



BATCH RECORDS AND PRODUCT RELEASE PROCEDURES

ARE YOU AT RISK?

If ever you want to be jolted out of your early morning slumber just pick up a recent edition of 'The Gold Sheet'. If this publication is new to you get a copy immediately; it provides a sobering reminder of what the FDA is finding in the pharma world and the devastating consequences of 'getting it wrong'.

'RECORD DRUG RECALL TOTALS FOR 2009 RESULTED FROM GMP BREAKDOWNS' (MAY 2010)

'ENFORCEMENT ON STEROIDS: FDA DELIVERS TWICE THE DRUG WARNING LETTERS' (APRIL 2010)

Once read, and suitably 'jolted', obvious questions quickly come to mind; "How did this mess happen?" "How can such catastrophic failures go unnoticed?" Any recall also brings into question the security and integrity of the Batch Manufacturing Record (BMR) and Product Release procedures that allowed the batches in question to escape.

The BMR and the Product Release procedure is a critical part of your Quality System. Vital information on the who, what, when, how and where is reviewed and

considered before that all important decision is made. "Do I or don't I?" "Do I release, reject or what?" For those involved in this process the pressures are immense. Decisions are rarely 'black and white' or clear cut; more usually a shade of grey. Time and commercial pressures are usually acute and the ever increasing complexity of your supply chain doesn't help. Despite these challenges the Product Release process must be efficient, robust and above all safe.

Based on the worsening recall statistics some companies are clearly falling short of the mark; way short. So how good is your BMR? How safe is your Product Release process? Are you 'at risk'? Consider your responses to the following:

1. DO YOU RELEASE PRODUCT JUST BASED ON THE BMR?... IF YOU DO, START WORRYING!

Product can only be released when you are absolutely sure that the quality system supporting manufacture is 'in control'. Release can only be justified when you know, rather than assume, that fully trained operators have used the right materials and components, followed procedures, operated clean, fully calibrated and maintained equipment within its validated state and followed the rules of GMP. To support batch release you simply must have access to Quality System 'performance measures' that tell the truth and nothing but the truth. Releasing product without accurate and reliable performance measures is a bit like a pilot landing 'blind' without dials and gauges; very dangerous. You may get away with it for so long but you will eventually crash. Before any 'yes' decision you must have the data to prove the Quality System is in control. This means having immediate access to information such as:

- > Audit and self-inspection reports for the entire supply chain



- > Change control history: have all changes been implemented successfully? What is the cumulative impact of minor changes?
- > Repeat deviations: why have they happened again?
- > Equipment calibration and maintenance status and trends: is equipment being operated within validated parameters?
- > Contractors: are they being managed and controlled?
- > Training and education 'status' of all involved, including contractors and 'temps'
- > Performance of key utilities (trend data for water, steam, gases, etc)
- > Environmental control
- > SOP status: are they all current, available and being followed?
- > Cleaning and sanitisation

2. HOW MANY DOUBLE CHECK SIGNATURES DOES YOUR BMR CONTAIN?... IF YOU HAVE LOTS START WORRYING!

Some people have this bizarre, but understandable, notion that lots of double check signatures mean the process is safer and more secure. We now know that the opposite is true.

Signatures are there for a purpose. They tell us who did what and when. Signatures are also very personal, reminding people they are responsible and accountable for their actions. Double or 'check' signatures are also there for a reason. These are reserved for those vital tasks that, if done incorrectly, can have a dramatic impact - weighing and adding materials and components, calculations, line clearances, reconciliations, approval of sterilisation charts and the like.

When we insist on too many check signatures two things happen. Firstly the importance of the genuinely

important tasks gets lost when operators are told everything is important. As operators struggle to get the job done there is also the danger that 'signing' becomes a 'tick box' exercise. The second consequence of excessive signatures is even scarier, encouraging less accountability and responsibility.

Years ago I was involved in helping a company investigate a costly packaging related recall. The cause was simple enough, an incorrect expiry date. What I found fascinating was that over 80 people had seen and signed to confirm that the expiry date was correct. Not one person picked up the error... I'm convinced many had signed without even checking the label and accompanying documents, assuming that others before them had done the job. So there you have it, the more signatures you have the more worried you should be!

3. SIZE MATTERS. THE BIGGER YOUR BMR THE MORE WORRIED YOU SHOULD BE

We were recently called into a company to help reduce their BMR 'error rate'. Over 38% of BMRs were returned to manufacturing because of mistakes and errors; the usual missing signatures, incorrect calculations and missing data causing costly delays and huge frustration. It became clear that the operators, a disciplined and committed bunch, were actually being distracted by the size and complexity of the 270 page BMR.

BMRs are usually a product of evolution. As the product and process evolves through to Phase 3 Clinical Trials the BMR inevitably gets thicker and more complex before it finally becomes 'registered'. No one sits down and thinks about content, format and design and making the documents easy to use. We helped one of our clients reduce the size and complexity of their BMR, achieving dramatic results... all in three days.

- > A 270 page document was reduced to 20 pages in total
- > Data entries were reduced by 27% (you will be amazed what you record and don't use!)
- > Double signatures were reduced by 68%



- > The 270 page BMR took, on average, 60 minutes to review and approve. The slimmer version took only 15 minutes
- > Most importantly the BMR 'error' rate reduced dramatically. After six months of use less than 1% of BMRs required correction

So, as far as most BMRs are concerned, less is more.

If you would like to dramatically improve the security and robustness of your BMR and Product Release process please drop me a line at martinlush@nsf.org.

Our intensive two day course: How to Simplify and Improve Your Batch Record Review Process will provide you with the tools and techniques to:

- > Decide what should stay in the BMR and what can be removed
- > Reduce the number of unnecessary signatures that do more harm than good
- > Improve document design to make your BMR user friendly
- > Reduce the time required for review and approval
- > Reduce the number of errors and reworks
- > Improve the security and robustness of your Product Release process

We come to you and run this workshop on your premises working alongside your subject experts.

ABOUT THE AUTHOR



Martin Lush has over 30 years' experience in the pharmaceutical and healthcare industry. He has held senior management positions in QA, manufacturing, QC and supply chain auditing and has conducted audits and education programs for many hundreds of companies in over 25 countries.

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