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NEWSLETTER

Tony Dunford Editor

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A STEP CLOSER TO THE ELIXIR OF LIFE ?

The Editor

Wouldn't it be nice to **live 25% longer** than you will likely do now, with the same quality of life?

This is the promise of a drug which has increased the lifespan of laboratory animals by nearly 25%. The treated **mice** were healthier, stronger and developed fewer cancers than their unmedicated peers. Can it also slow human ageing?



The Research

Whether it would have the same anti-ageing effect in people it is currently unknown, but the drug is already being tested on humans.

Look at it as the continuing quest for the **elixir vitae**, the Elixir of Life. Chinese Taoists looked for it as “the pill of immortality”. More recently the team at the **MRC Laboratory of Medical Science, Imperial College London, and Duke -NUS Medical School in Singapore** investigated a protein called **interleukin 11**. Levels of this increase in the human body as people age.

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It contributes to higher levels of inflammation and the team believe it triggers some “biological switches” that control the pace of ageing. (Scientists have known for quite a while that the **ageing process** is malleable. eg Lab animals live longer if you significantly cut food intake).

They conducted 2 experiments:

- In the 1st, mice were genetically engineered so that they were unable to produce interleukin 11.
- The second experiment started on 75 week old mice (equivalent to 55 year old humans) regularly giving them a drug to purge them of interleukin 11.

Results, in the journal **Nature**, showed that mouse lifespans were increased by 20 to 25% depending on the experiment, & sex. Older laboratory mice often die of cancer, however, the mice lacking interleukin 11 had far lower levels of it. They also showed improved muscle function, were leaner, less frail, & had healthier fur.

Interleukin 11 does have a role in early human development. Rarely there are people born who are unable to make it. This alters necessary skull bone fusion, & affects joints & tooth emergence. In resume useful to us early on, but playing a negative role later by driving ageing.

The drug, a manufactured antibody that attacks interleukin 11, is being trialled in patients with lung fibrosis.

The trials are incomplete, but the data suggested the drug was safe so far. (Other **unapproved** drugs being tried for treating ageing are the type 2 diabetes drug metformin, and the generic rapamycin to prevent transplant rejection).

Is the data too good to be believed? Could the same effect be achieved in people as in mice?? **It would be transformative for society.** Will there be intolerable side effects of this drug or similar? Future hurdles include the lack of evidence in humans, the cost of making such drugs, and the chaotic clamour for it, if successful.

In the meantime, don't wait for the drugs



LIVE LONGER BY EXERCISING

you are on holiday – get started !

Yes, elderly people who exercise live five years longer, (as does giving up smoking). Researchers say regular exercise in old age has a powerful effect on life expectancy. For example, an analysis carried out in Norway on 5700 elderly men and showed that those doing 3 hours of exercise a week lived half a decade longer than the sedentary.



In the British Journal of Sports Medicine (2015), the authors called for campaigns to encourage fitness in older people. The study, conducted by the Oslo University Hospital, found both light and vigorous exercise extended life expectancy. The trial tracking 68 to 77 year olds found that doing less than an hour a week of light exercise had no impact, but overall, those putting in the equivalent of 6 x 30minute sessions of any intensity were 40% less likely to have died during the 11year study. It added, even when men were 37 years of age on average at the start of the follow up, active guys had five years longer expected lifetime than the sedentary.

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For elderly man public health strategies should include efforts to increase physical activity. (The report did not look out at how active people were early in their lives). The British Heart Foundation has also warned against people getting too little exercise. Countrywise, Britain is in the middle of the pack with 44% doing no moderate exercise. It's 69% in Portugal doing none! whereas Netherlands had only 14% slouchers. Official advice in the UK recommends 150minutes of moderate exercise per week for > 65s.

Now for a cool drink....



Refreshed ? time for a good book:

Our suggestions:

“From the Holy Mountain”

“Free...”

“A Short Walk in the Hindu Kush”

William Dalrymple

Lea Ypi

Eric Newby



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Water Systems

Not the Elixir of Life, more the
“Vector of Contamination”.



By Steve Biddulph

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

(We've been running a number of articles about contamination & avoidance. In this one, Steve explains how he first became so interested in this aspect of Quality Assurance. Ed.)

Many years ago, when I was working for a major French pharmaceutical company, a colleague there, also from the UK, had previously worked as an MRHA inspector. Before joining the French company, he had previous experience with a couple of leading British pharmaceutical companies. He became a close friend during and after his time with the company and went on to lead the European Medicines Agency Inspectorate.

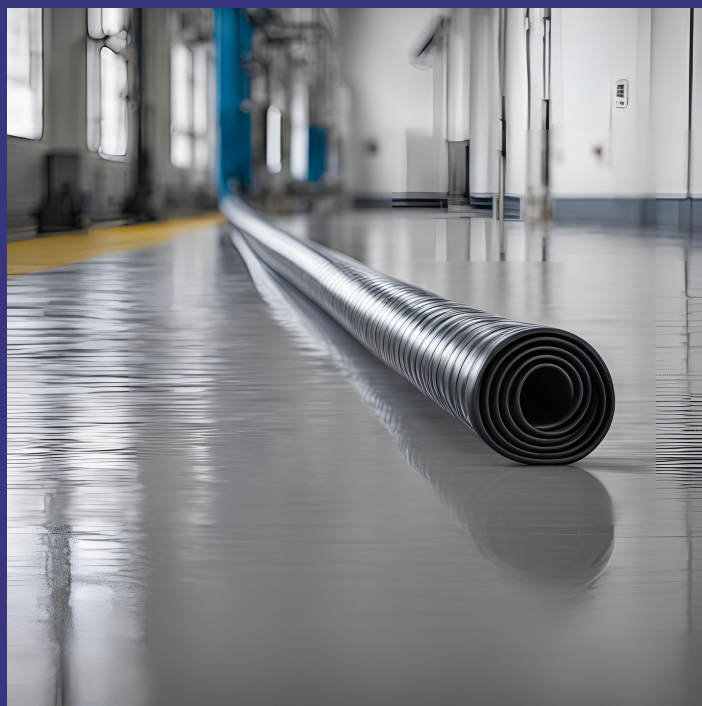
The major vector of contamination in the Life Sciences is found in the production and use of water.

When we first met, we went out into the world to audit, and assist the upgrading of manufacturing sites in the different company affiliates. At our first audit together, he told me “If you want to find out where the problems are on a site, look at the water systems, and any and all uses of water”.

How right he was !! Some of my most vivid memories major compliance issues - and regulatory crackdowns that followed, came in this period.

Any water, be it purified, potable, or WFI, will grow tremendous numbers of bacteria in a very short time. This can be seen in washed equipment and pipelines, particularly with flexible hoses if they are not allowed to dry.

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Water systems can harbour bacterial colonies as biofilm on the inner (often unseen) surfaces of system elements, and pipelines. As a qualified microbiologist, I'm aware of the need for careful design of water systems, and that definition of their performance characteristics will avoid the build-up of high levels of contamination and protect products from the contamination risk which I've found in many of my audits, even in some very expensive systems. Galenisys can certainly assist companies in designing their water systems, troubleshooting water linked issues in existing systems, or defining low-cost corrective actions to cure problems.

If we apply the right lessons, then the major common area of contamination risk in pharma facilities will be eliminated, in a compliant fashion. It is amazing to see in the world today, that the lessons from issues with water in years past are still with us. See the next issues of our newsletters for the bad examples that we have encountered over the years, & how they were dealt with.

**If you've got a water issue already, or want to avoid them, call
Galenisys**

The Project Manager's Notebook: WHAT?

WHO, WHAT, WHEN, WHERE, WHY, ON WHAT CONDITION, HOW MUCH, HOW OFTEN
by "Aubonne"

Last time the boss said **How Much** do you want? The next question is **What's** it for?

THE PROJECT SCOPE is the quality and quantity of **what** is proposed; defines the Project for which Capital is requested. Since $\text{Cost} = \text{function}(\text{Scope})$; the more precise the **project scope** then the more accurate the capital budget cost.

(Early on you can ask the boss "what do you want to see when the project is completed". If you get a simple answer, do follow up with "could you let me have a little more detail on ?")

PERSISTENCE: Management can be very equivocal when it comes to making capital commitments. It may need various budget **iterations** to get to an agreed definition, (which means more work & time). I found that **management** may be very keen to "get going" before Scope is agreed. Nevertheless, the Project Director should be determined to get management commitment to a sound Scope, before **he or she gets charged with** delivering it.

PROCESS: When the project is related to a particular development product, (group of products or particular galenical form), **it's important that the process is defined**, that is chemical route, fermentation specifics, ingredient specifications etc....

UNDERSTANDING THE PROCESS: I will illustrate the importance of understanding the process by referring to an exercise I used to give postgraduate Project Management students at University.

They were asked to calculate the **minimum lead time** for making **4** cups of **leaf** tea, from **the moment** of deciding to make it. And then to provide **cost estimates** for the equipment & materials required.

This example may seem simplistic. But the purpose was that all the students should appreciate the value of **understanding the process** in order to get an **accurate** cost & timescale.

(As a result, the leadtimes to a good cup of tea & the costs involved, were very similar for each team of students).

If the example had been building a nuclear plant?

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SCALE: Clearly project scope should include scale or quantity. Examples would usually be several parameters such as packs per annum, tonnes per year, square metres of sterile suite, personnel numbers, daytime or 24/7 etc.

CONTEXT: the capital cost is hugely dependent on **context**. So, the markets to be served, the facility location, geography, climate, & country need defining. Then the costs of complying with FDA, WHO, and other local regulations, requirements & norms can be covered. It's generally easier (but more costly) to carry out a project on a Greenfield site than within an existing facility when interruptions to services or production need careful scheduling.

DESIGN: The project scope may or may not include a design phase. If this has already occurred, then the cost estimate should be more accurate. **Do ensure** the planned Validation ("Qualification") has been matched to this design, in a Validation Master Plan.

With the project defined by the above parameters, the respective engineering disciplines can prepare their cost estimates for various modules or packages in the "WORK BREAKDOWN STRUCTURE" which I'll cover next time.



In short.....

The Editor

Trending - H5N1

- In 2023 the H5N1 virus acquired genetic changes allowing it to spread between marine mammals.
- Since the virus first emerged, around 900 human infections have been confirmed. Half were fatal, but as asymptomatic infections aren't counted, the real fatality rate is lower.
- All 5 new human cases of H5N1 in July were involved in culling infected poultry in Colorado, & appeared to have the same strain that has been spreading in dairy cows across USA.
- The US Centre for Disease Control is now testing people on farms that have had H5N1 outbreaks, for antibodies.
- Current (stockpiled) H5N1 vaccines are thought to primarily prevent severe disease rather than infection.
- However, humans are probably better prepared to face H5N1 than COVID, say experts, owing to their earlier exposure to other viruses.

TRENDING: A new more serious form of mpox virus.

This newly discovered strain of the monkey pox virus (now politely known as mpox) was first detected in the DRC & it looks like spreading into the neighbouring countries. Initial fatality rates are approximately 10% in children and 5% in adults, as it exhibits different transmission patterns and disproportionately affects youngsters. The new strain was initially identified in eastern Congo, & is **more** efficient at human to human transmission - alarming since the earlier version spread worldwide in 2022.

Don't monkey around.

Mpox exists in wild animals in several African countries and occasionally jumps to humans, for example through the consumption of "Bush meat". However, the new strain is spreading through heterosexual contact, particularly among sex workers, - about 30% of recorded cases - since the outbreak began around mid-september 2023.

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In Congo, the new strain is behaving quite differently from other strains of Inbox, with **cases also suggesting transmission through close nonsexual contact.**

Preventing this new inbox strain from becoming another global health crisis requires swift and coordinated action, and the WHO is raising an emphatic alert.

NEW - EU approves Sanofi Lung Disease Drug

Following a recommendation by the EMA) at the end of May, the EU Commission approved Dupixent to treat chronic obstructive pulmonary disease (COPD) in patients that cannot be helped by standard inhaled drugs, Sanofi announced in early July.

Sanofi & partner Regeneron won the EU approval for wider use of their Dupixent injection as an add-on maintenance treatment for adults with uncontrolled COPD, before it cleared in USA where it reviews in September. COPD (colloquially 'smoker's lungs') primarily affects cigarette smokers, is potentially deadly, and affects some 40 million people in Europe & US.

Sanofi said in April it expects the target patient population eligible for the drug to be roughly 300,000 patients in the U.S. alone. Dupixent revenues in 2023 were euros 10.7 bn, as it is already marketed for various immune system-related conditions like asthma & eczema in many countries, & is expected to bring in euros 13bn in 2024.