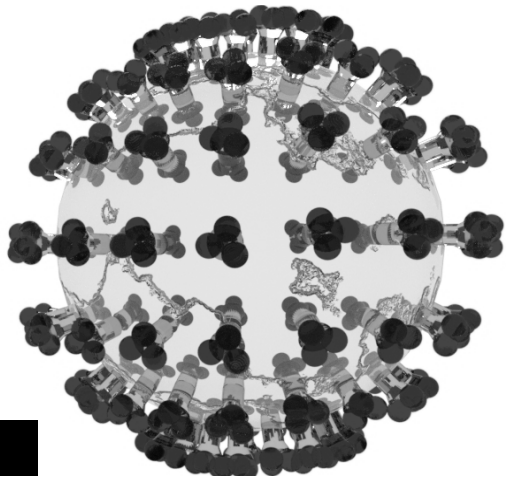
PD2M Newsletter

August 2020



A quarterly update for Pharmaceutical Discovery, Development and Manufacturing Forum Members

Note from the Editor

The pharmaceutical industry has changed over the last 20 years. Today, traditional small molecules and biologics coexist with novel therapeutic modalities that can offer extremely valuable treatments for common and rare diseases. The molecular complexity of drug substances and the presentation of drug products has also significantly changed, and that change was only possible by the adoption of advanced processing platforms. Efficiency, agility, and flexibility were the key aspects that enabled progress.

Ultra-rapid discovery, development, and manufacturing is essential to develop treatments and vaccines for biological threats such as COVID-19. Innovations that were deemed optional just a few years ago, are today a 'No-brainer'. A global pandemic put light into pharma strengths but also highlighted gaps that could prevent pharma from delivering an ultra-rapid response.

In this issue of the PD2M Newsletter, we interviewed many Andrews: Dr. Andrew Adams (VP New Therapeutic Modalities @ Eli Lilly), Andrew Rutter (Director, RutterDesign) and Andrew Livingston (Professor of Chemical Engineering @ Imperial College London & Interim Director, Rosalind Franklin Institute UK). We asked them the same questions about the academic/industry response and preparedness to a global pandemic, strengths, major technical advances, and gaps.

Learn why PD2M forum is vital in this discussion.

In This Issue

Carla Luciani

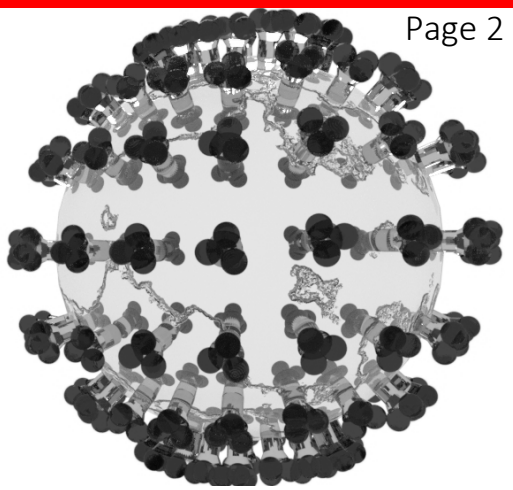
Pharmaceutical Discovery, Development and Manufacturing Forum, Newsletter Chair

RNA-Tx, Lilly Research Laboratories, Eli Lilly

Andrew Adams

VP New Therapeutic Modalities

Eli Lilly



Pharma's rapid and unified response to develop COVID-19 treatments and vaccines has emphasized the depth of the industry, academic and government scientific and technological strengths. Let's look closer at the word "unified". *Could you please comment on any unprecedented collaboration that you think could be key to win the race against this global pandemic?*

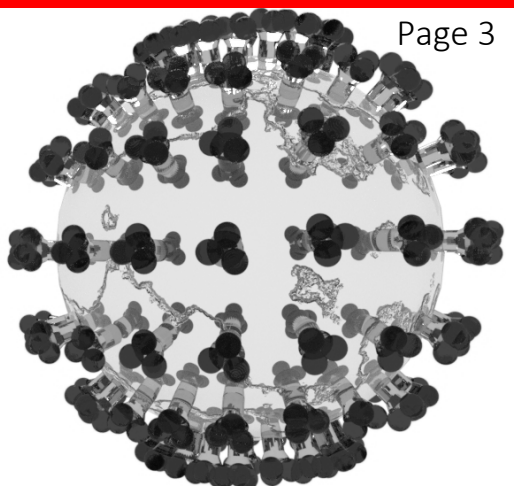
Success against the virus in the types of compressed timeframes we need has required collaboration at a scale our industry seldom sees. Specifically, using Lilly as an example, we have worked on our own COVID-19 programs with biotechnology companies, academic collaborators and specialist CROs to drive our programs forward with speed. We have also been part of industry level discussions which are aimed at coordinating the response to the pandemic. These efforts are critical to allow us to best leverage the strengths of individual organizations, labs and even individual experts.
As we and others move forward to hopefully deliver effective therapies, even further collaborative efforts will be needed to deliver at the kind of scale the world needs.

"Success against the virus has required collaboration at a scale our industry seldom sees"

In your field, what are the major discovery, development, or manufacturing advances that you think will be vital for a rapid response?

Neutralizing antibodies have been used successfully previously to treat infections like Ebola, however, nothing has been attempted at the scale that may be required for a pandemic like the current COVID-19 crisis. In the case of RNA delivered vaccines, such as those pursued by companies like BioNTech and Moderna, the COVID-19 pandemic has substantially accelerated the timeline for clinical evaluation of this new modality at scale. As my passion is the application of novel modalities to areas of high unmet need, I am excited to see these new types of medicine come to the fore at such a critical juncture.

Andrew Adams



As you see it, what are the major technological gaps that prevents us to act faster?

Historically, we have not moved at the speed needed to rapidly combat emerging threats like COVID, and development cycles for new drugs are not particularly amenable to the rapid response required in a pandemic. Thus, to tackle these kinds of issues in the future we will need a deeper focus on both the technological aspects of pandemic response which can be deployed quickly.

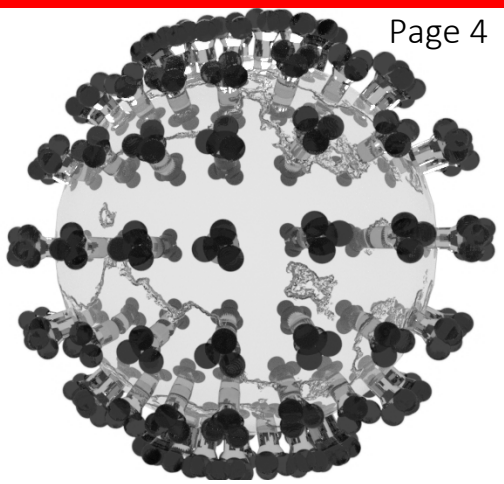
At the top of my list would be the development and maintenance of robust platforms for the identification and characterization of antibody therapeutics. Indeed, as part of our work with AbCellera on COVID-19, we were able to go from sample to clinical trial in less than three months. Additionally, if we look at the vaccine work done at places like Oxford, there is the potential to have these types of platform waiting in the wings for the next issue to arise. It is important to point out, that for these technologies to be applied, we need global surveillance for emerging pathogens to be robust, to give us as much time as possible to prepare and deploy our tools.

"We must elevate our work in terms of surveillance of pandemic threats"

When the dust settles, industry, academia, and regulatory agencies will be revisiting their approaches to pandemic preparedness. In your opinion, what approaches work well and what do you think could be revisited?

We can and we must elevate our work in terms of surveillance of pandemic threats. The key to an effective response is by providing as much time as possible to develop and subsequently deploy effective countermeasures, thus anything we can do to expand this early warning buys us time to develop more effective therapies. As an industry, we need to continue to invest in this area, especially in the intervening years when these investments may seem less attractive to ensure that when the need arises we can rise to meet the challenge with speed. Despite the dire situation, COVID-19 has shown the best of what our industry is capable of, when we choose a single priority and pursue it we can make a difference for patients around the world.

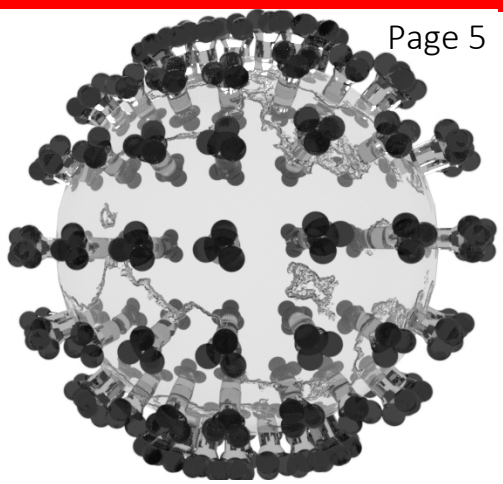
Andrew Adams



The Pharmaceutical Discovery, Development and Manufacturing Forum (PD2M) promotes the interchange of ideas, concepts, know-how, and experiences within and outside of the American Institute of Chemical Engineers (AIChE). *What would be your message to the PD2M Newsletter readers? How could this group help?*

Eventually, the COVID-19 pandemic will pass and life will return to a new normal, and as individuals we have a great capacity to forget. I would encourage the PD2M readership to consider application of their skills to science that could potentially advance our capabilities to combat threats like COVID in the future. Our tools to combat COVID today are the result of decades of iterative work in diverse disciplines from antibodies, small molecules to oligonucleotides, and these fields will continue to be part of our toolkit in the future.

"Our tools to combat COVID today are the result of decades of iterative work in diverse disciplines"



Andrew Rutter

Director, RutterDesign

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I believe agree with the starting point, that this crisis shows the scientific strength is there in the discovery side of making a medicine. My personal view is looking forward, the next phase will stretch the supply infrastructure, because of a business model driving utilization (i.e., not keeping factories idle) has shaped factories, not pandemic responsiveness.

The consequence could be capacity may need to be repurposed for COVID vaccine and adjuvant manufacture, testing the supply of existing day-to-day vaccines. Alternatively, supply may have to be rationed and phased as new capacity is slow to build. This is on top of a regulatory and clinical framework that is fragmented. Winning this race will need a similar mobilization on the supply side as the discovery phase to succeed.

"Winning this race will need a similar mobilization on the supply side as the discovery phase to succeed"

In your field, what are the major discovery, development, or manufacturing advances that you think will be vital for a rapid response?

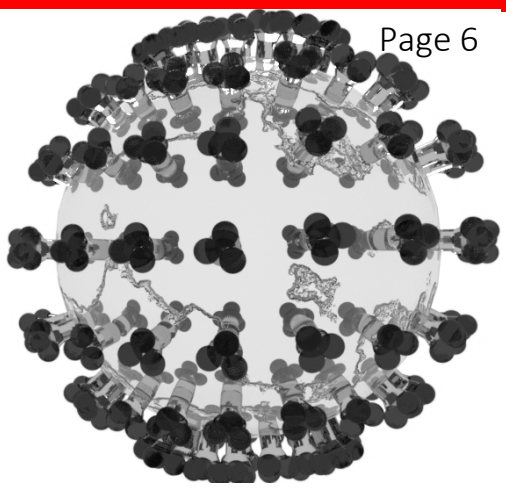
(i) *Manufacturing Capacity that can be added to demand quickly, with precision to meet regulatory expectations.*

(ii) *Capacity that is resilient – this means the ability to supply locally or regionally.*

(iii) *I think this comes from a combination of advances; Intensification technologies like catalysis, synthetic biochemistry and continuous manufacture, modularization/standardization of manufacturing platform (both unit operations and factories) and digitalization (twins and the link to the design process)*

(iv) *Rethinking the business model.*

Andrew Rutter



As you see it, what are the major technological gaps that prevents us to act faster?

Most are not technological – most are around workflow and people. For example, there has to be a collaboration to standardize modular plant. The area most ripe for technology is the integration of modelling to augment design and operation. An intensified process brings greater design challenges, and if speed is of the essence, these need to be brought to the forefront to integrate chemistry, biology and engineering. I also think these disciplines need to be taught differently to reflect this.

When the dust settles, industry, academia, and regulatory agencies will be revisiting their approaches to pandemic preparedness. *In your opinion, what approaches work well and what do you think could be revisited?*

I think I have already touched on this. Going further, what I would like is we openly think about the world that we are in; one where climate change/emergency, greater political instability are present, and answer the question: What would be the best partnership between companies and Government, States and Society to sustainably bring medicines to those who need them in this emerging world?

"the world needs engineers and scientists to step up, to change, to collaborate, and move medicine development manufacture forward.""

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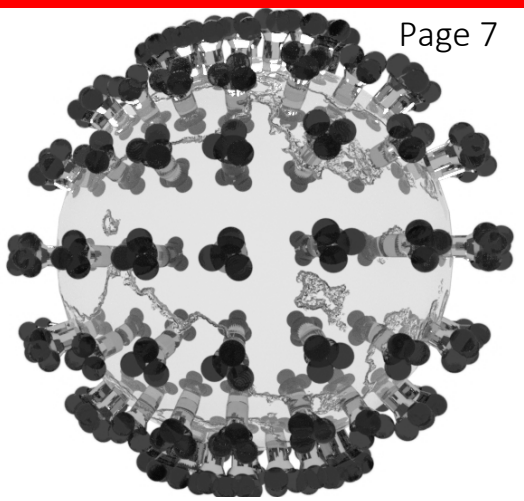
Now is the time to make change happen, the world needs engineers and scientists to step up, to change, to collaborate, and move medicine development manufacture forward. Do great things.



Andrew Livingston

Professor Imperial College London
Interim Director Rosalind Franklin Institute UK

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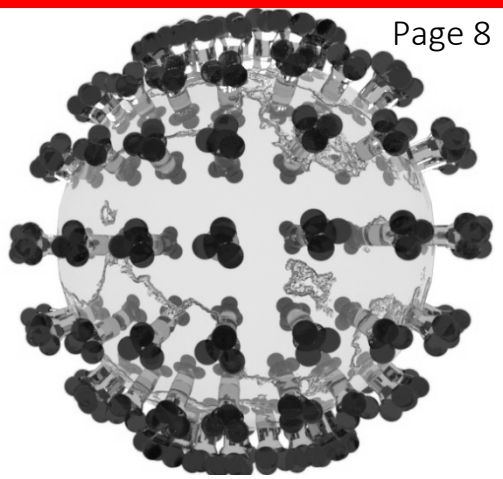
Here in the UK there are two collaborations which are key to the fight against COVID-19. One of these is the collaboration between University of Oxford (Jenner Institute) and AstraZeneca to rapidly develop a new vaccine through clinical trials and manufacture. The other is a collaboration between AstraZeneca, GSK and University of Cambridge that has set up a high throughput screening for COVID-19 testing and to explore the use of alternative chemical reagents for test kits in order to help overcome current supply shortages.

In your field, what are the major discovery, development, or manufacturing advances that you think will be vital for a rapid response?

It is interesting to see how the rapid move into clinical trials at unprecedented pace has exposed manufacturing as a bottleneck, for example for manufacture of vaccines, but also therapeutics. Gilead's website explains that they have shortened the time for manufacturing batches of remdesivir from 9-12 months to 6-8 months – this still seems like a long time in the dynamic of a pandemic. It seems to me that we need to come up with much faster processes for making these advanced medicines if they are to have an impact in halting the spread of potential pandemics.

"When you can measure what you are speaking about, and express it in numbers, you know something about it"

Andrew Livingston



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*In the UK, we had a lot of press about politicians "following the science" – and yet there was little capacity available for measurement of the spread of the pandemic. One of my favourite quotes that I repeat to my graduate students is from William Thompson, Lord Kelvin "When you can measure what you are speaking about, and express it in **numbers**, you know something about it; but when you cannot measure it, when you cannot express it in **numbers**, your knowledge is of a meagre and unsatisfactory kind". So, it was not clear to me that we had much real science, as we had few measurements. To act faster, and use science more effectively, we need greater capability to rapidly develop and deploy assays that follow the development of the condition throughout large populations.*

When the dust settles, industry, academia, and regulatory agencies will be revisiting their approaches to pandemic preparedness. *In your opinion, what approaches work well and what do you think could be revisited?*

It has surprised me how quickly regulatory approval for trials of new vaccines and drugs have been. If we could keep up this pace, that would be wonderful.

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I think we can help by working to increase the pace of process development, and to search for technologies which are fast to scale.

"I think we can help by working to increase the pace of process development, and to search for technologies which are fast to scale"