How Efficient Batch Records Serve Thorough Tech Transfer — Optimizing Aseptic Fill For Development Projects

Article | Oct 2021

Technology transfer — the process of moving drug manufacture from one line or site to another, usually to facilitate a scale-up in production or transferring manufacturing facilities — occurs several times throughout the development process. Each tech transfer demands meticulous attention to detail, including the equipment used, methodologies, and raw materials. Still, this dynamic process can be hampered by employing strategies that fail to optimize timelines and risk loss of knowledge.

Efficient, thorough, and timely tech transfer can benefit from a streamlined batch record process, one that prioritizes populating batch records with the necessary information to reduce drafting time and ensure consistent operation. Too often, though, tech transfers are held up by a missing piece of non-critical (for the current step) information, and the CMO's processes are not designed to push ahead despite critical information being in place.

Such strategies fail to acknowledge that, while nearly all tech transfers follow a similar path, each sponsor encounters its own challenges. Sometimes, different equipment will be used to accommodate scale-up. Other times, a formulation that worked in the laboratory must be modified to perform as expected at production scale. In many cases, sponsors simply are unprepared to manage the sheer volume of documentation associated with a technical transfer. Most of their experience and data is in R&D, rather than cGMP production and its accompanying regulatory burden.

Many of these challenges are difficult to overcome using any batch record system, as some batch record documentation can be started, but gaps exist that prevent certain steps from being completed (i.e., in terms of the CMO reviewing the documentation and then returning them to the client for review, revision, and sign-off). But, CDMO has developed a tech transfer process that can drive expedient batch record generation concurrent with these issues being corrected, adapting to each customer's needs while maintaining transparency and adherence to regulatory mandates.

Batch Record Innovation Drives Optimized Tech Transfer

CDMO's tech transfer process begins, essentially, with an overview document we work with the client to complete. Some clients can provide a significant amount of formulation and process information; others may only know their process works at small scale in a lab, but they are eager to progress to animal or clinical testing. In either scenario, this technical transfer "checklist" usually provides the bulk of data we need (e.g., formulation, fill volumes, type of glass, tolerances, etc.) to proceed with batch records.

The more information we can gather up front, the quicker and more accurately we are able to generate our batch records, as well as our unique specification sheets: client-specific documents detailing each customer's distinct needs and demands alongside the more templatized batch records. Specifically, CDMO's filling, inspection, and finishing are standardized processes, so batch records adequately capture these operational parts. Due to this, we can partner our batch records with specification sheets to decrease the records' drafting time:

Formulation Batch Record (Form BR; custom to each client) – The Form BR is dependent on the client's process, how their product is formulated, and any filtration processes. It varies based on, for example, whether

the process blends several excipients with the client's API, or we work from bulk drug substance only requiring a filtration step.

    - CDMO occasionally verifies client processes in the lab before transferring the process to filling to ensure the recipe scales to higher volumes and accommodates the fill method. We ensure test methods applied in early development are well-documented and account for all sources of variability. However, a standard small molecule or a monoclonal antibody (MAb) obviously presents fewer unknowns or chance of variability based on our previous experience.

- ***Manufacturing Batch Record (MBR; same for all clients)*** – The MBR is a standard internal batch record, comprising the aseptic filling process. It guides how we set up and process our robotic filling isolator, decontamination procedures, loading, etc.
    - Utilizing ready-to-use container formats in common sizes (e.g., 1 ml long syringes, 2R vials, 4R, 10R, 30R, etc.) allows us to have predetermined fill settings appropriate for most products.
    -
- ***Manufacturing Specification Sheet (MSS; custom to each client)*** – The MSS includes all filling parameters, including dosing and stoppering, tied specifically to client-provided information on the "recipe" for operation of the filling unit.
    - Beyond dosing parameters, elements like choice of delivery device and minimum extractable volume are critical to ensuring a precise, functional product.
    - Having filled multiple batches and conducted numerous studies across each of these formats, CDMO provides our clients a wealth of applicable knowledge in pump fill speeds, pump acceleration/deceleration, how long dosing will take, etc., all of which can be plugged directly into the MBR.

- ***Inspection Batch Record (IBR; same for all clients)*** – The IBR is a standard internal batch record detailing the inspection process.
- ***Inspection Specification Sheet (ISS; custom to each client)*** – The ISS is a short document describing all inspection parameters.
- ***Finishing Batch Record (FBR; same for all clients)*** – The FBR is a standard internal batch record covering the finishing process.
- ***Finishing Specification Sheet (FSS; custom to each client)*** – The FSS is a brief document that includes all finishing/kitting and labeling parameters.

Most CMOs perform a unique client draft for each record, adding time and expense to each project. CDMO's deliberate separation of non-client-specific batch records from client-specific operations is beneficial because it allows for greater attention to critical details while purging unnecessary documentation activity.

Instead of drafting (for example) a 30-page batch record, attempting to make sure every step aligns during review, the use of specification sheets allows us to keep client-specific information clear and concise, covering just a few pages. This succinctness minimizes time spent drafting batch records, as well as the up-front "leg work" associated with completing them and ensuring documentation flows properly.

Final Thoughts

CDMO's tech transfer process is enhanced by this innovative approach to batch records, but we also implement traditional, proven tactics for success: weekly meetings internally and with the client, accessibility to our project manager, and the utmost transparency.

Processes like receipt of materials, documentation reviews and exchange, and release testing from the lab all take place in parallel wherever possible, ensuring batch record drafting can transpire as soon as possible. A client that approaches us knowing exactly how they want to formulate, but unsure of some filling information, does not need to wait. We'll start operating with what is available, focusing on individual segments to expedite the process.

Depending on our current filling schedule, we operate with a 6- to 12-week lead time between signing of the project plan and executing their first fill. Still, in some cases, our flexibility allows us to move more quickly. A recent client came to us with a pre-formulated drug substance, requiring just a filtering step and a fill. We were able to have batch records drafted and prepare for a fill run within four weeks. While this is an atypical outcome, it is a typical example of our operation’s batch record drafting adaptability, as well as our capability to take advantage of an ever-changing, flexible schedule for the benefit of clients.

Source
How Efficient Batch Records Serve Thorough Tech Transfer — Optimizing Aseptic Fill For Development Projects (bioprocessonline.com)