and waste).[47] Students, furthermore, should receive updated education on the structure (and history)[1,2] of the fine chemical industry, including changes that occurred in the first 25 years of the 21st century and the drivers of said changes. The analysis and the conclusions of this study may inform further practice-oriented education on the industrial aspects of the chemical enterprise.

■ AUTHOR INFORMATION

Corresponding Authors

Rosaria Ciriminna – *Istituto per lo Studio dei Materiali Nanostrutturati, CNR, 90146 Palermo, Italy*; Email: rosaria.ciriminna@cnr.it

Cristina Della Pina – *Dipartimento di Chimica, Università degli Studi di Milano, 20133 Milano, Italy*; Email: cristina.dellapina@unimi.it

Rafael Luque – *Universidad Espíritu Santo (UEES), Samborondón EC091650, Ecuador*; Email: rluquealvarez@gmail.com

Mario Pagliaro – *Istituto per lo Studio dei Materiali Nanostrutturati, CNR, 90146 Palermo, Italy*; orcid.org/0000-0002-5096-329X; Email: mario.pagliaro@cnr.it

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.oprd.5c00010

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

R.C. and M.P. thank Ministero dell'Università e della Ricerca for funding, under Progetto "FutuRaw", Le materie prime del futuro da fonti noncritiche, residuali e rinnovabili, Fondo Ordinario Enti di Ricerca, 2022, (CUP B53C23008390005).

■ REFERENCES

(1) Pollak, P. *Fine Chemicals: The Industry and the Business*, 2nd ed.; Wiley: New York, 2011.

(2) Pollak, P.; Vouillamoz, R. Fine Chemicals. In *Ullmann's Encyclopedia of Industrial Chemistry*; Wiley-VCH: Weinheim, 2013. DOI: 10.1002/14356007.q11_q01.

(3) Chandler, A. D., Jr. *Shaping the Industrial Century: The Remarkable Story of the Evolution of the Chemical and Pharmaceutical Industries*; Harvard University Press: Cambridge, MA, 2005; p vii.

(4) Section XX of *J. Soc. Chem. Ind.* **1908**, *27* (18), 956–959. .

(5) Cybulski, A.; Moulijn, J. A.; Sharma, M. M.; Sheldon, R. A. *Fine Chemicals Manufacture*; Elsevier: Amsterdam, 2001.

(6) Ramakers, J. The finer things: where does pharma sit in the fine chemicals market? *European Pharmaceutical Manufacturer*, August 1, 2016. https://pharmaceuticalmanufacturer.media/pharma-manufacturing-news/the-finer-things-where-does-pharma-sit-in-the-fine-chemicals/ (accessed November 15, 2024).

(7) Fine Chemicals Market Outlook (2023 to 2033). *Future Market Insights*, Newark, 2024. https://www.futuremarketinsights.com/reports/fine-chemicals-market (accessed February 3, 2025).

(8) Rajagopal, R. Fine Chemicals: Technology and Products. In *Kirk-Othmer Encyclopedia of Chemical Technology*; John Wiley & Sons: New York, 2000.

(9) Search carried out on September 2, 2024, at scopus.com with the query "fine chemical industry" searching within "Article title".

(10) Ramakers, J. A fine art. *EPM Magazine*, 2016, Vol. *16*, p 4. www.jan-ramakers.com/Jan%20Ramakers%20in%20EPM%20June%202016.pdf (accessed February 3, 2025).

(11) Chemgineering International. Multi-purpose plant for fine chemical production, Münchenstein: 2014. www.chemgineering.com/en/references/chemicals/multi-purpose-plant-for-fine-chemical-production (accessed November 15, 2024).

(12) Peter Pollak on the World of Fine Chemicals. *CHEManager*, October 26, 2011. https://www.chemanager-online.com/en/news/peter-pollak-world-fine-chemicals (accessed February 3, 2025).

(13) The great medicines migration. *Nikkei Asia*, April 5, 2022. https://asia.nikkei.com/static/vdata/infographics/chinavaccine-3/ (accessed February 3, 2025).

(14) Zinkina, J.; Christian, D.; Grinin, L.; Ilyin, I.; Andreev, A.; Aleshkovski, I.; Shulgin, S.; Korotayev, A. The First "Golden Age" of Globalization (1870–1914). In *A Big History of Globalization. World-Systems Evolution and Global Futures*; Springer: Cham, 2019; p195. DOI: 10.1007/978-3-030-05707-7_11.

(15) Sheldon, R. A. Engineering a more sustainable world through catalysis and green chemistry. *J. R. Soc. Interface* **2016**, *13*, No. 20160087.

(16) Ramakers, J. Fine Chemicals: The Top 10. *CHEManager*, May 30, 2011. https://www.chemanager-online.com/en/news/fine-chemicals-top-10 (accessed February 3, 2025).

(17) 360 Market Updates, *Global Pharmaceutical Fine Chemicals Market 2024 by Company, Regions, Type and Application, Forecast to 2030*, Pune, India, 2024.

(18) Bruggink, A.; Straathof, A. J. J.; van der Wielen, L. A. M. A 'fine' chemical industry for life science products: green solutions to chemical challenges. In *Process Integration in Biochemical Engineering. Advances in Biochemical Engineering/Biotechnology*, Vol *80*; von Stockar, U., et al., Eds.; Springer: Berlin, 2003. DOI: 10.1007/3-540-36782-9_3.

(19) Netscher, T. Vitamins and nutraceuticals from the perspective of process research. *Chimia* **2018**, *72*, 485–491.

(20) Rouhi, A. M. Fine Chemicals. *Chem. Eng. News* **2004**, *82* (36), 49–58.

(21) Schaber, S. D.; Gerogiorgis, D. I.; Ramachandran, R.; Evans, J. M. B.; Barton, P. I.; Trout, B. L. Economic analysis of integrated continuous and batch pharmaceutical manufacturing: a case study. *Ind. Eng. Chem. Res.* **2011**, *50*, 10083–10092.

(22) Ciriminna, R.; Della Pina, C.; Luque, R.; Pagliaro, M. Reshoring fine chemical and pharmaceutical productions. *Org. Process Res. Devel.* **2024**, *28*, 3026–3034.

(23) Flownetics Engineering, game changer, Bangalore, 2024. https://flownetics-engg.com/en/Flownetics_Brochure_EN.pdf (accessed February 3, 2025).

(24) Bamberg, A.; Urbas, L.; Bröcker, S.; Bortz, M.; Kockmann, N. The digital twin – your ingenious companion for process engineering and smart production. *Chem. Eng. Technol.* **2021**, *44*, 954–961.

(25) Simon, L. L.; Kiss, A. A.; Cornevin, J.; Gani, R. Process engineering advances in pharmaceutical and chemical industries: digital process design, advanced rectification, and continuous filtration. *Curr. Opin. Chem. Eng.* **2019**, *25*, 114–121.

(26) Schmidt, A.; Helgers, H.; Lohmann, L. J.; Vetter, F.; Juckers, A.; Mouellef, M.; Zobel-Roos, S.; Strube, J. Process analytical technology as key-enabler for digital twins in continuous biomanufacturing. *J. Chem. Technol. Biotechnol.* **2022**, *97*, 2336–2346.

(27) ICH guideline Q8 (R2) on pharmaceutical development, step 5, 2009.

(28) Sheldon, R. A. *The E Factor*, 2025. https://www.sheldon.nl/EFactor.aspx (accessed February 3, 2025).

(29) Ciriminna, R.; Pagliaro, M.; Luque, R. Heterogeneous catalysis under flow for the 21st century fine chemical industry. *Green Energy Environ* **2021**, *6*, 161–166.

(30) Saito, Y. *Multistep Continuous Flow Synthesis of Fine Chemicals with Heterogeneous Catalysts*; Springer: Singapore, 2023.

(31) Coin, G.; Jiang, T.; Bordi, S.; Nichols, P. L.; Bode, J. W.; Wanner, B. M. Automated, capsule-based Suzuki–Miyaura cross couplings. *Org. Lett.* **2024**, *26*, 2708–2712.

(32) Miller, F. A.; Young, S. B.; Dobrow, M.; Shojani, K. G. Vulnerability of the medical product supply chain: the wake-up call of COVID-19. *BMJ Qual. Saf.* **2021**, *30*, 331–335.

(33) Emerson, D. Frontline: Red Sea Pharma Crisis Pushing Logistics Advancements. *Area Development*, June 17, 2024. https://www.areadevelopment.com/logisticsInfrastructure/q2-2024/red-sea-pharma-crisis-pushing-logistics-advancements.shtml (accessed February 3, 2025).

(34) *Bold Goals for U.S. Biotechnology and Biomanufacturing*. The White House Office of Science and Technology Policy (OSTP): Washington, DC, 2023.

(35) Arzneimittel-Lieferengpassbekämpfungs- und Versorgunsverbesserungsgesetz (ALBVVG). *Bundesministerium für Gesundheit*, Berlin, July 26, 2023. https://www.bundesgesundheitsministerium.de/service/gesetze-und-verordnungen/detail/albvvg.html (accessed November 15, 2024).

(36) Wada, T. Japan to subsidize antibiotics supply chain to reduce China exposure. *Nikkei Asia*, July 5, 2024. https://asia.nikkei.com/Spotlight/Supply-Chain/Japan-to-subsidize-antibiotics-supply-chain-to-reduce-China-exposure (accessed February 3, 2025).

(37) Egelske, B. Batch-to-continuous case studies for specialty chemical manufacturing, *RSC Symposium 2024, 37th Chemspec Europe*, June 19–20, 2024, Düsseldorf, Germany.

(38) Ni, X.-W. Continuous production of a functional consumer care product through process innovation, *RSC Symposium 2024, 37th Chemspec Europe*, June 19–20, 2024, Düsseldorf, Germany.

(39) For example, the seminar organized in Milan in late 2023: Ekato, *Modernization of Existing Equipment: Success Stories. Modern Mixing + Drying Solutions for Fine Chemicals & APIs*, Milan, October 12, 2023. https://www.ravizza.it/public/upload/Invitation_EngDay_Italy23_rev2.pdf (accessed February 3, 2025).

(40) Search carried out on September 17, 2024, at google.com using the query "flow chemistry job offers". Companies advertising job offers in continuous manufacturing through flow chemistry included CordenPharma, Sterling Pharma Solutions, Fairbrics, Piramal Pharma, Sanofi, and Adesis.

(41) China issues plan to bolster development of fine chemical sector. *Bastille Post*, July 20, 2024. https://www.bastillepost.com/global/article/4011466-china-issues-plan-to-bolster-development-of-fine-chemical-sector (accessed November 15, 2024).

(42) Reddy, R. R. Corning, Telangana govt. sign MoU to strengthen workforce in advanced manufacturing and chemical engineering technologies. *The Hindu*, August 8, 2024. https://www.thehindu.

https://doi.org/10.1021/acs.oprd.5c00010
Org. Process Res. Dev. XXXX, XXX, XXX–XXX

com/news/national/telangana/corning-telangana-govt-sign-mou-to-strengthen-workforce-in-advanced-manufacturing-and-chemical-engineering-technologies/article68497382.ece (accessed November 15, 2024).

(43) Ciriminna, R.; Della Pina, C.; Luque, R.; Pagliaro, M. The fine chemical industry, 2000−2024. *ChemRxiv Preprint* **2024**, DOI: 10.26434/chemrxiv-2024-pv7p1.

(44) National Aspects of the Fine Chemical Industry. *Nature* **1921**, *106*, 821−822. https://www.nature.com/articles/106821a0.pdf (accessed November 15, 2024).

(45) Pagliaro, M. "Catalysis: A unified approach": A new course in catalysis science and technology. *J. Flow Chem.* **2021**, *11*, 53−58.

(46) Kairouz, V.; Charette, A. B.; Collins, S. K. Implementing flow chemistry in education: the NSERC CREATE program in continuous flow science. *J. Flow Chem.* **2021**, *11*, 13−17.

(47) Jeraal, M. I.; Sung, S.; Lapkin, A. A. A machine learning-enabled autonomous flow chemistry platform for process optimization of multiple reaction metrics. *Chem. Methods* **2021**, *1*, 71.

https://doi.org/10.1021/acs.oprd.5c00010
Org. Process Res. Dev. XXXX, XXX, XXX−XXX