Medics Day 2022: Speech from Dr June Raine

DR JUNE RAINE: Well, thank you so much, Namine and Principal, colleagues, friends, the association. It's a tremendous honour to be speaking. How to follow Kate? Because I wouldn't be here if it wasn't for Kate and the absolutely incredible job she did. The prescient selection of those vaccines, which is why I'm here and probably why most of the people in this room are here. And I think you deserve another round of applause.

My purpose really is to take Kate's story a little bit further and tell you how the Covid pandemic has catalysed the transformation of a regulator, from a watchdog to enabler. And when I say that these are exciting times in the world of regulation, there are probably quite a few who've never had 'exciting' and 'regulation' in the same sentence. But I do hope to be able to convince you otherwise, just now.

The story of this transformation is effectively a tale of two cities: of London and of Oxford. And I think I hardly need to say to this audience that Oxford University has made a contribution to defeating this vicious virus far beyond any other institution in the world. And there are millions of people alive today because of this university. The Founders Dinner last night was just a wonderful opportunity to celebrate Somerville. And when we sang the Somerville song, some of us had in mind those early days of the 20th century, the days of writing that song and thinking about what Somerville did, not just at the end of World War One, but when the Spanish flu pandemic clouded the efforts to get systems working again, to get back to normality. And there is a lot to learn when there is a shock to a system. You discover things that work well and things that don't work so well.

So fast forward 100 years and here we are. We have been hit by a massive shock. All of our systems are under review now. They're testing every part of our infrastructure and we're getting a new appreciation of how we need to build back. I nearly said 'build back better'.

Oxford minds, of course, were busy working, and I first had my shock to the system, it was an email message from Professor Sir Andrew Pollard late one night, exactly two years ago today, 'Are you available for a brief discussion about work going on here in Oxford, which will lead to extensive interaction soon?' And of course, well, you might not believe this, I replied in 7 minutes – and friends who know me know that that doesn't often happen. But things were already starting, starting to prepare about that manufacture at scale, the Oxford Biomedica, that needed to be, at risk, preparing for the most massive preparation manufacture of vaccines.

In London, meanwhile, thoughts were on something else: Covid tests. How would we get the Covid tests at the volume and scale that we would need? Where would we get them from? So I was dashing into Number 10 – I didn't realise the Telegraph had managed to take a snapshot of this as I scuttled in for a meeting in the Cabinet Office about Covid tests. Sitting rather peacefully, the question arose as why a regulator was in the room? Was a regulator going to be able to do anything about this? And our PM, who seems to be able to notice things, shot a comment to me, 'Well, the MHRA will stop us killing people,' and for some reason I immediately was able to respond, 'No, the MHRA will help you keep people alive,' – and that is the signal of the watchdog to the enabler.

Many colleagues will have asked and thought, ‘What is the MHRA?’ We’re on two sites. It’s a government body, an arm’s length body of the executive agency, it’s an executive agency of the DHSC. And I think the general view is that rules are written on tablets of stone and there’s a lot of policemen in these places that go around factories, find problems with trials and generally hold things up. And to add to the complexity, as we’ve already heard, not just the vaccine taskforce doing this incredible work to locate the products, we’ve got the other body, the Joint Committee on Vaccination and Immunisation, working out how to deploy them.

And while we collaborated across these boundaries as never before, we knew that independence was going to be the key to public trust – independence in our decision making. And so that became a very, very real focus.

So, you’ve heard from Kate a little bit about how we began immediately to transform our processes. We tore up the rule book, and we allowed companies to immediately start juxtaposing not sequential phases of clinical trials, but overlapping, beginning the next one before the previous had been finished. And that large scale manufacture being prepared, at risk. We did not know if any of these vaccines would be effective.

We spent a long time on guidelines and we decided in the end that 50% efficacy would really be fine. So the data began to flow in and we began, in the middle of June, six months ahead of time, 2020, to start to prepare what safety surveillance we would need. And this is where I look at Kate, because Kate at that point had thought that once the purchase had been made, the approval had been signed, home and dry. And what I was able to share with you was we only really learn about benefit/risk in

clinical use. And we knew that there would be a vast influx of reports of side effects. No effective medicine or vaccine is without them.

But you can see the layers of parallel working that went on and that can never be turned back now. An interaction with a developer that, at each stage, looks at the protocols for the design and feeds in further important directions. So it all happened in parallel.

And so, by the time we were able to look at the interim analyses that was so exciting, we actually knew we were very close to an approval. And there were the data that Kate described in numbers, that separation of the curves around 12 days between the group that had been vaccinated and the placebo group that told you this was a highly effective Pfizer BioNTech vaccine.

Many times I was asked, 'Was that a difficult decision?' Well, I would ask anyone in this room to look at that – and bearing in mind that the side effect profile was much as you would have expected, the sore arm and the temperature, fatigue, whatever. I sometimes wondered if it was about being a female. Did I find it difficult? But actually, it made itself.

And here we see Margaret Keenan, 91-year-old grandmother in Coventry. And I'm glad to say well boosted now and I think still a very happy and outgoing lady. And she was such a sport that day. The Oxford-AstraZeneca vaccine, of course, followed very soon after. And as you've heard from Kate, this is the incredible story of global, a vaccine for the world, 2.5 billion doses administered worldwide, well ahead of the

others. And the fact that it is 183 nations, 20 manufacturing sites set up to deliver at cost.

And it's worth saying this again, it came from Oxford University. That email from Andy Pollard about what Sarah Gilbert's team were doing. It is absolutely phenomenal. It's hard to calculate how many lives were saved by that one research group alone, but probably in excess of a million as we speak. Something quite incredible. And I think more than a quarter of the 10 billion doses of vaccine given worldwide are the AZT vaccine.

And this is Ghana beginning its rollout on 1st March. We're very close to the Ghanaian situation, and we exchanged safety signals with Ghana, with Nigeria, Ethiopia, South Africa and Kenya. Every week we are looking at signals just to condition that local decision making and confidence in benefit/risk.

So maybe I'll change focus and tell you a bit about some of the other flexibilities, if you want to call it that. I won't say 'tearing up the rule book' for anyone who's a bit more insightful about the regulations we have to enforce, but we were very flexible. We were out there in the Nightingale hospitals ensuring manufacture on site of particular medicines that are needed to be prepared for patients. And so, the Excel Centre, as it was transformed, was another home for some of our staff.

This is an interesting story of collaboration. Some colleagues in the room might recognise a CPAP, a Continuous Positive Airway Pressure. The contact was made by University College Hospital, their intensivist and their bioengineers. 'We think we can invent something that will keep people off ventilators.' Cast your minds back to

before we had vaccines or therapeutics, people didn't want to go into an ambulance in case they were put on a ventilator with a 50-50 chance, it was that bad.

So, we were contacted around March 8th, Mercedes-Benz were commissioned, 750 of their engineers, to manufacture at scale. We approved in nine days and by April, 10,000 were going out to the NHS. And it may not be the most robust scientific data, I'm not thinking about the Medics Group this morning, that was treated to some wonderful science, but mortality in the UK intensive care units fell by 21%, coinciding with a 26% fall in the use of ventilators, despite an equivalent severity of disease. And so that hypothesis, about getting oxygen into people without having to ventilate them, really seemed to bear that out. And it's now used, it was given to the WHO, it's used in countries right around the world, particularly in low and middle income countries like Uganda, Palestine, etc. So a great step forward and another brilliant piece of work relying on collaboration.

Back to Oxford again. Now, this is something to celebrate. The Recovery Study, the world's biggest Covid treatment trial, co-run by professors Martin Landray and Horby. And just listen to those statistics. From the first protocol to the first recruitment: nine days. And as we know, many trials fail to get enough participants. It's well over 40,000 now. Many trials don't give results for a long time. Within 100 days, we were able to start using dexamethasone, which reduced mortality by a third. That knowledge that was available – and not even so much the things that work, but you remember all the press from the US about hydroxychloroquine, for example, convalescent plasma for example, where there had to be a real switch back from what the advice had been on the basis of robust data. So here in Oxford, something to be

astonishingly proud of. And I think again, it's widely quoted by the March of '21, the data from Recovery had saved at least a million lives.

And another interesting fact, the US FDA set about analysing trials and their likelihood to produce actionable data. Now, that might sound to a non-scientist, 'Why would a trial produce data that isn't actionable?' We can think about that. But of the 2,800 odd trials they looked at, 5% produced data that you could act on. And when I saw a list of countries around the world, of all these trials, the UK was nowhere. But then the list of actionable studies there we were. And it went from us asking the FDA what they were doing to regular calls from the commissioner of the FDA, 'What's the latest in Recovery?' And that's something to be astonishingly proud of.

Still with Oxford, and as we sit here today, another amazing study which is very close to the real world, PANORAMIC is being done. And I suspect there might be some colleagues even in this room who are either part of it or participating in it. Looking at the first oral antiviral pill, Molnupiravir, to see if what we saw from the earlier data releases is really going to be borne out, when you know that for it to work, you need to have it very quickly, within about five days. And so that work's ongoing and Paxlovid will follow. And I'd like to pay tribute particularly to that GP research unit, which is doing phenomenal work to make sure that we have robust data on which to base prescribing decisions.

A quick frolic through a couple of other things. The work on tests we produced target product profiles. And one of my proud moments was a call from South America, saying they were waiting for these target product profiles to be able to have tests of

their own. And that means that – and this was London, of course – no, it wasn't, it was informed by Professor Derek Crook from Oxford University. So yet again, the science from Oxford was informing this.

And I think you can see in the top right, there's a rather nifty AI reader for your test, if you can't see where that pale line is appearing, it will read it for you and artificial intelligence will tell the NHS. We used artificial intelligence to analyse our yellow card reports. And I know some of your colleagues have got a strong interest in this, with close on half a million, to get the data you need to detect safety signals needed additional help. And so regulation, again, is using the latest tools to be able to be on top of safety in real time.

I think an important aspect, right from the outset, was that public trust would need to be maintained with openness about how decisions are made and the data on which they're based. And it troubled us a lot with the early surveys that said that about 50% of people would not take a vaccine. How were we to proceed? Well, I would like to pay tribute to Sir Munir Pirmohamed, who has been a pillar of openness about the data that we hold and has gone out and briefed, relentlessly, to let people understand how his independent committee has made decisions.

The downside, of course, is that we attract the anti-vaxxers and this is outside our front door and some of it can be quite assertive, I think you might say. I think the verdict from this one was that four burly Met officers had been injured. But none of our staff, thankfully.

And the statistics on uptake now are stellar. 90% plus – it's 91.6% of over 12s – have had a first dose, 85.3% second dose, and it's two thirds are now boosted of adults, of people over 12. So this is a remarkable outturn where we are today.

Repeatedly, Somerville has stepped into the spotlight, and I'd like to highlight the work, brilliant mathematical modelling, done by Professor Dame Angela McLean. Of course, she has another important claim to fame, is that her mother created the Medics Group. So she isn't just on mathematical modelling and the chief scientific adviser to the MoD, and I do hope she's on the list for future lecturers, because her work has been incredible.

And we enlisted the help – I'm afraid we had to look to the other university, but sometimes one has to – Professor Sir David Spiegelhalter. Although I did locate the fact, and it has to be why he is where he is, that he was at Keeble, a contemporary of mine when I was here. But he's at Cambridge at the Winton Centre and helped enormously with communicating risk openly. And it's when you see data displayed in this way, by age – and this is the side effect that's been reported with the AZ vaccine – and you're trying to weigh up benefit, preventing ITU admissions against the risk of a clot, you begin to see how you might advise. And JCVI was able to take this and say, 'Let's have another vaccine under the age of 40.'

And it's conditional, though, on the environment. And this was a time of a medium risk of being infected. So a very clever way to look at your risk of being infected, your risk of an adverse reaction and your risk of having to be admitted through ITU.

So, back to Oxford again. And in the middle of the year, last year, the G7 health ministers met at Mansfield College, and I was privileged to go there – big demonstration outside, as you might expect. And what came out of that, because we're so good at delivering here in Oxford, was the Clinical Trials Charter, which will facilitate compatibility of trials. We heard from Kate how, when infectivity is going down somewhere, a trial may have to move and the AZ trial certainly had to do that. If we have compatible protocols and interoperability, we can start to work internationally and get good data more quickly. Our own revision of the clinical trials regulations will now follow these concept.

The main output though was music to Patrick Vallance. The Hundred Days Mission. He's created it and he uses this wonderful expression that 'we have to make the exceptional the everyday'. Well, that's no trouble here, Jan, is it? We make the exceptional the routine. We use best practice. And key to that is a joined-up regulator that's using every collaborative opportunity, but maintaining independence.

So the big question you're asking is, 'Will . . .' oh, no, you're not yet. This is the Prime Minister coming back to say, in response to some of the things that Kate has said, 'We will have good science to inform our policy.' And he was able to choose our organisation to launch this new initiative around the science and technology space. So I'm hoping that now that Patrick has a bit more time, he'll be doing some more work here.

So the question then: will we be able to maintain this change in regulation permanently? And I believe in our own regulatory world, we've changed our

processes. There's no going back now. We can ensure that we're as speedy as possible with our approvals without cutting corners, and that we don't ever again keep patients waiting. We will work in partnership, for example, with the Health Research Authority, vital that we look at the ethical approvals and the regulatory approvals in tandem, and would involve patients and the public really much more in all our regulatory activities and be much more open and transparent. So all of those commitments can be done. But importantly, we'll plan ahead for the next pandemic because there will be one.

Reflecting on today, I think the trickiest part about speaking to you is actually drawing conclusions. There's going to be a public enquiry. There will be an opportunity for all of us to pitch in with what we've achieved, what we've learnt, what we'll do differently the next time, and what needs to be put in place for the future. And it will dig very deep. And no one, I think, can, at this stage, predict the extent of the conclusions. I tried to think about some analogies, but I don't know as much as JVT about football. That would have been one idea. And I did try the one about reaching the base camp at Everest when we were about to have the last analyses of the Pfizer data, but I don't think it panned out quite as well as football.

I think to round off, I will simply return to the words of someone who's much better able than me to summarise. 'It was the best of times. It was the worst of times. It was the age of wisdom. It was the age of foolishness. It was the epoch of belief. It was the epoch of incredulity. It was the season of light. It was the season of darkness. It was the spring of hope. It was the winter of despair. We had everything before us. We had nothing before us. We were all going direct to heaven. We were all going direct the

other way. In short, the period was so far like the present period, that some of its noisiest authorities insisted on its being received, for good or for evil, in the superlative degree of comparison only.' And I believe that we as a country, our leadership, our scientists, our great university, our NHS and, most of all, our people have all been in the superlative. People who came forward in their thousands to be part of trials for vaccines and medicines that might benefit others, or who volunteered to help at the vaccination centres. Simply took food to the housebound. We have been in the superlative, and if I've contributed to that, I'm very proud. But everyone in this university can be more than proud. Thank you very much indeed