RE-EVALUATING STRATEGIES TO IMPROVE PROCESS EFFICIENCY

A conversation with Robert Dream, HDR Co.

ABOUT

Robert Dream in a biopharmaceutical industry consultant who has over 30 years of experience in project management, licensing, CMCs, operations, regulatory affairs. Susan Dana Jones is a recognized leader in bioprocessing, She has over 30 years' experience in managing complex biopharmaceutical development programs from discovery through late-stage clinical trials and commercialization.

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Susan Dana Jones: You urge biopharmaceutical companies to develop an holistic vision when they are looking for opportunities to make manufacturing operations more efficient – how do you define the approach?

Robert Dream: To have a holistic vision you have to consider everything from pre-clinical through clinical to commercial manufacturing. Then, within that, you need to look at the technology involved, the workforce, the patient and the business KPIs.

And the approach can be used irrespective of the size of company involved. For large companies it provides greater oversight of the process. And for smaller firms the approach is potentially even more important because in reality any successful small company is either going to end up as part of a large company or going to be a large company in the future.

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You have to plan ahead of a time. The industry is moving forward and bringing innovation into biologic manufacturing with things like automation and new facility designs. You have to have a model in mind.

There is a saying by George Box – a leading statistics scientist who created models for the life sciences sector – [which states] that "all models are wrong but some are useful." He said you create a model and the model has to work. If it kind of partially works then that is useful because I can modify it - and that's what we're talking about with a holistic vision.

SDS: And within that, how do you design a flexible technology framework? What are the strategies that biopharmaceutical companies need to use to build adaptability into their manufacturing operations?

RD: Well you need to understand the role the manufacturing facility performs. What work will take place there and how will you set it up to ensure it is flexible. When designing a facility you need a plant structure and to make it flexible you need a modular line setup, that is, a plant structure that has interchangeable lines. It also should have a multi-directional layout that supports design space using QbD, automation, plug and play and smart equipment system.

And as industry moves away from the batch to continuous production it makes it more feasible to do feed forward, feed backwards type of automation. So you have to have the equipment down the line that is capable of taking care of the product coming into it and feeding back information into the equipment before it. Beyond that you should think about digitization and things like smart robots, all of which need to be considered during facility design.

And digital tools also have a role to play in facility operations. Production simulations, for example, can be used to identify problems and understand where the faults are using real-time data analysis.

SDS: What role does automation have to play in the holistic manufacturing approach you advocate?

RD: First you have to look at what you are manufacturing. Do you want to have a closed system because you don't want to have the environment contaminate your product while you are making it? If so, then automation is an ideal solution, because it facilitates the use of closed systems and limits the need for manual handling.

In general, you need to know your product, you need to know your equipment and you need to know how to implement it correctly. There is not like an automating machine out there that can tell you how to meet part 11 from the FDA or annex15 from the EMA. But there are vendors you can talk to if you don't have an automation expert in-house.

SDS: We do have an audience question, it goes back to the discussion about automation. Is using AI on top of automation now common?

RD: Today AI is there whether we like it or not. AI is a tool you use to create automation. AI is basically the software portion of it then you have the hardware portion of it and you have the sensor portion of it.

You do need digital sensors to capture the data you need an inline or at line testing equipment that can take the data from the digital sensors. AI is basically a tool that we use to make the automation work in a better way.

SDS: And looking at implementation more generally, beyond just automation, what are the considerations manufacturers should keep in mind to achieve operational excellence?

RD: There's a couple things that you need to do to implement technology in an effective way. Firstly, you should create a vision and solidify it into a plan. The idea is to make a document that details your implementation plan - and it shouldn't go on the shelf, this should be a living document.

The plan is a fully integrated value chain. You need to have a system integration and control method. The good thing about these plans is that they can reduce costs by improving production flexibility, quality and set up speed.

But you also have to be realistic and only make changes when it is appropriate to do so. For example, for people who have old equipment and existing facilities that have been running for 20 years making operational changes is difficult. If you have a product coming out of that - let's say you have a four billion dollar product – you don't want to try it with that. You want to try it with your new product or you want to try it on a side line.

Involving external expertise can be very helpful. I did one operational excellence implementation plan for a company in the UK that had some difficulties with a facility that made eight products. They didn't want to build new facilities, they wanted to automate and to use whatever equipment that could be used and remove any obsolete systems.

So we went through the process and we made a presentation to the board that we have about seven solutions for you. And literally we created a process for them. They needed a 20 percent a product increase in five years and we gave them about 30 percent product increase and instead of spending 85 million sterling we spent only 3 million sterling.

And the meeting was supposed to last for three days but the director that was responsible for the project two hours later said “we don't need any more presentation, I got what I need let's talk about what we're going do with it.”

SDS: How should a biopharmaceutical company go about emphasizing safety, quality, efficacy and regulatory compliance in its manufacturing operations?

RD: Safety, quality and efficacy are not only regulatory requirements. If you're making a drug product that goes to a patient you need it to be safe, you need it to be as good as what you claim to be and you need your production of it to be efficient.

So how do we achieve these things? Well, using a holistic approach, these are achieved by using a combination of technologies, lean management and patient-centricity.

For safety, a lot of organizations basically take feedback from doctors and patients to see where the problems are with the product. Also when you do your clinical trial you should gather data from similar products. This data allows you to make improvements as you find faults.

Regulators allow you, within a frame of work, to modify your manufacturing process. And, as long as you report it, you don't have to reapply unless you change it beyond the approved process. As a result you can continually improve your process and product manufacturing and just report it in your annual report. If you look at it ICH Q12 basically tells you exactly what needs to be done.

The other thing is continuous process verification. The days of manufacturing three verification batches are over. You have to be in control of your process and your line manufacturing the product all the time. You need to continually verify the process is operating as expected.

And if the process does go out of spec, you have to be able to say why. Is it faulty equipment? Is it a faulty process? Is it faulty material? Sometimes you might get a vendor change the material on you and you don't know and obviously you have a problem. You need to basically look at it continuously while it's running because that is what regulators look at these days.

SDS: So you've spoken about the holistic approach from the point of view of product quality and safety as well as how it can be used to achieve operational excellence on the factory floor. How can the holistic approach impact your bottom line? Is it worth the investment?

RD: If you incorporate a vision that is a holistic and you incorporate all the stuff we talked about and you maintain it, your efforts will usually result in a better ROI.

But really we need to talk about a few things here besides just ROI based on the bottom line for business. There are the parameters that control the process and make regulators happy and make the patient happy - CPPs, CQAs, CMAs - and then you have the KPI.

A lot of people think business KPI is a focus for regulators, but regulators do not care. KPI is just bottom line for business and you make sure basically that you make a good enough product and not too much waste and do it efficiently and cost wise within a limit to make profit.

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A company has to make profit to make products. They are not - I hate to say this - in love with patients. They like the patient. They want the patient to basically receive good product, but if they can't make profit they get out of business.

Profit is the main aim of it but if you run your manufacturing operation in a way that just focuses on KPIs you are unlikely to be successful. For example, in 2022 there were a couple companies that got in trouble with the regulators because they used more limited risk assessments, rather than taking a more holistic, all-encompassing approach.

So while we need to be cognizant that ROI is an important part of manufacturing, we need to keep in mind it is not the only thing. If you incorporate everything we talked about in a holistic manner it should give you a good ROI and good KPI.

This case study was originally presented at Evaluating Biopharma's Biomanufacturing Optimization online and interactive event.

You can watch Robert's presentation in full and on demand here.
Details of future Evaluating Biopharma events can be found here.

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