

Active Pharmaceutical Ingredient Manufacturing's Accelerating Agenda

From in-house capability to engaged strategic contract service providers, API processors are advancing operations and implementing next-generation thinking to drive efficiency and quality

Few categories in pharma are as “active” as the active pharmaceutical ingredient (API) segment, or as central to the world’s pharmacopeia. Entering 2017, the dynamic continues. At the heart of most all prescriptions, generics and OTC drugs, APIs are responsible for delivering the intended therapeutic effect to patients. Elemental, APIs are traditionally the focus of intensive research and development investment. Now in the post-blockbuster era, recent development is robust and accelerating, especially in high-potency first-in-class small-molecule compounds and drug substance/drug product development in the large-molecule biologics space.

Research and Markets announced the API market is expected to reach \$213.97 billion by 2021 from its current 157.95 billion in 2016. Not surprisingly, Research and Markets finds cancer a major target with the oncology segment accounting for most of the global API market in 2016. The research firm notes many pharmaceutical companies are focusing development on novel oncological treatments and targeted therapies using anti-body drug conjugates to treat cancer.¹

Research and Markets’ segregates the APIs market into innovative and generic APIs. Innovative API development accounted for the largest share in 2016, the research firm attributing its ascension to the increasing number of FDA approvals for new molecular entities, higher prices commanded by innovative APIs (compared to their generic equivalents) and growing focus on developing novel innovative APIs to create therapies to meet the “unmet” medical needs of the market.

API Manufacturing Leadership

Research and Markets’ data revealed the tendency for drug owners/innovators to keep commercial manufacture of innovative APIs in-house and for a time it appeared that might slow growth in the contract services sector. Although there is still plenty of inertia and investment behind traditional drug innovation and processing in-house, the fact remains a significant portion of API development and manufacture has shifted to the pharma supply chain. That contract development and manufacturing is at the forefront of API processing is reflected by the results of the 2017 Nice Insight Contract Development and Manufacturing Survey. Most companies (54%) acquire or plan to acquire small molecule API R&D services (57% of those in Asia, 47% of those in the EU and 61% of those in North America). More than half (57%) of companies outsource small molecule API clinical-scale manufacturing and about one-third (35%) outsource small-molecule API commercial scale manufacturing.²

2017 Nice Insight Contract Development and Manufacturing Survey covers a market sustaining more than 300 contract services companies. It is a robust market, and judging by all the capital being invested in the sector by venture capitalists, it is maneuvering decisively to meet all that demand and growth. Although roughly half of the CDMO population Nice Insight surveys bring in more than \$20 million in annual revenue, a list of approximately 30 dominate. Those top companies, including venerable names like Cook, Patheon, Catalent, Pfizer CentreOne, Abbvie, were identified as leaders by Nice Insight’s 2016 survey of contract services buyers seeking their awareness and perceptions of CDMO companies they

know and engage. According to Jim Miller from PharmSource, this top group is responsible for approximately half of all revenues in the contract manufacturing space.³ He also notes demand for API manufacturing services, in particular small-molecule oral solid dose (OSD) related products, is driving billions in business and billions more in investment in the contract services sector.⁴

API manufacturing leadership is emerging at an accelerating pace with development and investment in optimizing capacity, processes and operations going on around the world. Competitive, regulatory and social imperatives are driving all of pharma to achieve the competence and technical capabilities required to manufacture defect-free APIs at commercial scale as cost-efficiently as possible. To get there, most recent analysis and trend data point to the industry moving inexorably to transition capacity from its science/lab-based fixed-scale legacy to that of more contemporary commercial, flexible, cost-effective processing and manufacturing strategies. The optimization of both in-house and contract service provider's process capacity is now increasingly being supported by strong, external engineering and technology partners who increasingly are becoming closer to their customers and more strategically essential to successful operations than ever before.

Synthetic APIs likely commanded the largest share of the market in 2016. Research and Markets, like others, cited an increasing number of new product approvals as one source for the growth, but perceptively identified technological advancements in the *method of synthesis* as a major factor contributing to the growth of the synthetic APIs segment. Although similar dynamics are occurring in large molecule development and biotech APIs, which are expected to grow at the highest CAGR in Research and Markets forecast period.

API Processing and Technical Innovation

All aspects of drug quality, safety and effectiveness cascade from the manufacturing process. Pharma understands this, as do regulators and the engineering and technology suppliers serving the industry. Although the pace of innovation and "change" in pharmaceutical processing appears to some to be a "one step forward, two steps back" sort of exercise, the year-after-year rise in equipment spending budgets identified by Nice Insight's 2017 Pharmaceutical Equipment Survey reveals an ongoing emphasis by the industry to shed obsolescent capacity, invest in high-value operations and forward advanced manufacturing strategies.⁵

"Pursuing advanced manufacturing strategies" is turning out to mean one thing to one manufacturer and perhaps something entirely different to another depending on their particular circumstances. For Janssen that meant instituting one of the first commercially viable continuous manufacturing processing trains in pharma's brief industrial history. For AstraZeneca it meant completely transforming an existing batch oriented facility for optimal performance. For others it means taking advantage of prefabricated, prevalidated process modules that can be whisked to a given location and commissioned within months - similar to what Patheon and GEA are developing to meet the challenges of delivering on-demand, flexible processing to its customers. In 2016 INTERPHEX recognized GE and its KuBio offering as a technological leader for its modular offering for the biopharmaceutical space.⁶

More discrete underlying technologies like automation, control and process analytical technologies are at play advancing pharma processing and operations. These technologies support modern digital age manufacturing environments and lend tremendous control and transparency to pharmaceutical operations.⁷ These technologies are being increasingly adopted to not only control and optimize

traditional batch operations but the complexities of highly-potent APIs processing.⁸ Lastly more available affordable automation and control have proven essential to developing continuous manufacturing processes now being explored and implemented by the industry.

Cash and technology continue to flow into API research and manufacturing. The investment is fueling innovation and new products and that activity is supporting both the traditional pharma R&D innovation pipeline as well as a more optimized and efficient pharma manufacturing base that now spans the industry. With it, pharma is creating not only a more cost efficient infrastructure to make their products, but a more sustainable platform to deliver the safe, affordable medicines to meet the world's demand for effective high-value medications.

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