Paolo Magrì
President at DCAT (Drug, Chemical and Associated Technologies Association)

Paolo Magrì, Senior Vice President, Business Development at Advitech Advisory and Technologies, was recently elected to a one-year term as President of the Drug, Chemical and Associated Technologies Association (DCAT). Mr. Magrì has over 28 years of experience in the active pharmaceutical ingredient (API) sector. Prior to joining Advitech, he served as Vice President of Business Development at Infa Group. During his tenure (2005–2016), Infa grew by acquisition to include sites in Italy and Spain and a contract manufacturing division. Prior to Infa, Mr Magrì served as Marketing and Sales Director at Sicor and in Teva's Active Pharmaceutical Ingredient (API) division after the acquisition of Sicor by Teva in 2004. His strong track record in the industry also includes previous roles at Archimica/Pro.Bio.Sint. and Fordras. Mr. Magrì earned his master's degree in chemistry and pharmaceutical technology from the University of Milan, Italy.

Mr. Magrì shared his thoughts on trends in the fine-chemicals sector, including specialized manufacturing technologies and the future of a one-stop-shop business model with *Chemistry Today*.

LOOKING AHEAD OVER THE NEXT FIVE YEARS, WHAT CHALLENGES AND OPPORTUNITIES DO YOU SEE IN THE FINE-CHEMICALS SECTOR?

Like the pharmaceutical industry as a whole, the fine-chemicals sector is grappling with the increasing complexity of the pharmaceutical supply chain. This is probably the single biggest challenge that we face.

Over the next five years, companies that invest in developing long-term strategic relationships with their key suppliers, as well as new technologies to help them manage this vital network, will have an advantage in the marketplace.

On a global basis, we are seeing growth opportunities in the fine-chemicals sector for both new players in emerging markets and companies in the well-established European fine-chemicals market. European API producers are growing and finding new opportunities in the drug-substance sector through a combination of new projects for custom synthesis and a revival of "classic" generic APIs.

HOW DO YOU SEE THE PRODUCT MIX BETWEEN SMALL MOLECULES AND BIOLOGICS EVOLVING? WHAT ARE THE IMPLICATIONS FOR THE INDUSTRY OVERALL AND FOR SUPPLIERS?

Biologics have become a fundamental component of the global pharmaceutical market, and their market share is increasing in key therapeutic areas, such as oncology and autoimmune diseases. In addition, much of the new investments in terms of technological innovation focus on biologic-based drugs.

But small molecules remain critically important. For the 20 top-selling drugs, the mix of small molecules and biologics on a value basis is similar, about half for each modality, so you can see the rising role of biologics in the global marketplace.

If we look however, at recent new drug approvals, small molecules represented approximately 70% of approvals of new molecular entities in 2017 by the US Food and Drug Administration's Center for Drug Evaluation and Research. Small molecules still represent an important part of new drug development.

Moreover, a closer look at the chemical structure of new chemical entities (NCEs) for pharmaceuticals reveals an interesting evolution of small-molecule APIs; these new molecules are very often based on more complex chemical structures and the corresponding therapeutic effect is available at very low doses. The increase in API complexity and activity has an immediate and valuable implication for our industry. New capabilities in product handling, for example, for high-potency drugs, and being able to achieve economy of scale even for lower-volume drugs become more important, and API producers are adapting their sites to these new requirements.

As Professor K. C. Nicolaou of Rice University noted in an essay published in the January 2018 issue of the *Israel Journal of Chemistry*, it is important that we champion and support the discovery and invention of new synthetic methods, strategies, and technologies. It's good for science, our industry, and society.

WHAT SPECIALIZED MANUFACTURING TECHNOLOGIES ARE EMERGING? HOW WILL THEY IMPACT SUPPLIER'S CAPABILITY SETS?

I see several important trends in the fine-chemicals sector and for production of small-molecule APIs:

- Organic synthesis has been continuously evolving to higher levels of sophistication, and with that evolution come new technological platforms. Continuous processing and biocatalysis are two examples of technologies with a growing potential in terms of industrial applications in the large-scale production of APIs and intermediates.
- The benefits of "green chemistry," from human health to the environment to the economy and business, have been clearly established. We are seeing the use of enzymes and of flow-chemistry to reduce the environmental impact of some chemical reactions, and we should expect to see more innovations in the future.
- Looking to other industries for inspiration could help API producers create powerful ideas for innovation. A case in point are membrane technologies used for water purification, which are being adapted to address more complex separations in API production.

HOW DO YOU ASSESS THE BUSINESS MODEL OF THE SO-CALLED "ONE-STOP-SHOP," WHERE CONTRACT DEVELOPMENT AND MANUFACTURING ORGANIZATIONS/CONTRACT MANUFACTURING ORGANIZATIONS (CDMOs/CMOs) BECOME END-TO-END PROVIDERS OF BOTH APIs AND DRUG PRODUCTS, EITHER THROUGH ACQUISITION OR THROUGH INTERNAL INVESTMENT?

This trend, which I believe will continue, is driven by a number of factors:

Technology acquisitions: An important percentage of overall mergers and acquisitions (M&A) in the pharmaceutical sector is represented by the acquisitions of small API sites, and they contribute to a global reshaping of the API manufacturing landscape. In terms of geography, the majority of the "targeted" companies in M&A were located within Europe or the US, and one of the key drivers for target selection was the opportunity to acquire highly "demanding" technologies applied within a cGMP environment. As a result, an increasing number of CDMOs/CMOs in the pharmaceutical industry are becoming end-to-end providers, with several strategic implications.

Risk-mitigation: Creating a "one-stop-shop" offering two capability sets—APIs and drug products—can be a risk-mitigating strategy for CDMOs/CMOs to respond to an ever-increasing complex supply chain being faced by their pharmaceutical customers.

Diversification: Another form of risk-mitigation, diversification can help an organization increase sales and expand into new markets. Combining business models, such as API and drug-product capabilities, is an effective method to increase a CDMO's/CMO's overall market stability.

The successful end-to-end CDMO/CMO of the future will offer a "one-stop-shop" experience for their customers that provides the benefits of integration, including increased responsiveness, cost reductions, and security of supply while preserving the quality of the customer–supplier relationship.