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NEWSLETTER

Galenisys wishes all our Newsletter readers and subscribers a very Happy & Prosperous New Year 2024

"No doubt 2024 will bring new challenges for many companies. Galenisys are bringing new associates into the company, and our clients require our services throughout the world in China, India, the USA, Europe, the Middle East and Australia.
However, whatever our client's needs in the Life Sciences in 2024, Galenisys is ready to step up and provide them with the necessary professional and expert services."

Steve Biddulph

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NEWSLETTER

Tony Dunford Editor

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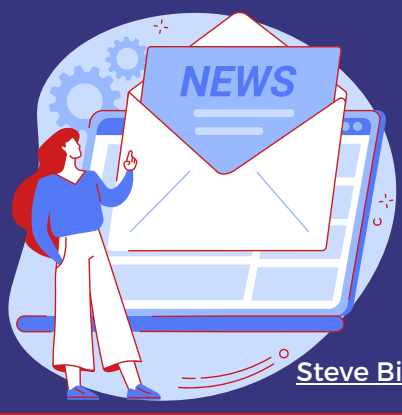

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The Food (and Drug?) Administration

The FDA, us, and the cultivated meat industry
by the Editor

In the famous “hierarchy of human needs” top of the list is **Food**. Health is further down. We have remarked elsewhere that many people continue to consume the (“wrong”) food they like, despite their obesity and its implications for their health.

A look at the recent developments in **the cultivated meat business** suggests food will continue to rise in the FDA's “hierarchy of priorities”.

In June 2023, **Eat Just** and **Upside Foods**, Californian startups, both won the first US regulatory approval to market cell cultivated meat. (It's been on sale in Singapore since 2020).
All sorts of other companies are also trying to bring cultivated meats to market.

The headline that “meat and dairy production accounts for 12% of humanity's greenhouse gas emissions” is often repeated and simple to remember. Consumer surveys show that many are trying are restricting their meat consumption on environmental grounds and this provides strong motivation for the cultivated meat developers.

In 2021 a Consultancy forecast a $25 billion industry worldwide by 2030, but realism is setting in. **Beyond Meat**, one developer, went public in 2019 & capitalization zoomed to $14 billion however it's now just $600 million. What's happened?

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Demand and Cost

Firstly, the slumping demand for plant-based meat has introduced realism to valuations. These alternative meats had reported sales in the US of $483 million in 2021 but were down to $338 million last year. In Europe sales are still growing but more slowly than before.

The **Good Food Institute** found the reasons (50% of) people don't like plant-based meat are **taste and texture**. Developers hope to overcome both these objections.

Cultivated meat is derived from cells taken from livestock or poultry animals. If developers can identify which genes in cells are responsible for providing taste and structure, they could counter the difficulties. One solution being used now to address the problem of texture is to grow the cells on a “scaffold” encouraging them into a certain shape and thus provide more fibrous “meat”.

And there are reasons to believe the taste “problem” maybe transitory. One only has to look at how 20th & 21st century menus compare; and how new flavours have moved our buying habits. (The Editor now prefers “sour cream and chives flavoured crackers”, to the plain “old” ones).
Perhaps more difficult to resolve are the high costs, and production scale up issues that developers have encountered.

A manufacturing alternative to scaffolds is to use bioreactors (which are already familiar features of biotechnology production). In this **batch process** the cells are grown in a nutrient rich liquid and after a period the meaty slurry is harvested and purified. The cost of these nutrients is high particularly if they are of pharmaceutical grade. So, the approval of industrial grade alternatives (“90% cheaper” says one analyst), and approval of their manufacturers, will become important.

The other inhibiting factors are the energy costs of production and the capital costs of bioreactor type manufacturing facilities (as we know only too well).
Given that the processes of creating protein derived from soya or wheat are more amenable to continuous processing, than bioreactor batch manufacture; **hybrid meat** - that is to say a mixture of plant protein and cultivated meat maybe the answer to both cost and consumer preference.

The products now approved for US market are just such combinations. And one only has to look at the ingredients listed on the labels of pork sausages in EU supermarkets to see the accepted precedents for both protein types.

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The FDA and the regulation of cosmetic products

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

Continuing our focus on **the FDA and the regulation of cosmetic products**, we have already noted that on December 29, 2022, the United States President signed the Consolidated Appropriations Act, 2023 (Pub. L. 117-328) into law, which included the Modernization of the Cosmetics Regulation Act of 2022 (MoCRA).

Among other provisions, MoCRA added section 607 to the Federal Food, Drug, and Cosmetic Act (FD&C Act), establishing requirements for cosmetic product facility registration and product listing. This replaces the voluntary system that ended in March 2023. Manufacturers should note that information from the Voluntary programme will not be transferred to the new system so Manufacturers will have to file new submissions for facilities and products in the new electronic systems described below.

The FDA has now issued a Guidance for Industry document on the ¨Registration and Listing of Cosmetic Product Facilities and Products¨.

Cosmetic manufacturers can now provide comments on the Guidance document for the 30 days after its publication in the Federal Register. Following this period, the FDA will publish the Final Guidance Document.

As stated above, the FDA has also developed an Electronic Submission Portal – Cosmetics Direct – such that manufacturers can streamline their registrations. FDA has also an Electronic Submissions Gateway which manufacturers may use for facility and products registration.

Since product formulations are constantly evolving in the cosmetics industry, FDA advises manufacturers to use the electronic submission systems such that registration can move forward with the minimum of delay.

THE EU NEW LIST OF CRITICAL MEDICINES

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

The European Medicines Agency (EMA) has published its first list of critical medicines in the EU for the EU on 12.12.23. It was developed by The European Commission (EC), the Heads of Medicines Agencies (HMA) and EMA, and will be of interest to generic manufacturers and those planning major pharmaceutical plant expansion.

The EMA commented on its **methodology** as follows:
"A critical medicine is identified by combining two criteria, the seriousness of the disease they target and the availability of alternative medicines."
Criticality was decided (and will be decided in the future) based on the following two criteria:

- The **therapeutic indication** (criterion 1) of the medicine
- The availability of **appropriate alternatives** (criterion 2).

For criterion 1, all authorised medicines in a Member State were classified, irrespective of their marketing status. For criterion 2, only authorised medicines marketed in the respective EU Member State were classified.

For each criterion, 3 **risk levels** (low, medium and high) were defined. Once a risk level has been assigned for each criterion, a risk matrix is applied to assign the medicine to either of the following **3 categories: "critical medicines", "medicines at risk" and "other medicines".**
And this provides a useful means of checking what medicines for human use are considered critical in the EU healthcare systems, and for which continuity of supply is a priority.

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The EU is anxious to avoid the sort of shortages we have seen and reported on in the last few years, for example antibiotic eye drops. It remains to be seen whether EU agencies or national governments reconstitute security stocks as a result.

The list contains the following 268 APIs and therapeutic areas, decided by wide consultation:
1.Alimentary tract and metabolism (group A): 11 APIs
2.Blood and blood forming organs (group B): 22 APIs
3.Cardiovascular system (group C): 23 APIs
4.Genito-urinary system and sex hormones (group G): 3 APIs
5.Systemic hormonal preparations, excluding sex hormones and insulins (group H): 11 APIs
6.Anti-infectives for systemic use (group J): 82 APIs
7.Antineoplastic and immune-modulating agents (group L): 45 APIs
8.Musculo-skeletal system (group M): 6 APIs
9.Nervous system (group N): 27 APIs
10.Anti-parasitic products, insecticides and repellents (group P): 3 APIs
11.Respiratory system (group R): 5 APIs
12.Sensory organs (group S): 10 APIs
13.Various (group V): 20 APIs
The list can be seen via the link: https://www.ema.europa.eu/en/news/first-version-union-list-critical-medicines-agreed-help-avoid-potential-shortages-eu. and will no doubt be updated from time to time.

Note also the WHO list of Essential Medicines.
José Zapata

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How to handle deadly epidemics

Some of the best lessons are those learnt from the past.
The Editor

The inquiry into how the British government managed the COVID epidemic is currently paused over Christmas - New Year. The Inquiry is said to last until 2026. (There must be a lot to learn given that similar inquiries in other countries have already been completed).
As always however, some of the best lessons are those learnt from the past.

London in the 16th century was a deadly place - every year more people died there than were born. The population only increased** because of the steady influx of provincials, refugees from the continent, and sailors / other travellers - all of whom continually refreshed the city's stock of deadly & infectious diseases. A plague was virtually always present somewhere in the city, flaring up into an epidemic every ten years or so.

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However, Londoners had tried & tested responses.The people lived in close quarters “cheek by jowl” in narrow streets. The bulk of the population was packed a total area of 450 acres (3/4 square mile). As this in turn was divided up into 100 or so parishes each with a church which recorded deaths, the spread of **the disease was very effectively monitored.**

Each time the death toll in the city reached 40, all public gatherings (except for churchgoing) were banned within 7 miles of London in a no-nonsense example of **prompt & compulsory lockdown**. Enforcement was facilitated, since even when there was no epidemic, the city gates were locked at dusk and a nighttime curfew took effect with darkness. (Admittedly the force of night constables and watchmen were usually portrayed as laughable dimwits by Shakespeare and others).

Thirdly, those who could afford to, left the city at every outbreak - energetically practising **social distancing**.

In other capitals, as Madame la Marquise de Sevigne remarked in one of her (many) letters to her daughter, **mask wearing was in force** - at the Court of Louis 14e, - and general restrictions had prevented her attending a production of Moliere.

Hopefully (!!), drawing on these lessons will enable the Inquiry to report a lot sooner, and some of the large fees of the participating Judges, Barristers, Solicitors, & Civil Servants, will be saved for the purchase of Personal Protective Equipment ,..... similarly unavailable in the 21st as the 16th centuries.

(** It increased rapidly from approximately 50,000 in the year 1500 to four times that number by the end of the century).
The Editor

Quality drug development - EMA & FDA joint document

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

Last month the EMA and FDA published some Questions and Answers (Q&As) documents on expediting Quality Drug Development (link below).

Such moves towards harmonisation can be beneficial to industry, and in this case the USA and Europe plan a joint panel to look at difficult areas in Quality Drug Development for any medicine intended for marketing in both areas.

This publication results from a 2018 meeting between EMA, FDA, and industry. The aim was to facilitate the development and preparation of the **pharmaceutical quality files for "PRIME" (priority medicines) and "BT" (Breakthrough therapies)**, (particularly for patients with unmet medical needs) thus potentially expediting the development and approval of these products without lowering the medicinal standards.

The document "EMA-FDA joint Q&As on Quality and GMP aspects of PRIME/Breakthrough therapy applications" and can be accessed both in the FDA and EMA websites.

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It is presented firstly in a Glossary of terms and secondly in four (4) annexes:

- Annex 1. Q&A on Control strategy considerations for PRIME/BT applications: with 7 Q&As
- Annex 2. Q&A on Process validation approaches for PRIME/BT applications: with 10 Q&As
- Annex 3. Q&A on Alternatives for determination of re-test period or shelf-life for PRIME/BT applications:
  - For Small Molecules/Chemical Entities and Well-Characterized Biotechnology Products: with 3 Q&As
  - For Small Molecules/Chemical Entity Products: with 3 Q&As
  - For Well-Characterized Biotechnology Products: with 1 Q&As
- Annex 4. Q&A on GMP considerations for PRIME/BT applications: with 8 Q&As

These documents are only intended to provide general information and do not constitute regulatory guidance. Industry will still need to discuss with the Agencies when planning to follow any of the published approaches, (as the EMA and FDA are not in full agreement) but at least we have both points of view:

The FDA information website says that "for EMA, these Q&As are applicable to chemical and biological medicinal products for human use, including complex biologicals (such as ATMPs), unless stated otherwise. For FDA, these additional discussions and the resulting annexes are only applicable to CDER-regulated products.

Therefore, all references in the annexes to biological products are intended to refer to CDER-regulated biological human drug products only. Center for Biologics Evaluation and Research (CBER) -regulated products, such as advanced therapy medicinal products (ATMPs), are not in the scope of these documents."

Visit the link: https://www.ema.europa.eu/en/events/stakeholder-workshop-support-quality-development-early-access-approaches-such-prime-and-breakthrough-therapies

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