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NEWSLETTER

Tony Dunford Editor

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by The Editor



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FEEDING FRENZIES

By The Editor

On Saturday a couple of weeks ago I was in Manchester, (which readers may recognise as the world capital of football).I had expected to see plenty of people sporting shirts of their favourite team, (Man City v Newcastle; & Man Utd v Liverpool that weekend) but what struck me most was the number eating chocolate covered ice cream.

In the concourse of Manchester's Piccadilly station was a quartet playing live classical music to draw attention to the fact that Unilever was there, giving away **free Magnums** – which are sticks of chocolate covered ice cream made famous by a most attractive young lady (Eva Longoria) devouring one.



I was puzzled as to why Unilever might be doing this until learning of the large and diverse effects that the **new weight loss drugs** were having on companies outlooks and

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Investors' appetites

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- There is clearly a feeding frenzy for the shares of companies involved in the new market for GLP 1 agonist type weight loss drugs, with investors' appetites driven to bubble territory. **Novo Nordisk** capitalization has expanded more than threefold to \$560 billion, whilst **Eli Lilly's** at \$740 billion has more than doubled since the start of 2023. Users of Novos' Wegovy shed about 15% of their body weight on average, those taking Lillys' Zepbound lost around 20%.
- When **Viking Therapeutics** announced trial data showing that its anti-obesity medicine helped patients lose more weight even than Zepbound, its share price more than doubled!
- Given estimates such as the world obesity federations, of 2.7 billion people being obese or overweight; predictions such as the size of the weight loss market reaching \$80 billion by 2030 are reasonable. It fuels the development frenzy with approximately 100 other companies having weight loss candidates in various stages of advancement.
- This demand feeds the requirement for greatly increased fill and finish and device manufacturing capacity, and as we referred to in our last newsletter**, the value of such sites & knowhow has also soared.

These GLP 1 agonists are extremely effective and relatively safe. Basically, they work by creating a feeling of fullness that suppresses patients' appetites. But clearly the drugs have no effect on investors' appetites.

But some **side effects** are already apparent:

- When Wegovy the first GLP 1 slimming jab was launched in USA the market value of WW, formerly Weight Watchers crashed by 90%. (A Director, Oprah Winfrey, started using GLP-1s & quit their Board). Other traditional weight loss companies are experiencing similar effects.
- "Obesity sufferers NEEDED" - With all the clinical trials of these "me too" companies planned & ongoing; plenty of overweight folks will be required. Eli Lilly alone are conducting one trial with 15,000 participants studying the effect of the active ingredient in Zepbound and Mounjaro.
- The food companies such as Nestle & Unilever clearly understand how more modest appetites reduce sales of sugary & fatty products.

Are free Magnums a reminder to customers how nice their old favourite is, before the weight loss drugs go mainstream?

The Editor

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COSMETOVIGILANCE



By Steve Biddulph

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

We continue the series on Cosmetics, with a look at Cosmetovigilance ie the Post marketing surveillance for cosmetic products.

Companies that manufacture health products for sale are well aware of the need for **post marketing surveillance** of their products. However, these requirements are increasingly being demanded **for cosmetic products**.

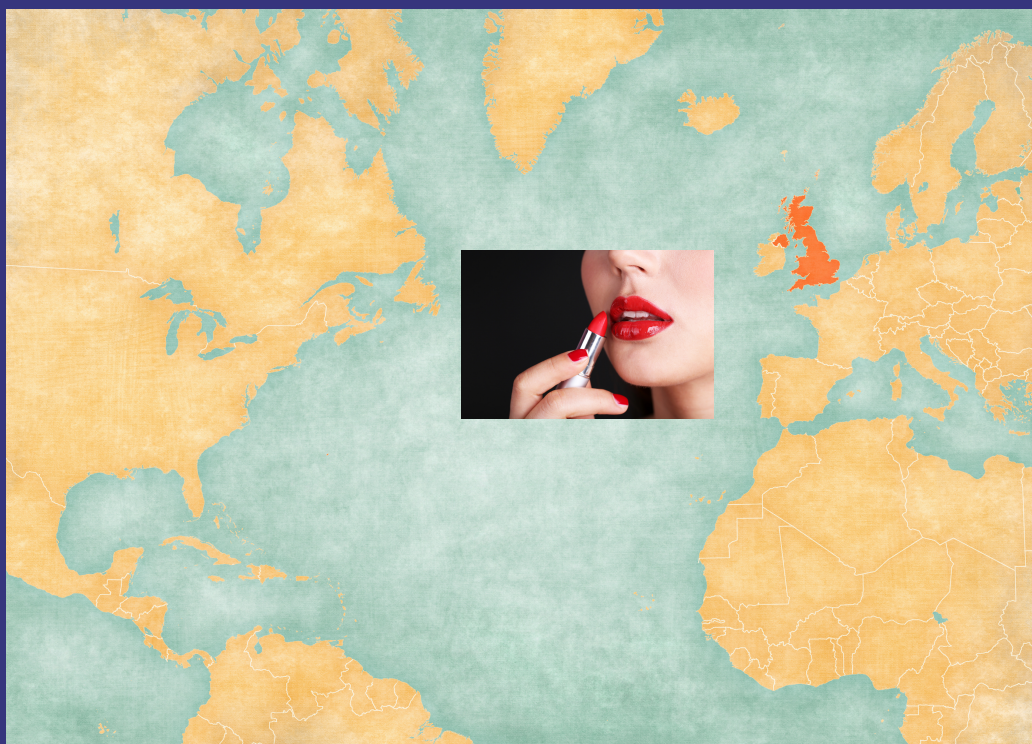
Pharmacovigilance is the collection, detection, assessment, monitoring, and prevention of adverse reactions occurring with **medications**. All regulatory agencies require companies to implement a Pharmacovigilance system. And Medications (drugs) are defined by their intended use in the diagnosis, cure, mitigation, treatment, or prevention of disease.

Cosmetovigilance refers to surveillance activities for the collection, detection, assessment, monitoring, and prevention of adverse reactions due to **cosmetic products**. Cosmetics are defined as products for cleansing, beautifying, promoting attractiveness, or altering the appearance.

And so, Cosmetics include moisturisers, lipsticks, perfume, deodorants, make up, shampoo, etc.

In the USA there are differences with Europe over the requirements for cosmetics and with regard to legal definitions of drugs and cosmetics. If products, **improve human wellbeing**, then they will be defined as drugs in the USA, whereas in Europe they may remain defined as cosmetics. Europe. This will apply to such European cosmetic products as sunscreens, anti-dandruff shampoos, toothpaste containing fluoride and lip balms to prevent dryness.

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Cosmetovigilance was initiated by the French health products safety agency as a part of a pharmacovigilance system for cosmetics. Most other Health Regulatory Agencies in the world have now adopted this requirement for the post marketing surveillance of cosmetics.

Common undesirable effects can be, for instance, skin reactions from fragrances, balsam of Peru, neomycin, thiomersal, formaldehyde, and other preservatives. These ingredients are frequently found in nail polish, perfumes, shampoos, lotions, and cosmetics including foundations, mascara, and lipsticks. Since reporting systems in different countries differ considerably, understanding the causes of these effects can be very difficult.

This is further complicated because cosmetic formulations can be modified quite often and the effects of some of the constituents are not well documented. Given that many people suffer from allergies to many other materials in the environment that can give rise to skin conditions it is a very difficult for cosmetic companies to judge which undesirable reactions are caused by their products and which ingredient is the real cause.

With increasing comprehensive surveillance of cosmetics and their use and the standardisation of reporting, companies will acquire more meaningful data with which to evaluate the possible unwanted effects of their cosmetic products and to introduce actions to correct the issues.

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Here are some of the areas which we would cover when establishing Cosmetovigilance Systems & Procedures for cosmetics clients:

- ADVERSE EFFECTS REPORTING ("ADRs")
- ASSESSMENT OF ADRS
- RISK MANAGEMENT
- RESULTING CAPAS (more on this topic next month)

It's over a decade since the European Commission issued the following:

"Regulation (EC) No. 1223/2009 on cosmetic products ('Cosmetics Regulation') 1 created the basis for a uniform approach to the management of serious undesirable effects (SUEs) attributable to the use of cosmetics. It provides for notification of SUEs without delay to the Competent Authorities of the Member State where the effect in question occurred, as well as the notification of any corrective measures taken by the Responsible Person or Distributor. Data on SUE become part of the Cosmetics Product Safety Report (CPSR) 2 and have to be made available to the public 3 .

In order to facilitate the implementation of Article 23 of the Cosmetics Regulation, which constitutes an essential part of a cosmetovigilance 4 system, and to establish a management and communication system on SUE throughout the EU, the Commission, in conjunction with Member States and industry, established the following guidelines describing the system.

Their aim is to ensure harmonized notification of SUE by the Responsible Person or Distributor and follow-up on SUE notifications by Competent Authorities, Responsible Persons or Distributors".

Note the responsibilities put on the "Responsible Person or Distributor..."

Galenisys has worked with cosmetic manufacturers on their Quality Systems, and Inspection readiness. We have successfully helped them with troubleshooting, and correcting issues that arise within cosmetic manufacturing, control, facilities, equipment, and utilities.

Contact us if you would like to know more about our experience and services.

YOU GOT IT!

By The Editor

“You got it!” is the refrain I'd expect when ordering a Big Mac and fries. Apparently, it's also the likely response if you asked a virologist if you are infected with the Epstein Barr virus, since up to 96% of us are!

This month is the 60th anniversary of the medical breakthrough* which the discovery of the Epstein Barr virus (“EBV”) represents. The key findings were published in The Lancet in 1964 by Epstein, Achong, and Barr, relating to EBV & the form of cancer which is known as Burkitt Lymphoma. EBV is remarkable being the most common viral infection in humans. When we get infected it's with us silently for the rest of our lives. (And probably > 96% of us have never heard of it). Work by Werner and Gertrude Henle at the Children's Hospital of Philadelphia in 1967 - 68 showed that EBV can directly immortalize B cells after infection (subsequently an important in vitro research tool).

It spreads easily through saliva eg via kissing or sharing a drink. Most people get infected as babies or youngsters and have no ill effects whatsoever. However, get infected in early teenage life or early adult hood and there's a 50% chance of getting “kissing disease” - glandular fever, and increased chance of many other afflictions.

The groundbreaking discovery then*, was that for certain individuals, this virus can spark of cancer. Since then, other viruses like hepatitis C and HPV have also been linked to cancer this has led to lifesaving developments eg the HPV vaccine to prevent cervical cancer.

Since the 1960s EBV a member of the Herpes virus family, has been implicated in multiple sclerosis and other autoimmune diseases. Following natural infection with EBV, the virus is now thought to execute some or all of its repertoire of gene expression programs to establish a persistent infection. The site of persistence of EBV may be bone marrow. Epstein-Barr nuclear antigen 1 (EBNA1) is a multifunctional, dimeric viral protein associated with EBV. It is the only EBV protein found in all EBV-related malignancies.

Studies of regional diseases suggest that it's the complex interaction between the virus the ethnicity, and diet of the individuals, that affects the way the body responds “logically” to infection.

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The scenario therefore is, infection, ethnicity, lifestyle, and diet, plus the multiple mutations with the virus contributing an essential key component on the pathway that leads to cancer, plus the body's immune system attempting to control the variety of outcomes. So, studying these viruses really elucidated other pathways that are common in all cancers not just virus associated cancers. It's estimated that probably around 15% of human cancer worldwide is associated with virus infection.

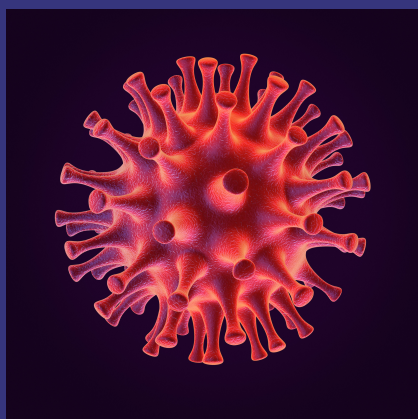
Working to towards an MS vaccine

EBV has also been linked to multiple sclerosis ("MS") an autoimmune disease that affects one in 500 people in the UK. Massive epidemiological studies over many years in the USA showed that you can't get multiple sclerosis unless you are EBV positive, and data from years ago showed that there's an increased risk of developing multiple sclerosis if you've previously had glandular fever. Current studies are looking at whether the continued behaviour or reactivation of EBV is contributing to the disease, but researchers are absolutely convinced now that the EBV is the major causative agent of MS.

There are currently 2 MS vaccine approaches:

- Generate a therapeutic vaccine that can be used to treat MS & hopefully to treat certain cancers.
- Even if EBV infection can't be prevented in the 1st place; then dampen the initial effects of it to avoid glandular fever hence protecting against later MS. This is being followed up in the USA with a Moderna vaccine.

Friend or Foe?



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If EBV is linked to so many illnesses, should we just vaccinate everybody against it in the first place? For many years there was work on such a vaccine including that by Epstein himself, but none were found to prevent infection. And because this virus is so infectious at a young age, it is very difficult to vaccinate the whole population, & hard to justify it. Although under active research, an Epstein–Barr virus vaccine is not yet available. It's said the development of an effective vaccine could prevent up to 200,000 cancers globally per year.

However, if you were to completely eliminate the virus what would that do to our immune system? In an evolutionary sense has this ubiquitous virus helped develop our immune system? Apparently, there is some evidence that perhaps suggests great importance in helping us control infection by bacteria. Other emerging evidence suggests that in later life EBV supports the development and effectiveness of our immune system.

In resume, if we completely eliminate EBV from the human population could it cause untoward and unknown problems? Natural selection suggests that there would be no reason to retain the potentially dangerous EBV in our systems unless it gave us some evolutionary advantage. One idea is that it helps our B cells to remain effective. Perhaps combinations of more effective vaccines and better drugs will help us control these diseases without necessarily completely eradicating the EBV from our bodies. Or is it still there because it's so damned versatile?

What are my main takeaways from all this:

- 1.How ignorant we are of things so linked to our mortality and illnesses.
- 2.The value in following up a certain, ostensibly narrow, line of research because it will / could open up a whole window of knowledge about far bigger health issues.
- 3.Although it's now 60 years since the breakthrough, in that time multiple pieces of this enormous (unfinished) jigsaw of knowledge, have been put into place.
- 4.However, even a brief reading of EBV research usefully illustrates the enormous complexity of its role & capabilities, and what remains to be discovered.
- 5.And, until a safe vaccine arrives, kissing your baby is a good thing!

The Editor

Adapted & resumed, interalia, from a recent review of EBV research by Lawrence Young, virologist, and Professor of Molecular Oncology at the University of Warwick UK medical school.