

NEWSLETTER



Tony Dunford Editor

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Best Wishes for Christmas & New Year to all our readers from the Galenisys Team



IT'S A WATERY WORLD!



By Steve Biddulph

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

In this article Steve wraps up the series on the continuing challenge of waterborne contamination in our industry.

Water is the environment in which the first life forms developed on earth and bacteria were amongst these first life forms. Bacteria have continued to exploit water in its different forms ever since. Now they can be found in fresh and salty water, very cold water, the water of hot springs, and by the lava eruptions on the ocean floor.



Many diseases were and still are, spread by water - cholera, typhoid fever, and bacillary dysentery. The pathogenic *Escherichia coli* strains and emerging pathogens can be found today in potable water despite treatment with chlorine or fluorine. Why is this?

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Agriculture puts fertilisers into the soil, animal waste is spread on fields, and all of this will drain into the water table. Potable water companies take water from the water table, treat it, add chlorine, usually and pump it out to the local population as potable water.

Potable water has a low bioburden and all countries in the world have stringent specifications for the bacterial contamination potable water. Of course, despite treatment and testing of the water, there is still a small bacterial bioburden present and, at times, very low levels of pathogenic bacteria.

In the Life Science Industries, potable water is probably the most employed starting material. Given that this water will carry a bacterial bioburden, companies must ensure that this is removed, if possible and in all cases that it is not allowed to proliferate. In our series of recent articles on water use and treatment, we have emphasised that companies must have well designed, carefully used, and regularly maintained water systems for the production of Purified Water and Water for Injection. Systems like these will ensure that water does not become a vector for allowing bacteria to enter into production processes and to present risks to products and patients.

During my career, I have seen many water systems that were not well designed, to say the least.

Here's a summary of the various causes of high levels of water contamination, that I have discovered:

- Bacterial retaining filters used in water distribution systems
- "Rusty" 316L stainless steel distribution pipework
- A purified water system that was so designed that river water by-passed it completely and went straight into the manufacturing process
- A long series of ultrafilters to remove pyrogens without treating the primary cause of pyrogen formation
- Deionisation resins that were allowed to be used for several weeks without regeneration
- Water system drains that were piped directly into the local sewage system

Each of the above incidences caused massive contamination and needed considerable resources to try to find out what had gone wrong and how to fix it. The companies involved had never considered that defective built-in design features were the cause.

If you are having issues with the bacterial or pyrogenic contamination of water, contact Galenisys and we will find the cause(s) and tell you how to correct them in a sustainable fashion.



Drug Delivery Dream On.

The Editor

In the 1960s, Fisons, a British company, invented a new medical device for dispersing a dry drug powder by inhalation into asthmatic lungs. A few years later, while I was working in Japan, a pharmaceutical executive there told me that this novel method of administration had prompted them to look at all possible ways of delivering drugs including, for example, impregnating socks!



I was reminded of this recently by a new paper published in Nature where researchers revealed that they were using tiny spring-loaded devices capable of releasing high velocity jets of drugs into digestive tissues of pigs, consistently to a sufficient depth at sites in the oesophagus, stomach or intestines. One of the minute devices resembles a moon lander, the other a cylinder.

What's the rationale for doing this, you may well ask. It goes something like this. Novo Nordisk is Europe's largest company by market capitalization. It's built up its business based on treating patients reliant on insulin injections sometimes several times a day. Latterly Novo has the blockbuster semaglutide products (Ozempic for diabetes, & Wegovy for weight loss) on the market.

However, many people have a serious aversion to needles. This leads to one in six American adults skipping vaccinations for example or failing to maintain their insulin regime. So, Novo and researchers from MIT, the Women's Hospital in Boston & the Royal Institute of Technology in Stockholm; collaborated on the above mentioned devices and others.

Like the impregnated socks, only the future will tell if the ideas catch on

The Project Manager's Notebook.

In this, the 5th article in our series, the theme is WHEN?

By Aubonne

If you're a project Manager, you will invariably be asked “when will it be finished?”

A good definition of a project is that it is “a non-routine activity with a beginning and an end, undertaken within defined cost and time constraints, to achieve a stated business or organisation objective”.

This definition mentions the 3 key project parameters - Cost, Time, & Scope - between which there may be necessary trade-offs during the project.

“Time is Money” This old adage is nowhere truer than in project management. A drilling rig on location, and nowadays the huge vessels (there’s a limited number) hired to erect offshore wind farms, are clear examples. Towards the end of a project, the cry of “get that crane and scaffolding off hire” may well be heard.

The Project Duration will normally have been determined before Project Approval by reference to completed projects of a similar nature, and advice from within & outside the organisation. Once it’s approved more detailed project planning will need to be undertaken, & refreshed during implementation.



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Critical path analysis.

So how do we plan in detail & reduce the overall project lead time? Enter critical path analysis. Here are its essential elements:

- 1.Experienced project planners knowledgeable about the processes, plus a software package, (there's a big choice, all are only as good as quality of the input).
- 2.Brainstorming by the Team in detail to list (& number) every activity.
- 3.Estimation of the duration of each activity
- 4.Establishment of the activities dependencies ie. identifying the precedence between activities. Eg ordering XYZ before installing XYZ.
- 5.Determining which can be simultaneously actioned and which are necessarily sequential.
- 6.With the above data entered, the software can show overall durations, "latest event time", "earliest event time", "activity float", and vitally the critical path which is the sum of the longest chain of sequential activities.
- 7.In large projects the planning network can be bafflingly complex, so presentation of it needs to be as clear as possible, and distribution of updates rapid.
- 8.Once the chains of sequential activities have been identified, it will be possible to work on shortening them by trade-offs.

Cost, Time and Scope.

A couple of examples will show the benefit of challenging the projects established view on cost, time and scope:

- 1.On a pharma site, the long lead-time standby generators & freeze dryers had to be ordered promptly since they were destined for the new building basement, and should therefore arrive before the entire ground floor concrete slab was cast in position ("the dependant activity"). This constraint was successfully challenged by accepting the extra cost of leaving a cut out in the concrete slab filled in after these long lead time equipment items were delivered, thus significantly advancing the completion date. (In general, it's vital to get the long lead time equipment items ordered asap in any case).
- 2.We had one city centre project where "Site Establishment" was an early "work breakdown structure" package.. This included provision of security fencing, portacabins, access routes, and four cranes. The contractor that was chosen for this was successful because he was able to show that he could cover the whole site in plan view with three cranes only.

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In the life sciences industry, there are however some constraints on the extent to which the project scope can be challenged and modified. This is because earlier R&D and clinical work will have defined much of the process, it's ingredients, & quality parameters. These will be, or will already have been, established in regulatory documents.

Time is the Essence For certain projects, eg vaccine development “time will be of the essence”. In this case, the project plans should assume success for all preceding activities. This will mean ordering equipment, product, and building facilities, **“at (financial) risk”** & the project manager should ensure all stakeholders are formally aware. In very competitive situations for patented products getting to market, the time is of the essence approach may well be justified.

Aubonne

The Galenisys Team have wide experience in varied Pharma Projects and will be happy to assist you resourcing yours.



Christmas: Be JollyCareful!

The Editor

After feeling a “bit rough” for a few days last week, I had a short stroll during which I met my neighbour taking his dog for its daily walk. “How are you now, which one was it?” he said, after I mentioned I’d had flu. He wondered if it was the norovirus.

Oh, yes, the Norovirus. The first recorded outbreak of this virus was some 40 years ago in the **Bronson Norwalk Elementary School** in Ohio, USA. Since it first caused vomiting and diarrhoea amongst the youngsters there, the Norwalk virus (now “Norovirus”) is now “credited” with infecting some 700 million people worldwide per annum (WHO). Extraordinary propagation! Not surprising, therefore, that it's become a target for eradication.

Scientists in the UK have shown how particularly infectious it is. Since only 20 or so virus particles are needed to infect a person, just one droplet of vomit or one gram of faeces is capable of infecting > 100,000 people.

Norovirus could be considered “the perfect pathogen” because it is highly infectious, spreads prolifically, can survive for weeks, and does not tend to be lethal to its hosts. For most of us, the infection is very unpleasant but short lived. But in the case of babies, young children, the elderly, and people with compromised immune systems the situation is very different. The WHO estimate is of around 200,000 deaths p.a. amongst these groups, including from contaminated water.

This virus is, however, only one of many viruses from three different families causing gastroenteritis or “stomach flu”. Like the mafia, none of the families do us any good. All use the same means of infection: “the faecal- oral route”. Infection is spread from contaminated surfaces and unwashed hands.

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Wash your hands well !



The infection route is just us humans

There're no parasites, carriers, or side effects from medication to blame; just humans not being careful enough. Christmas & New Year is boom time for the Norovirus & the others. We're in enclosed spaces more because of cold weather, and there's lots of communal catering, & close contact.

Vaccines have been developed for one of these gastroenteritis viruses, the Rotavirus. The WHO first recommended using these 20 years ago and they are currently used in more than 100 countries.

Moderna now have a mRNA vaccine targeting various strains of Norovirus, in a large global late-stage clinical trial, which started in the summer of 2024. But although research is ongoing to tackle other strains of gastroenteritis viruses for many, there are no vaccines for these yet.



In the meantime, BE JOLLY CAREFUL, & ENJOY CHRISTMAS

The Editor

