COVID-19 and Chemical Engineers

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What is a Major Hazard?

It is not clear what the definition of a major hazard is within chemical engineers' sphere of influence. Certainly, those covered by the Seveso III Directive (COMAH in the UK) are major hazards relevant to chemical engineers. The Bhopal disaster killed over 3,000 and injured over 500,000. However, in May 2021 WHO estimated that the death toll from COVID-19 was over 3 million and the estimated death toll from Malaria in 2019 was 409,000. Clearly these diseases are Major (Bio) Hazards but are they relevant to chemical engineers?

Chemical Engineers and Major Diseases

Major diseases and pandemics are not (bio)chemical plants, but they are biochemical systems that are recognisable to chemical engineers and there are many ways that chemical engineers can contribute to reducing the death toll. The most obvious way is by their contribution to the development and manufacture of pharmaceutical products such as vaccines, monoclonal antibodies and small molecule therapeutics such as steroids. However, there are many other ways that chemical engineers can contribute.

The engineering associated with biohazards is very similar to that relevant to the manufacture of high potency pharmaceutical products and processing of nuclear materials. If many of the relevant technologies were adopted by the medical profession the risks to medical personnel could be significantly reduced.

There are also other ways that chemical engineers can assist as discovered by the IChemE/ISPE UK COVID-19 Response Team.

IChemE/ISPE UK COVID-19 Response Team

This is a team of volunteer chemical engineers and other engineering professionals that formed in March 2020 to provide expertise in any way that could help. The team has looked are a number of aspects, including

1. Containment versus PPE
2. Layers of protection – Swiss cheese model
3. Risk analysis and data analysis – Chemical Engineers use correlations which scientist tend not to.
4. Manufacturing supply chain break down.
5. Training requirements
6. Tech transfer project as part of the degree course
7. Talking to new manufactures such as VMIC.
8. Increasing oxygen distribution in hospitals
9. Explaining the issues involved in replicating vaccine production from one location to another

This presentation will discuss the ways that response team helped to reduce the impact of the COVID pandemic and the lessons that have been learnt from this project and draws the conclusion that pandemics are Major Hazards that fall within scope of chemical engineering and chemical engineers. Also, presented are recommendations for further action.

Section 1 - What is a Major Hazard? COVID, COSHH and Process Safety.

Traditional Definition of a Major Hazard

The IChemE's billing for this conference opens with the following statement which give us some idea of the traditional definition of Major Hazards from a chemical engineer's perspective.

> *"Hazards is widely recognised as one of the world's leading process safety conferences. First staged in 1960, Hazards is an industry-focused event, providing a platform for sharing good practice, current thinking and lessons learned in process safety, as well as valuable networking opportunities."*

Based on the above, the traditional definition of major hazards is connected to process safety, but the COVID-19 pandemic has shown us that this definition is too narrow, and the definition should be far broader.

Major Hazards and Seveso III

Certainly, those hazards covered by the Seveso III Directive (COMAH in the UK), for example are major hazards relevant to chemical engineers. An example of a major hazard that had a significant impact on the view of process safety is the 1984 incident at the Union Carbide pesticide plant in Bhopal, India, which released at least 30 tons of a highly toxic gas called methyl isocyanate and killed more than 3,000 (possibly as high as 15,000 people) and injured over 500,000 people. This was clearly a major hazard relevant to chemical engineers.

But what about major diseases?

As we discuss later on, diseases kill millions of people per annum, and arguably all of these are preventable deaths just as the deaths at Bhopal were preventable.

COVID-19 with 4.5 m and rising is currently the number 3 largest killer of all diseases but even diseases such as flu and pneumonia combined have killed more than 60,000 people in a year just in the UK e.g., 1976 and 1999.

(See https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsduetocoronaviruscovid19comparedwithdeathsfrominfluenzaandpneumoniaenglandandwales/deathsoccurringbetween1januaryand31august2020)

Clearly major diseases cause considerably more deaths than industrial accidents and deserve the full attention of chemical engineers. They should be classified as major hazards of relevance to chemical engineers

Medical professional not chemical engineers

It could be argued that major diseases are the realm of medical professions and not chemical engineers. It true that they are the front line of the fight against disease but without the products and services provided by chemical engineers they simply could not function. Without the products and services provided by chemical engineers there would be no hospitals, no medicines, no medical devices and no surgical instruments etc.

Chemical engineers have always have a major role to play in fighting disease the COVID-19 pandemic has brought this to prominence.

COVID-19 and COSHH

COVID-19 is completely relevant to a number of areas that are very familiar to most chemical engineers.

The phrase “biological agent” is defined by reference to regulation 2 of the Control of Substances Hazardous to Health Regulations 2002 (COSHH) and includes any micro-organism which may cause infection. This definition is broad enough to include Covid- 19, unless one takes the view that viruses are not micro-organisms, but this pedantic view does nothing to reduce the hazard’s capability that the legislation is trying to counteract.

The COSHH regulations at least two area relevant to diseases such as COVID-19

1. Under COSHH employers owe a duty of care to their employees and third parties.
2. Employer’s duties include carrying out a risk assessment and adequately controlling exposure to COVID-19.

Both of the above requirements have the potential to make significant impacts in the workplace as it becomes clearer to employers the duties that they may have. The legal precedence created by the duty of care relating to secondary smoking could have a major impact in the future and the engineering protection measures required could fall within the sphere of chemical engineering competence.

COVID-19 and RIDDOR

The UK Health and Safety Executive has recognized that COVID-19 falls within the scope of Reporting of Injuries, Diseases and Dangerous Occurrences Regulations 2013 (RIDDOR), their guidance states (https://www.hse.gov.uk/coronavirus/riddor/index.htm)

You should only make a report under RIDDOR when one of the following circumstances applies:

1. an accident or incident at work has, or could have, led to the release or escape of coronavirus (SARS-CoV-2). This must be reported as a dangerous occurrence
2. a person at work (a worker) has been diagnosed as having COVID-19 attributed to an occupational exposure to coronavirus. This must be reported as a case of disease
3. a worker dies as a result of occupational exposure to coronavirus. This must be reported as a work-related death due to exposure to a biological agent.

This guidance quite narrowly worded so that it appears that only a release of Covid 19 from work to a worker is included. Transmission between work colleagues does not appear to be covered which would be more relevant to chemical engineers. However, we can see that to some extent COVID-19 falls into an area of process safety familiar to chemical engineers. How relevant RIDDOR is to COVID-19 will become clearer in the future.

COVID-19 and Process Safety

There are many aspects of process safety that are relevant to protecting employees from COVID-19 for example

1. COSHH Risk assessments

2. The Use of LOPA - as discussed later. See also "LOPA versus COVID - Return to Sustainable Living" By Ali Mokhber, Shivani Aggarwal, Pablo García-Triñanes, which is also included in HAZARDS 31
3. Containment, barrier technology and other engineering protection measures such as good ventilation
4. The correct use of PPE.

These are just a few examples and it clear from the activities of the IChemE/ISPE UK COVID-19 Response Team that there many other areas of process safety related to COVID-19

Section 2 - Chemical Engineers and Major Diseases

As discussed above it is clear that major diseases kill far more people than industrial accidents, they are covered by regulations relevant to chemical engineers and that many aspects of process safety familiar to chemical engineers. However, it could be considered that it is only of relevance to those chemical engineers working in the pharmaceutical industry and other areas of life science. However, the IChemE/ISPE UK COVID-19 Response Team volunteer project has illustrated that this is not true. Christopher Ross, Project Coordinator, for this project has written the third section of the paper and he has a petrochemical background, with very little involvement with pharma, biochemical or medical engineering till 2020.

What Chris has demonstrated is that his Process Support, Process Safety, Project, Management of Change, Systems Approach background all stood him in good stead and has been transferable to the requirements of the volunteer project.

Top 8 causes of death in 2019

To put the impact of diseases in context here are the top eight causes of death in 2109, these account for 51% of all deaths (Source: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death)

1. Ischaemic heart disease 9 m
2. Stroke 6.1 m
3. Chronic obstructive pulmonary disease 3.3 m
4. Lower respiratory infections 2.7 m
5. Neonatal conditions 2.0 m
6. Trachea, bronchus and lung cancer 1.9 m
7. Dementias 1.8 m
8. Diarrhoeal diseases 1.6 m

There have been 4.55 million deaths from COVID-19 so it probably stands as a number 3 on this list.

Involvement from Chemical Engineers

Chemical engineers are currently active in the following areas.

Industry Sections

1. Pharmaceuticals and biopharmaceuticals including the provision of pharmaceutical grade excipients and relevant consumables.
2. Medical devices.
3. Medical gases.
4. Food and nutraceuticals
5. Water purification, effluent treatment and sanitation

Application of skills

1. Pollution minimisation
2. Cleaning, sanitisation and sterilisation products and services
3. Understanding of risk
4. Safety systems
5. COSHH – containment, isolation, barrier technology, HVAC, PPE including face mask, hard hats.

For those of us who have worked in these areas for many years it is clear that the basic chemical engineer science that is taught to all chemical engineers is relevant to reducing the deaths from disease and that chemical engineers should become far more active in the professional space.

Practical Examples

COVID-19 has shown us many practical ways that chemical engineers can help to reduce the impact of major diseases.

Section 3 shows the progress to date achieved by the IChemE/ISPE COVID-19 Response Team. A project team within IChemE's Learned Society space.

Section 3 IChemE/ISPE COVID Response Team – Progress to date

Volunteer Response

The team was built up from the following

1. IChemE and International Society of Pharmaceutical Engineering UK Affiliate (ISPE UK)
2. Volunteers from membership-supported by staff
3. Other professionals including Architects, Clean Room Designers, Business Development specialist, Petrochemical engineers, Process Safety experts etc.
4. International- UK, Sri Lanka, ROI, Australia, Malaysia
5. IChemE SIGs, Pharma Bioengineering also Particle Technology

The COVID pandemic indicated that viral spread and impact is clearly a biochemical system, generating serious hazards and that there is room for other disciplines, beyond the immediate medical problem.

There were about 70 volunteers at the peak, many had been furloughed but have now recalled to work including one who pulled out to work on the Oxford vaccine and another to the Vaccine Task force.

Provision of therapeutics and vaccines are a big part of the defense against COVID-19, but not the only part. Understanding how the virus works as a biochemical system, how it spreads, the chance of infection encounter, the risk of death all relevant. In particular, the virus is not a static hazard-a vaccine or therapeutic can exert evolutionary pressure such that new variants of concern emerge

Project Approach

As IChemE/ISPE UK volunteers it became clear that:

1. We can define the various problems relating to Covid
2. We can identify possible options to solve and appraise them
3. We are not indemnified by IChemE or ISPE UK to design and implement.
4. Our other role is knowledge sharing and making introductions

An important lesson learnt with that the implementation of projects requires cooperation with partners such as industrial companies or universities.

The project approach has been to define the "Problem" or "Opportunity", then look at possible options which might be deployed. Selection of an option is case specific and may be beyond what we as a professional institution can do. Execution and operation were certainly beyond the team's remit.

Initial Emergency Phase

A number of activities were carried out early in the pandemic including:

1. Oxygen distribution in hospitals became a problem:
    a. due to increased demand with more patients needing oxygen, (standard hospital design is based on a diversity factor which means oxygen cannot be provided to each bed simultaneously) and
    b. higher oxygen demand resulting from the use of CPAPS masks (CPAPS masks tend to spill more oxygen but better medical outcome than ventilators. Less of a big deal to fit, no anaesthetic needed, no insert to the lungs as a ventilator.
2. Shared idea to enhance use of SS weldneck for oxygen distribution to enhance reticulation. This was a solution to the problem of qualified brazers for the brazed copper fitting normally used for medical oxygen.
3. PPE materials - one of our members sourced 0.1mm polycarbonate for visors

Barrier Technology

The team identified that barrier technology can be a better approach than the widespread use of PPE.

1. Cooperation with an entrepreneur using Perspex screen glove box technology
    a. Hierarchy of controls
    b. Cannot knowingly remove the virus
    c. Engineering solution next best
    d. Better than PPE
2. Piloted in GP surgery in ROI

This was an example of collaboration with others outside IChemE/ISPE UK, the practical solution had to be implemented by a third party. As a quid pro quo for the team, the third party did a webinar on protection against Covid using barrier technology.

PPE Reuse VHP Sterilisation

The response team created a break-out project which again was based on collaboration with third parties. The principal aims were:

1. Addresses shortages of PPE
2. Address the potential for better PPE, personalised to user
3. Reduce waste
4. Reduce cost

Although VHP sterilisation of PPE had been already adopted in USA for emergency use the UK NHS did not adopt the technology. The part of the project demonstrated that the NHS is an extremely difficult body / series of bodies to deal with. A document which claimed to be their management of change procedure was focused on gaining buy in from all employees involved and not particularly technical and certainly not helpful from the team's perspective.

Small Molecule Issues

The IChemE/ISPE UK COVID-19 Response Team carried out a detailed review of small molecule therapeutics that could help with the treatment of COVID-19. The following points arose.

1. Small molecules taken by ingestion, synthetic
2. Cost reduction tends to increase supply chain complexity and decrease security
3. Shortages of everyday drugs due to increased demands, shipping costs increase
4. Highly regulated, difficult to increase production
5. Skill shortages-education & training
6. UKRI UK Research & Innovation and NIHR National Institute for Health Research UKRI/NIHR sponsored Oxford run RECOVERY trial-to identify existing drugs with Covid potential
7. Small molecule drugs are by far the most common. Generally taken by mouth and ingested via the gut-small enough to digest. Synthetic drugs.
8. Shipping includes air freight-significant high value freight is carried as belly freight in passenger airliners
9. Consistency of drug Active ingredient and finished product is key, so it matches the licensed product.
10. Dexamethasone was a big success. Ruling other treatments out was also useful

Vaccine Issues

Another one of the team's streams was to consider the issues relating to vaccine manufacture

1. Extremely sensitive to process conditions, ingredients etc.
2. Replication of the Process difficult
3. Quote-about 10,000 items of data are required in the production of a vaccine-all have to be satisfied
4. Includes supply chain, fill finish, distribution, often cold chain
5. Various vaccine platforms-killed virus, adenovirus part of the Covid virus is spliced into a carrier virus, mRNA virus strands.
6. The killed virus platform requires live virus first, and will have to be handled in a facility rated to BSL- 3 or 4 (4 is the highest level of Bio Security, about 50 of these types of facilities in the world)
7. Cold chain for Pfizer vaccine -70C. Use within 6 hrs once warmed to ambient-needs to be deployed at a scale of 1200 doses (pack size) in 6 hrs

Technical Transfer Project

A separate Learned Society project was set up to look and the education and training gap relation to Technology Transfer. This project has moved to the point where IChemE is currently calling for volunteers to become involved in running a Technology Transfer education and training project

Technology transfer required advanced knowledge and skills to assess items when they cannot be fully replicated in the new location. The focus will be generally on biochemical engineering but not completely so.

RAEng Collaboration

Since the RAEng is effectively the gateway to HM Government for all engineering-all disciplines, the team sort to develop its contacts with RAEng and engaged in the following activities

1. Sir Patrick Valance "request"-Two of our volunteers contributed to the interim report "Infection Resilient Environments"
2. Ventilation identified as a major topic with the Chartered Institute of Building Services Engineers CIBSE, plus IMechE
3. Offer of LOPA tool for further work-based infection encounter as the initiating event. Infection encounter based on ONS sampling which gives an estimate of the total cases per 100k, and COVID map, giving total confirmed cases by UTLA Upper Tier Local Authority as cases per 100k. Using the tool indicated that usually the estimate of total cases exceeds the confirmed cases.
4. Also consider Association of Local Authority Medical Advisers (ALAMA) covering risk of death if infected. ALAMA have a tool to generate risk of death from COVID based on sex, race, age, BMI, health status

An important lesson learnt by the team was that collaboration with RAEng is an important way to get access to HM Government in the UK. Identifying ways to improve access to governments in other nations would be a useful future project.

International

The IChemE/ISPE UK COVID-19 Response has been an international effort. Areas covered include

1. A team in Sri Lanka, developed a mobile ICU
   a. Converted container with 3 beds, each with CPAPS ventilators and patient monitors
   b. Airlock for entry/exit, monitoring station for nursing staff
   c. Air purification unit, containing UV-C, HEPA filters

Pandemic Preparedness

The team also spent some time looking at pandemic preparedness and considered the following points.

1. Bio Security policy to monitor for pandemic outbreaks of disease. Loosely based on the UK and international response to Covid 19.
2. Standing organisation to carry out a watching brief for future pandemics, escalating to implementation of various projects to characterise and deal with the threat.
3. Creation and maintenance of an ability to develop, and scale up production of new vaccines and therapeutics, and to transfer to other sites.
4. Production and supply chain security against hostile and disruptive interference.
5. Policies are required to improve personal and public health, with regard to:
   a. Fitness, exercise, and nutrition.
   b. Understanding of hygiene, especially the importance and provision of clean water supplies and sewage treatment
   c. Understanding of viral and bacterial transmission, and basic steps to prevent this.
   d. Health of individuals key to their Covid outcome shown in ALAMA data.
   e. Good nutrition underpinning the immune systems
6. Basic understanding of the use (& misuse) of anti- biotics, vaccines etc.
7. Ability to track viral evolution in real time.
8. Development of testing and ensuring results are understood.
9. Overall, creation of a functioning series of organisations, often covering other disciplines that can co-ordinate pandemic preparedness.

Conclusions

1. Pandemics (like COVID-19) are clearly major hazards to human life and health. Typically, these present in the form of open, complex biochemical systems. Analysing and understanding such systems is the province of biochemical engineering, and in the case of disease spread, applying this knowledge to minimising the spread.
2. Understanding the risks involved with a view to minimisation appears to fit within the province of the Process Safety Engineers, albeit in a more open, less controlled system (i.e., the public domain) than is usual.
3. Access to authorities is key in order to allow Chemical Engineers to offer support. In the UK, the most appropriate route is via the RAEng who are the main conduit for HM Government for all engineering related queries.
4. Pandemics tend to stress supply chains due to world-wide demand for particular types of drugs, therapeutics, intermediates, vials, syringes, ancillaries, freight transport and PPE. Cost reduction measures tend to drive the complexity and security of supply chains upwards. Provision of medicines and PPE should be regarded as a security and sustainability issue, and not just a cost issue.
5. In the public domain there is a significant lack of understanding of the difficulties of vaccine manufacture, including supply and distribution chains, and replication of accredited manufacturing facilities from lab to production facility and from one production facility to another.
6. Pandemics are costly in terms of burden on health services and impact on the economy due to lockdowns. The CGD (Centre for Global Development) estimates that for every $ spent on Pandemic Preparedness there are potential savings of $1700 on health, $1100 on GDP, plus deaths averted of between 50-120 per 100k. Understanding the nature of Pandemics as biochemical systems and creating and managing organising of other disciplines and specialists is clearly within the remit of chemical engineering.
7. Public understanding of such things as virus spread and viral load, the difference between PCR and LFT tests, has not been good. Plus the potential to misuse anti biotics such that anti biotic resistant bacteria emerge is constantly present.

Recommendations

1. Chemical engineer should work more closely with RAEng and going a better understanding of the conduits to HM Government to allow them to be more effective in any future pandemic or major public health incident.

2. The weaknesses in the medicines supply chain highlighted by the pandemic should be included in IChemE's sustainability considerations.
3. Further work should be done on the use of personalised high-quality PPE for health professionals, using VHP (or similar) to sterilise for reuse.
4. A Technology Transfer project to assess the need for specialised advanced training to assess how to replicate manufacturing in another site where not all conditions might be exactly the same should be started. (This is now in hand.)
5. Understanding the nature of Pandemics as biochemical systems and creating and managing organising of other disciplines and specialists should be within the remit of chemical engineering.
6. Providing concise educational material on these subjects –akin to writing operating instructions is within the province of the chemical engineer, and within the education remit of IChemE and therefore consideration should be given to this within IChemE educational activities.