Galenisys 11 rue Notre Dame de Nazareth , 75003 Paris, France. Tel : +33145554414 or +33632329927

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NEWSLETTER

In this Edition :

The Editor.

Tony Dunford Editor

Steve Biddulph +33 6 32 32 99 27 Steve.biddulph@galenisys-pc.com

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Actually, we love bacteria – part 1

Bacteria, the Microbiome, Symbiosis, and Holobionts
The Editor

At Galenisys, our team spend a lot of time trying to stop bacteria from contaminating the pharmaceutical products of our clients, by advising these companies on the measures to take in training, during manufacture, and in quality assurance.

Given our business; you might think that we would be “antibacterial”, indifferent to the benefits of bacteria to humanity. So, in this article we take the opportunity to set out some new fascinating evidence to more than “balance the score card”.

In praise of “our other half”

We're told that there are around 37 trillion cells in the typical human adult weighing 70 kilos ie. “**our**” cells. However, if you add in the estimated number of cells of bacteria that **reside** in us as well, the total number of cells doubles to around 74 trillion!

These other bacterial cells represent what is called the **human microbiome**. (As you know, treatment by antibiotics we might use to combat infection can also play havoc with the beneficial bacteria there).

The human microbiome is made up of arcane bacterial, fungal, and protist cells which occupy the mouth, gut, skin, lungs, and almost every other surface nook and cranny of our body. (In general, these cells are much smaller than proper human cells so don't blame them for obesity!). Some of these extra cells are mere passengers **whilst others are actively beneficial to us.**

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Steve Biddulph +33 6 32 32 99 27 Steve.biddulph@galenisys-pc.com

This is the idea of **symbiosis** in which different species live together intimately and collaboratively.

What do we all have? answer "symbionts"

Modern research is providing an ever-increasing list of examples of symbiosis between bacteria and humans, animals, plants, and other bacteria. Now it's said that almost every multicellular organism, and even some single celled ones, have **symbionts**.

Enter "holobionts".

Some research biologists find it very useful when investigating cause and effect, to consider that the plant or animal and its microbiome are merely parts of a united meta-Organism whose components evolve together with each other in a mutually advantageous way## (remember natural selection); and to call this meta-Organism a **holobiont**. The occurrence of the terms holobiont & hologenome in scientific papers has been exponential in the last 20years, so this view has traction.

Thanks to a new technology called **metagenomics** it's much easier now to investigate symbiosis and investigate potential holobionts. **Metagenomics** analyses the genomes in complex samples, for example plants AND the soil around them, or a mashed-up part of an animal, at the same time. Obviously, such samples are likely to contain many bacteria. But to identify which bacteria by the traditional method of culturing, would require long and laborious research to establish which culture media & conditions the various bacteria would grow in.

Three examples will show the advantages of this different way of thinking:

- The honeybee has long been recognised as a very important and valuable pollinator. There is research into whether insecticides are responsible for the marked decline in the population of honeybees. If research is only restricted to investigating the honeybee genome, one excludes the possibility that the population decline is due to the effect of these chemicals on the honeybee's microbiome* (ie the bacteria that are of value to the honeybee species). *Hives likely exchange microbiomes via flowers their members visit.

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- Whereas honeybees are viewed as good, the public generally regard bark beetles as bad. But the bark beetles holobiont nature is emphasised by the fact that some have evolved special structures which carry fungal spores. The spores grow thin tendrils that allow them to digest wood that releases nutrients which bark beetles can metabolise. But if these fungi (one of the best known of which causes Dutch Elm disease) get out of hand they can devastate entire forests. So, this holobiont is well worth investigating.

- In the animal world, many amphibians are threatened with extinction by skin fungi called chytrids which have been spread from their Asian homeland by humans. Along with researchers at London Zoo, biologists are studying the diversity of amphibian skin microbiomes and whether this can give the amphibian meta-Organisms immunity to chytrid infections.

Theoretically the bacteria in/on the skin, surface or gut could be purged. Is it still the same plant, animal, entity? Well perhaps it would depend on the degree of “integration”.

One can question where exactly the borders of the term holobiont lie. But biology is full of concepts that are at once fuzzy and useful. Perhaps the most important advantage of the concept is to act as a reminder to biologists never to neglect a possible role for the microbiome (or a bacterium) in any phenomenon they're trying to understand.

The following examples show that in some organisms the bacteria or viruses are vital to, or completely integrated in, the holobiont, and that (if it existed) its behaviour and characteristics would be completely different without the bacteria or viruses:

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Steve Biddulph +33 6 32 32 99 27 Steve.biddulph@galenisys-pc.com

Good for a bean bug but not for a farmer.

- For example, the study of the evolution of pesticide resistance and insects usually (only) involves the genome of the insect itself. But resistance by pests - called bean bugs - to a key insecticide, is provided by bacteria of a certain genus which live in their guts. This is very (economically) important knowledge if you want to counter that resistance.

- The Australian termite relies on gut microbes to break down the tough wood it eats into molecules which the holobionts' animal part can metabolise. One of these microbes is itself a combination of a type of single celled eukaryote and 4 types of bacteria! A pioneering American biologist called this critter "the beast with five genomes".

- All aphids carry bacteria of the Buchnera genus, which is unknown elsewhere. These live INSIDE specialised aphid cells (called bacteriocytes) so comfortably that they've shed most of their genes over some 200m years of "co-habitation". The bacteria synthesise the needed amino acids as the insects can't. The insect part provides the other food.

References: Abridged from "What is an organism, anyway?" The Economist 17th June 2023

In our next Newsletter, & part 2 of "Actually, we love bacteria" we'll look further at homo sapiens and bacteria.

The Editor

At Galenisys our job is to help our clients

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

At Galenisys we are proud of our expertise in Quality Assurance and compliant QA Systems, frequently providing training in these areas. (We have a suite of some 200 training & presentation modules covering all aspects of a pharma QA System).

We are also mindful that our key role is to help our clients with solutions to their specific needs. So, when one of the clients we are helping with a large manufacturing project, wanted a bespoke technical training course including cell & gene therapy, upstream & downstream biotech processing; we set about finding him a solution:

educo life sciences

A training provider for Life Sciences Companies

We identified London based Educo Life Sciences, who provided an excellent service in putting together a tailor-made two-week course in vaccine manufacture, control, and the relevant regulatory aspects, for this client.

Educo Life Sciences are learning and development specialists providing technical training solutions to the pharmaceutical, biotechnology, cell & gene and medical device industries. Educo are focused on improving the skills and knowledge of life science professionals, so they perform with confidence, accelerate their careers and drive innovation.

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Educo provide a calendar of courses that cover many aspects of industry and regulatory requirements and they, also, provide courses that are tailored to a specific client's requirements. Eg:

- Pharmaceutical Training – development through clinical to routine manufacture and control
- Biotechnology Training – upstream and downstream development, manufacture and control methods
- Cell and Gene Therapy Training – regulatory, manufacturing and commercial topics and cell therapies, gene therapies and viral vectors
- Medical Device Training - regulations, quality, risk management IVDR, MDR and FDA requirements
- Regulatory Requirements – GMPs, EMA, FDA, WHO

Being a service provider to our highly regulated industry, they are ISO 9001 certified and have a 9001 QMS in place to ensure that activities deliver quality training courses that meet customer requirements. Educo is also a CPD member and this ensures that their approach to training is checked on an annual basis through audits, as we would expect, Educo also has a detailed quality policy which outlines the approach to training, managing feedback, and continuously improving training course delivery.

Galenisys look forward to working with Educo Life Sciences, in the future, in providing the training needs of many of our other clients.

Watching our backs

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

Covid is still around – who's keeping an eye on it & how?

The passage of time has provided the opportunity to rationally structure SARS - COVID 2 risk assessment facilitating a high level of coordination between WHO and other international bodies.

One of these is The ECDC (European Centre for Disease Prevention and Control, an agency of the EU) which is following the evolution of SARS-CoV-2 variants. An extract of one of their publications (below) gives an interesting outline of how this surveillance is carried out:

- "**Variant classification** serves as an important communication tool for alerting EU/EEA countries about the emergence of SARS-CoV-2 variants with concerning properties likely to impact the .. EU/EEA.

- ECDC utilises three categories of variant classification to communicate increasing levels of concern about a new or emerging SARS-CoV-2 variant:

1 variant under monitoring (VUM), 2 variant of interest (VOI) and 3 variant of concern (VOC).

- New evidence is regularly assessed on variants detected through epidemic intelligence, rules-based genomic variant screening, or other scientific sources. If a decision is made to add, remove, or change the category for any variant, the tables are updated to reflect this change. The tables are regularly sent for consultation to ECDC and WHO Regional Office for Europe's joint virus characterisation working group…

- There are currently no SARS-CoV-2 variants meeting the VOC criteria".

So, this is good news, even though there are still several VUM and VOI currently being tracked:

VOIs	Omicron BA.2.75	Omicron XBB.1.5	
VUMs	Omicron CH.1.1	Omicron XBB.1.16	Omicron BA.2.86

Just to remind you of the number of variants in the "covid era": there are 59 variants of the virus that have been **de-escalated**, meaning that the variant is no longer circulating, the variant has been circulating for a long time without any impact on the overall epidemiological situation, or there is scientific evidence demonstrating that the variant is not associated with any concerning properties.

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“But Watch this one”: the ECDC 10th August update mentions that: “…(BA.2.86) … carries 30 additional spike changes compared to the parental BA.2 lineage.

Due to the overall reduced genomic surveillance of SARS-CoV-2 it cannot be determined whether the variant is circulating undetected elsewhere. It is currently not possible to determine whether the variant is associated with any changes in transmissibility, immune escape or severity, the high number of mutations however, makes it likely that it is associated with significant antigenic differences

On June 15, 2023, …for the 2023-2024 formulation of the COVID-19 vaccines for use in the U.S. beginning in the fall of 2023 ….(following VRBPAC recommendation) …. **the FDA has advised manufacturers who will be updating their COVID-19 vaccines,** that they should develop vaccines with a monovalent XBB 1.5 composition.

New vaccines & facilities will continue to be necessary in future and Galenisys experts will be continue to support you in the field of the vaccine manufacturing, quality, & facility design, with their extensive experience.

José Zapata

Heads Up – Was Voluntary, Now Compulsory

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

Until March 2023, the FDA operated a **Voluntary** Cosmetic Registration Program for cosmetics manufacturers. (I briefed readers about this in our February 2022 Newsletter).

The program provided the agency with information about cosmetic products and ingredients, their frequency of use and businesses engaged in their manufacture and distribution.

In 2022, the approval of the Modernization of Cosmetics Regulation Act of 2022 (MoCRA) changed this. By the end of 2023, **registration and listing of cosmetic product facilities and products will become a requirement**, making information about cosmetic products, including the ingredients used in products and the facilities where they are produced, available to the FDA.

The draft guidance, "Registration and Listing of Cosmetic Product Facilities and Products: Guidance for Industry," describes MoCRA requirements for facility registration and product listing, and the exemptions under MoCRA for certain small businesses.

Under MoCRA, submission of information about existing cosmetic product facilities and products is required no later than Dec. 29. Facility registration information is to be updated within 60 days of a change and registration to be renewed every two years. Additionally, any updates to a product listing, such as a change in product ingredients, are to be provided annually.

The FDA will rely on registration and listing information to accomplish several objectives, such as identifying facilities producing products potentially causing adverse events, facilitating the recall of unsanitary products, administering product testing and surveillance programs, planning inspections and identifying products marketed in violation of the law.

The draft guidance is intended to play a critical role in helping to ensure the safety of cosmetic products that many consumers use day-to-day. It also serves as a milestone within the FDA's continued efforts to protect the public health.

The FDA is accepting comments on the draft guidance until Sept. 7.

See also Galenisys Newsletter March 2022 "Caring for Cosmetics".