Pharmaceutical manufacturing

Roland Berger

IMPROVEMENTS TO MAKE P. 5–6

April – 2020

Production efficiency

Boosting network and plant performance to reduce costs and create savings

OPTIMIZATION
IN 3 STEPS
P. 4

In brief

Tighter margins in the pharmaceutical industry and the anticipated high investments into new modalities (e.g., cell and gene therapies) increase the pressure to generate savings across all functions. In recent years the industry focus shifted towards production cost savings. Usually, these costs are more difficult to achieve and require longer implementation times than savings in SG&A and R&D. The experience of many projects and our cross-industry expertise in pharmaceuticals and operations helped us reliably identify the right improvement levers. We allocated these levers to three main topics – network optimization, production optimization and digitalization – and experienced a general savings potential of 8–12% in successful optimization projects.

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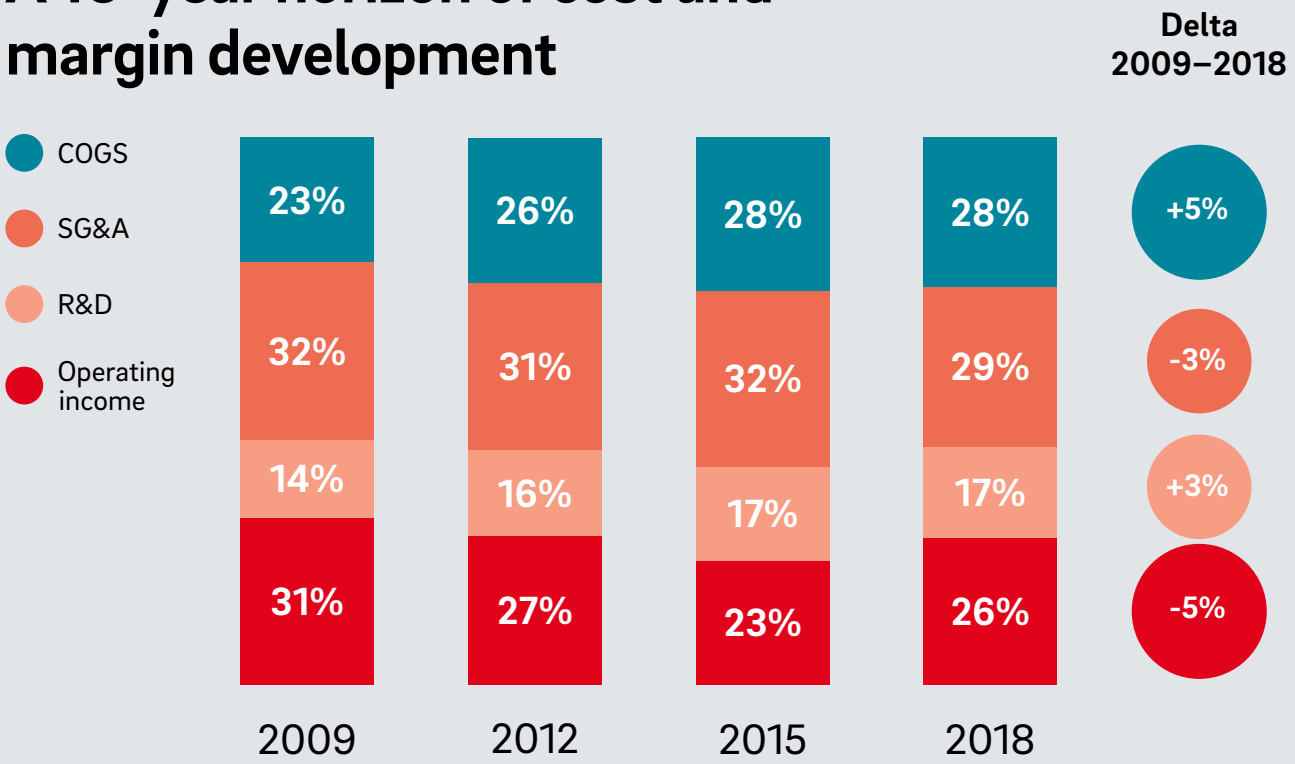
Efficient manufacturing – lowering pharmaceuticals production costs

In light of shrinking margins, decision makers across the pharmaceutical industry are looking at manufacturing costs like never before. The appeal of improving manufacturing costs has increased as product pricing has come under pressure and best practice examples of other industries have opened new perspectives on cost hsavings.

Drug makers are rising to the challenge of making manufacturing more efficient. Efficiency gains in areas like selling, general and administrative expenses (SG&A) and research and development (R&D) have been impressive, but companies cannot rely on them forever. At the same time, product prices are under scrutiny from politicians during the election campaigns in the US, health technology assessments (HTA) in the EU, and National Reimbursement Drug List (NRDL) negotiations in China. With their scope on both the cost and revenue sides narrowing, pharma companies are feeling the pinch.

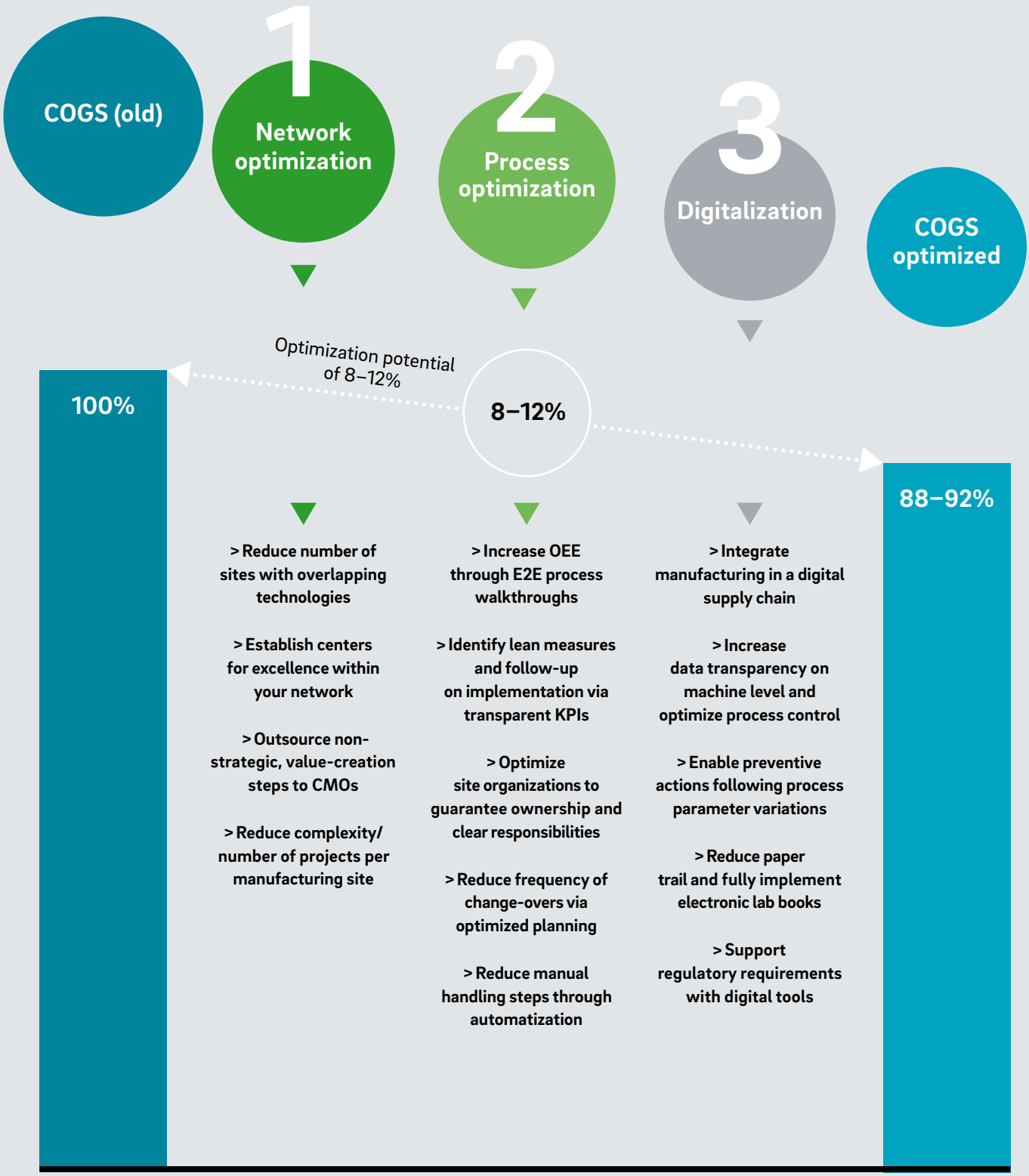
Drug makers have traditionally shied away from larger manufacturing optimizations. They cut costs by squeezing SG&A expenses and lowering internal R&D budgets, since this was simpler and faster than grappling with manufacturing costs. Highest technical requirements and strictest regulation – codified in the good manufacturing practice (GMP) guidelines, ▶

A 10-year horizon of cost and margin development



Source: Roland Berger

Three steps to manufacturing efficiency



Source: Roland Berger

for example – make pharma manufacturing uniquely demanding. Companies face major challenges if they want to make changes to operations – high costs, heavy documentation and ever-harsher regulation. Every product variation has to be registered and, in some cases, even requires new analytical and clinical data and renewed approval by regulators. As profit margins erode further, and even reach critically low levels in some areas, pharma companies are turning to manufacturing costs as a potential remedy. As their products compete mainly on price, manufacturers of small-molecule generics and biosimilars have been under pressure for several years. However, innovative drug makers are increasingly feeling the pressure because of higher R&D costs and new product categories that require large investments. In addition, companies making large-molecule drugs have had to deal with increasing competition from biosimilar manufacturers in Europe and also in the US.

All branches of the pharmaceuticals industry have seen the cost of manufacturing drugs rise over the last 10 years. In general, the cost of goods sold (COGS) currently accounts for a larger part of total expenses than a decade ago. Tighter regulation and higher quality and testing standards have raised pharma manufacturers' so-called conversion costs, the expenses they incur by employing personnel and installing, running and maintaining machines.

Technical and pharmacological challenges are making manufacturing more complex. Using the same manufacturing equipment for different products has become more difficult as regulatory cleaning requirements have tightened. Large product portfolios mean generic companies and contract manufacturing organizations (CMO) have to contend with cross-contamination more than other companies. At the same time, the expense of switching production lines from one drug to the next is also an issue for branded drug makers.

Pharmaceuticals manufacturing is also grappling with ever more evident pharmacological limitations. Novel compounds that dissolve in water and easily permeate human cell walls are increasingly rare. Today, they more usually have limited bioavailability and water-solubility and demand more intricate manufacturing processes like spray drying and hot-melt extrusion.

Branded drug companies had to deal with huge drops in demand when blockbuster drugs lost patent protection and generic pharma companies began to claim a share of the market. This roller-coaster ride has encouraged branded drug makers to switch from high-volume to high-value products. The shift from manufacturing blockbusters to orphan drugs means branded drug companies are making some products in lower volumes and straining to adapt large-volume production sites.

Lastly, industry consolidation has led to the formation of large companies with complex manufacturing networks. As the cost of relocating production has risen and lead times lengthened, companies have shied away from optimizing production networks. However, companies see they have to start tackling the cost burdens created by these inefficient manufacturing networks and streamline production capabilities to reduce complexity.

Improvements to pharmaceutical manufacturing go hand in hand

All these factors demand that pharmaceutical companies tackle the cost and structure of their manufacturing operations. They need to re-assess production strategy, overall network design and plant performance management. Specifically, drug makers have to:

1.1 Optimize their global production footprint in light of strategy, regional patterns of demand and manufacturing attractiveness. A cut in the US corporate tax rate led to new investment in pharmaceutical manufacturing there. For example, Pfizer recently invested $465 million in a sterile injectable-pharmaceutical production facility in Michigan.

1.2 Raise operational efficiency by making production networks less complex and less inefficient. Teva, for example, is well on course for realizing cost savings of $3 billion as a result of a cost-cutting program that includes comprehensive optimization of its production network. After the acquisition of ▶

Actavis, Teva had around 80 production sites that it estimated could in theory have been replaced by 20 greenfield sites. In the last two years, the company has closed 13 plants in its manufacturing network.

2.1 Pursue lean production by reducing non-value-adding activities and aligning production with consumer demand. Manufacturers must identify and prioritize selected improvement levers. This can bring both quick improvement gains and long-term improvements in production KPIs. For example, Johnson & Johnson developed an in-house network of experts focused on continuous improvement to optimize every process in its supply chain. 1,000 separate insights improved processes and supply-chain outcomes and saved $1.8 million in operating costs and raised lean-capability review scores by 52%.

2.2 Revise production processes to free up machines. Companies can cut production complexity by reducing the number of package sizes or introducing multinational packaging formats for selected products. For example, we have observed that a number of our clients saw a significant increase in conversion costs after continuously raising the number of SKUs on offer. Reducing packaging variety and simplifying commercial functions helped claw back efficiency, especially that of packaging lines.

2.3 Move towards continuous manufacturing operations. Research and development advances suggest that production is shifting from manufacturing drugs in batches and in distinct phases to a continuous process. This begins with the raw materials being fed into the production line and ends with a packaged product coming off it. For example, GEA worked together with Merck subsidiary MSD on a 120-hour continuous manufacturing trial: 15 million tablets were made from 6,200 kg of raw materials in a single production area. Continuous manufacturing allowed GEA to test fully integrated and closely controlled processes as an alternative to less efficient and more time-consuming manufacturing in batches.

3 Digitalize operations to better understand and control manufacturing processes. Many manufacturers still rely on analog, paper-based processes that make digitalization and data collection and evaluation difficult. Collecting and analyzing data allows drug makers to understand and control production and product specifications in unprecedented ways. For example, Boehringer Ingelheim is using data analytics to pursue the "golden batch" in manufacturing, the batch that renders both excellent yields and product quality. The German company used multivariate data analysis and batch-evolution modeling to fully control the drug-fermentation process and produce in golden batches.

Recent project examples show COGS saving potential of 8–12%

Roland Berger has deployed such improvement levers in a string of successful projects. We have helped small and medium-sized companies and the largest corporations to craft manufacturing strategies based upon corporate visions and mission statements. We have helped our clients tailor their production network exactly to their requirements, taking into account their markets and the entry hurdles and state support that might exist. This includes evaluating whether a pharmaceutical manufacturer should itself invest in an additional site or contract out production to a CMO. Roland Berger regularly also designs optimization programs for production facilities that can raise efficiency across the board or in specifically targeted areas, and helps organizations adjust to changing demands and environments. Best results are achieved by approaching manufacturing costs from different angles, targeting network, site and organizational issues at the same time. Pharmaceutical companies advised by Roland Berger have been able to reduce COGS by 8–12% and to raise overall operating margins by 2–3% as a result.

Manufacturing trends in the pharma industry

	LEVER	COMPANY	CHANGE STORY
1.1	Optimize global footprint	Pfizer	▶ Reduction of US corporate tax rate leads to investment in US pharmaceutical manufacturing ▶ Pfizer invests $465 million to build a sterile injectable pharmaceutical production facility
1.2	Raise operational efficiency	Teva	▶ Due to debts, high costs and falling sales Teva carried out a cost-cutting program, including a comprehensive network optimization with site closures ▶ As a result, the company could cut about $3 billion in costs
2.1	Pursue lean production	Johnson & Johnson	▶ The company developed a network of professionals focused on continuous improvement ▶ 52% increase in lean capability review scores could be achieved leading to positive effects on customer experience, operational capabilities, compliance and the bottom line
2.3	Move towards continuous manufacturing (CM)	GEA MSD	▶ During a 120-hour trial more than 15 million tablets have been made in one single production area ▶ Benchmarking against a typical batch process showed that producing the same quantity of tablets in the same time would have required a team of operators working in parallel in three production areas
3	Implement digitalization: golden batch analysis	Boehringer Ingelheim	▶ The company aims to achieve the golden batch – a repeatable process that consistently optimizes yield and quality ▶ By using multivariate data analysis and batch evolution modeling, the drug fermentation process could be fully controlled, enabling the team to produce in golden batches
	Artificial Intelligence	Pfizer, Roche, Sanofi, Takeda, GSK, Merck, Janssen, AbbVie	▶ According to MIT only 14% of drugs successfully pass clinical trials. Furthermore, a company can expect to pay between $161 million to $2 billion for any drug to complete the entire clinical trials process and get FDA approval. ▶ Deployment of AI increases the success rates of new drugs and decreases operational costs at the same time ▶ Most major pharma companies are now exploring AI-driven solutions for manufacturing and support functions

Key benefits for implementation along multiple levers can be:

- ▶ Improve OEE >10 p.p.
- ▶ Reduce deviations and increase quality >40 p.p.
- ▶ Reduce individual time spend >50 p.p. on non-value-add activities

Source: Roland Berger

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