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NEWSLETTER

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The Editor

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Africa Health Excon June 2023

We proudly participated in the 2nd Africa Health Excon alongside one of our clients, in Cairo, on Wednesday 7th & Thursday 8th June 2023.

It was a great pleasure to meet clients again, and potential clients, face to face, at this unique event which brought together manufacturers of diagnostics, pharmaceuticals, biological products, medical devices, and recognised international industrial equipment & service suppliers. Many start-up companies in the Life Sciences business were also present.

Galenisys was able to meet with many of the people and companies involved in the project to build a vaccine manufacturing facility in Egypt, to answer their questions, and provide advice.
We assisted at an open discussion forum on the supply of essential vaccines to Africa and at a ceremony for the formal recognition by the Egyptian Administration of the establishment of a training Academy by our client. Galenisys is actively involved in this Academy and the courses that it will offer.

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Cosmetics and the FDA

By Steve Biddulph
Fellow of Royal Institute of Microbiology. Board level pharma experience. QSM and Aseptic Manufacturing & Control Expertise

Galenisys is currently assisting a major international cosmetics company to prepare for an FDA manufacturing site inspection.

For the FDA, any product marketed in the USA that purportedly improves ¨well-being" will be treated as a drug and therefore be subject to 21 CFR 210, 211 and relevant FDA guidance documents.

This policy applies to such products as anti-dandruff shampoos, toothpaste with fluoride, suncreams and lotions and lip balms. Suncreams prevent sunburn and lip balms prevent dehydration and although neither type of product will have a registration dossier (NDA) the FDA will treat them as "Over the counter" (OTC) drug products.

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There are between 100,000 and 300,000 OTC products on the market in the USA. Since 2017, the FDA has increased its efforts in attempting to regulate the OTC market. It has used several initiatives for this :

- The requirement for OTC manufacturers to be registered. Registration must be renewed annually. It is important to note that a foreign drug OTC manufacturer also requires US FDA registration UN listing if the drug from the manufacturer is marketing in the USA

- Registrants are required to submit initial listing information on all (their) OTC drugs in commercial distribution at the time of establishing registration with the FDA. Owners and operators of all registered establishments must update their drug OTC listing information with the US FDA every June and December.

- The creation of monographs in the USP/NF for OTC products. These monographs provide a rulebook for each therapeutic category, established in conditions, such as active ingredients, uses (indications) doses, route of administration, labelling, and testing under which an OTC drug is generally recognised as safe and effective (GRASE)

- The requirement for OTC drugs to carry expiry dating based on stability studies -accelerated for six months, or real time studies.

In addition to the above, the FDA performs on-site inspections to check that OTC manufacturers are in compliance with cGMPs and other relevant FDA requirements.

This is why forward-thinking OTC/Cosmetics manufacturers look to Galenisys to assist in the preparation for on-site FDA inspections. We are pleased to have successfully provided this service to several such International companies over the last few years.

Steve Biddulph

What's involved in a good batch review process

By Jose Zapata
Galenisys Pharma Senior Expert. Pharmacist with frontline experience in Quality, Operations & Project Management.
PDD Certified

Pharmaceutical companies with dynamic managements often acquire a range of products to add to their portfolio. When they do this they also take on responsibility for batch release of course.

This growth creates an additional workload for the QA function. However compliant batch record review & release requires the relevant knowledge & experience of the product form & regulatory requirements.

Given the cost & lead time of appropriate training for additional QA resources a good and prompt solution is to subcontract the **batch record review** to an expert group, whilst long term arrangements are implemented.

At Galenisys, we are used to accepting such client mandates, to review the batch record documentation, and make recommendations concerning release (or not).

We have found that a range of situations cause clients to turn to us for this tailored support:

1. A new product or group of products is acquired from outside & added to the portfolio.
2. One of the clients' pharmaceutical plants, or their CMO/CDMO, starts manufacturing of a new product(s) after a technology transfer process.
3. The clients QA department needs to focus in-house resources on key expansion projects and requires support for the review of routine products.
4. The new production location is distant & may have travel or language implications.

When we at Galenisys are commissioned for such a batch review project, it's because of our core knowledge & long experience. This is notable in the injectables field, or where considerable microbiology expertise is required. The products concerned may be medicines, APIs, LBPs...

Additional benefits of our involvement can include reassurance concerning existing practice which comes from outside experience, and the training of new staff.

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At the beginning of a Batch review project, we take into account the following general points:

- We are conscious that our role is to provide support to the clients QA department and finally the QP (EU) or the Quality Head (US) for the final batch disposition.
- In the case of observations (critical/major/minor) in a certain batch (production or QC), - the need to highlight these.
- The knowledge of the process & factory where the product is manufactured is key for the understanding and quick implementation of the project. This is why we strongly recommend visiting the plant if possible, as well as reviewing documents like validations and qualifications.
- Defining the system for documenting the reviews, and the relevant contact person(s)/group are essential aspects at the project outset.
- We know timelines nowadays are important for clients, & at Galenisys we keep to the required planning for batch review.

Typically, the list of documents normally & routinely reviewed after our deployment starts are:

- Production: batch record, IPCs, different graphs (autoclave, freeze drier, isolator…)
- Analytical: analytical record, chromatography results, audit trails…
- Microbiology: EM documents, bioburden, sterility, endotoxins…
- Deviations
- Change controls

Galenisys reviews are documented in reports with any necessary comments and sent to the contact person defined in the project, for response and explanation if appropriate. We will follow up if required to close any open point like a complex deviation.
And finally, we will provide a **final disposition document** recommending release, or eventually rejection.

We look forward to supporting you in such projects - reviewing batch processing, carrying out comprehensive document review, highlighting batch deviations, suggesting CAPAs, and defining process improvements.

Should the need arise, don't hesitate to contact Galenisys. Jose Zapata

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MORE PARACETAMOL NEEDED (more prunes?)

More than three decades ago I visited Agen, in southwest France; for a pre-contract assessment.

It was at the time when the manufacture of paracetamol was being consolidated worldwide, with the entry into the market of Asian manufacturers. Paracetamol of course is an important ingredient in many OTC and prescription painkillers. However, one of its mild adverse effects is relieved by prunes, and this struck me as excellent synergy for the local economy of Agen, which excelled in the production of both at that time.

Last week the French President's announcements, carried on the national evening news, which outlined the "onshoring" measures his government would take to relieve the shortages of paracetamol-based products, reminded me of the trip to Agen.

A headache for France

The President was visiting the pharmaceutical company Aguettant* and unveiled a list of the essential medicines that should be "onshored". A government adviser characterised the current situation as an "important deindustrialization giving rise to unacceptable dependence", and cited for example, that the number of products in the industry from outside France now represented 40% compared to 30% 20 years ago.

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A spokesman continued that “depending for 60 to 80% on foreign production, particularly China, is evidently unacceptable”. This “unacceptable dependency” was in sharp focus during the COVID epidemic when the shortages of personal protective equipment, and certain medicines to combat COVID and its effects were so evident to the Governments & populations of France & elsewhere.

Apparently, a paracetamol factory in Roussillon, in Isère is planned, meaning that first production from this facility would be unlikely before 2026.

However, it's not just paracetamol that is in short supply, antibiotics such as amoxicillin are also limited in France & the rest of Europe. In our previous newsletter, we wrote about the shortages & problems of delocalization and price pressure. ANSM, the French organisation concerned with the security of supply of medicines and healthcare products, has indicated the huge increase in out-of-stock situations between 2021 and 2022.

Annual price reductions!

It is clear that offshoring alone has not caused these shortages. LEEM, the trade body representing pharmaceutical companies in France, pointed in January 2023 to the annual price reductions on (generic) products demanded by the French Social Security financing law (“LFSS”). This was euros 800 million in 2023. As an example, “the price allowed on a bottle of amoxicillin eye drops was 76 centimes”.

The geopolitical situation is such that we can expect more changes to key supply chains in the next few years; with accompanying funding requirements.

* He also spoke on this subject during a visit to a Sanofi site near Lyon. During this event the Sanofi CEO announced an investment of 610 million euros for the construction of a new vaccine production unit Neuville-sur-Saône (France).

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