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for
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I O C D

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# One-World Chemistry for a Sustainable Future

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## 1. Introduction

This lecture has three components. In the first part, I will make the case that the chemical sciences have been central to global progress – and that they will go on being essential to meeting oncoming global challenges, especially sustainable development.

But I will argue that, to be able to make its optimal contribution, chemistry must change substantially and I will propose that 'one-world' chemistry offers a framework for how to do this.

And finally, as an example, I will look at the field of 'the chemical sciences and health' and outline why I think this area needs to make some systemic changes.

So, let me begin with the claim that "the chemical sciences have been central to global progress". I'm going to take wealth and health as two indicators of global progress. But before I get started on this, there's a general point I want to make:

People promoting the field of chemistry often like to focus on just one side of the coin and to emphasise the global 'goods'. They like to say ***"Look at all the great things that chemistry has done for us!"*** An example is the slogan that the DuPont chemical company used 1935-1982: *"Better things for better living… through chemistry"*,[1] which was subsequently contracted to *"Better living through chemistry"*. But where there are 'goods' there can be 'bads' as well: so, for example, increasing wealth over the last few centuries has been associated with increasing pollution of the environment; the development of new pharmaceuticals and agrochemicals has been intended to give us better health and nutrition, but it's sometimes led to severe problems of toxicity for human beings and animals. And when faced with the bad side of the coin, the temptation for those who promote chemistry is to try to ignore it and just say that '*The bad things are the fault of people, not of chemistry!'*

When talking about chemistry, it is very important to openly acknowledge three things:
- All chemistry knowledge can be applied for good or bad: it's people in every part of society, (including scientists, policy-makers and the public) who decide;
- Chemistry literacy is about acquiring the capacity to make informed choices;
- All choices have implications beyond the immediate setting, so that systems thinking is essential – which means that chemistry literacy must be taught in the context of real-world applications

## 2. Achievements

So let's ask the question: Have the chemical sciences been good for wealth and health?

### Wealth

Let's look at how overall human wealth has changed over time: this graph plots average global Gross Domestic Product (GDP) per capita, expressed in constant dollars, over the last 2000 years.[2] We can see that global GDP per capita remained pretty constant until just a couple of hundred years ago, but then began to rise increasingly steeply. Now, I'm going to distort the timescale on this chart, stretching out the last couple of hundred years to allow a more detailed focus on the more recent events. An important precursor to the steep rise in average global wealth was the Agricultural Revolution, which in Europe took place in the 17-19th centuries. By greatly increasing agricultural output, it liberated large numbers of people from the business of growing food and they flocked to the towns and cities, where the industrial revolution was able to benefit from their labour.

The chemical sciences made a major contribution to this growing global wealth:[3]

- Since 1800, the field of electrochemistry laid the foundations for the electrochemical industry, including the generation of electrical power, its storage in portable forms in batteries, and electrolysis processes providing valuable industrial materials.
- Synthetic chemistry began making big advances in the 1840s and 50s with work on the aniline dyes. As well as directly stimulating new fashion industries, the expertise that began to accumulate in the scale-up and commercialization of synthesis processes very soon led to major growth in organic chemicals industries.
- The foundations of biochemistry were laid in the 1860s and paved the way for the development of the biotechnology industry.
- From the 1830s to the 1930s, work on polymer chemistry created a new set of industries manufacturing materials such as rubbers, fibres, polymers and plastics.
- Studies on the first synthetic drugs around 1900 created many of the basic principles of medicinal chemistry and gave rise to the modern pharmaceutical industry.
- The development of spectroscopy and chromatography provided the basis of analytical sciences with applications including food, medicine and the environment.
- The second agricultural revolution had its origins in work in the early 20$^{th}$ century on nitrogen fixation and later on the insecticidal properties of DDT. These were precursors to a wide range of agrochemical industry products.
- The demonstration of the first semiconductor effect in 1833 and work over a century later on semiconductors and transistors were important milestones in solid state chemistry. We are currently witnessing an ever-expanding range of applications of solid state display devices and microchips that are transforming our lives.

Overall, current gross world product is something in the region of US$ 80 trillion per year. It's difficult to exactly quantify the total contribution of the chemical sciences to this total, but it's clearly very large – globally, the bulk chemicals sector alone is worth over US$5 trillion; the pharmaceutical industry alone passed the US$1 trillion mark in 2014; and the global agrochemical industry contributes over US$ 200 billion per year to the global economy.

Of course, the huge rise in global GDP per capita during the last couple of centuries has not been evenly distributed around the world. Looking at a global map of income distribution, as measured by GDP per capita,[3] we find that average country incomes vary by one to two orders of magnitude, according to whether they are high-, middle- or low-income.

I will just very briefly give one pair of examples [from many I could have chosen] of the direct role that chemistry has played in economic development at the national level.

Belgium is a high-income country, with a current GDP per capita of over US$40,000. A large part of Belgium's economic and industrial development since the 19$^{th}$ century can be traced to the chemical industry and life sciences, which currently account for around a quarter of the total manufacturing sector.[4]

Taiwan provides an example of a HIC country (with a current GDP per capita over US$ 20,000) which transformed its economy during the second half of the 20th century, with national planning and investment in chemistry capacity playing a key role. Between the 1950s and 1990s, Taiwan's per capita GDP rose eight-fold to over US$ 7,000 and in the 1990s the chemical industry was the largest industrial sector, contributing a quarter of the total production value. As well as technical and strategic factors, there was a crucial political component to Taiwan's success in the chemical industry sector – there was strong support by the government, including well-planned industrial zones and tax, investment and export incentives.[5]

## Health

Was there not some golden age, before human beings began the industrial development of the planet, when people lived healthy, clean and long lives close to nature? No, actually: at the dawn of human history, life expectancy was less than thirty years – and, strikingly, average global life expectancy remained below 30 years until the second half of the 19$^{th}$ century. It then began to increase very rapidly and more than doubled during the 20$^{th}$ century.[6] Over the past 150 years, average global life expectancy at birth has increased by roughly 3 months per year.

So, what roles might the chemical sciences have played in this dramatic increase in average global life expectancy?

- An important underpinning development was the Agricultural Revolution, which ensured that, on average, people were better fed and not malnourished.
- The field of immunization began with the demonstration that cowpox could be used to inoculate against smallpox. Subsequently, the chemical sciences have been fundamental to the development vaccines against a wide range of deadly diseases.
- The demonstration around 1830-50 of the anaesthetic effects of certain volatile liquids and gases that had recently become available by chemical synthesis was a vastly important step for medicine, enabling advances in surgery and dentistry that were completely impractical before the development of anaesthesia.
- The era of public health dates from work by John Snow and others in the mid-19th century on contaminated public water supplies. Water purification and analysis remains one of the cornerstones of modern public health.
- The foundations of biochemistry and of our understanding of the bacterial origin of infections were laid by the work of Louis Pasteur in the 1860s.
- As we've seen, the foundations of medicinal chemistry were laid around 1900 with the synthesis of analgesics and antibiotics.
- The basis for metabolic medicine came from work by Casimir Funk, who isolated the first vitamin compounds and published his vitamine theory in 1912; 10 years later Frederick Banting showed that diabetes was the result of a deficiency of the hormone insulin, which he isolated and successfully used to treat diabetic patients.
- The modern antibiotic era really took off with Alexander Fleming's discovery of penicillin and introduction by Gerhard Domagk of the synthetic sulfa drugs in 1935.
- The anti-cancer era began in the 1940s with the work of Louis Goodman and Alfred Gilman on nitrogen mustard agents and anti-folate compounds.
- The transplant era was initiated in 1954 when Joseph Murray carried out the first successful human organ transplant – a transplant of a kidney between identical twins – but the real benefits could not become more generally available until the natural product cyclosporin was isolated in 1969 and its immunosuppressive properties were discovered. It first began to be used clinically in 1980 to prevent organ rejection.
- 'Science-based' drug development began in the 1960s, as a more systematic, experiment-led approach to discovering compounds with desired biological activities.
- And the new era of gene-based medicine that we are now witnessing can trace its origins, among other things, to the development by the 2-times Nobel Prize-winning chemist Frederick Sanger – and others – of methods for the chemical sequencing of DNA, which enabled the inception in 1990 of the project to map the human genome.

But like average wealth, average life expectancy is not evenly distributed around the world among different countries. As the chart shows, national average life expectancies for some countries now exceed 80 years (and for girls born in S Korea its now above 90 years), while for others national average life expectancies can be as low as half that.[7]

So, these two dramatic rises, in human wealth and human life expectancy, have run in parallel over the last couple of centuries, and it may be tempting to argue that increasing life expectancy is simply a result of economic development. However, it turns out that this is not the case.

We can explore this if we look more closely at the relationship between wealth and health. A plot of average national life expectancy against GDP per capita is known as a Preston curve (after Samuel Preston, U Pennsylvania). The first thing that you notice about the Preston Curve is that it's not linear – it rises steeply for poor countries and then begins to flatten out, so that beyond a certain wealth you don't go on getting an increase in average life expectancy.[8] This is an important indicator that wealth cannot be the only factor involved. But perhaps it is just that at a certain point you reach the natural lifespan of human beings?

Plotting a set of Preston curves for the last century covering different time periods and in constant dollars, you find something very interesting. In any one time period, there is a similar trend for the relationship between life expectancy and GDP per capita – but between each succeeding time period there is an overall increase in life expectancy. So in constant dollars, the same amount of national wealth correlates with more life in a later period.[9]

Preston himself attributed 75% to 90% of the increase in life expectancy to improvements in health technology, while income growth was responsible for the rest. This conclusion was supported by other eminent economists – for example, Richard Easterlin concluded that the decline in 20th century mortality had its origin in *technical progress* – where the term 'technical progress', as used by economists, refers to technological advances; their diffusion and uptake in different countries; and the capacities of the countries themselves to conduct and apply research.[10]

Ismail Serageldin, the Director of the Library of Alexandria in Egypt, has commented[11] that, increasingly, a nation's wealth will depend on knowledge and that the 'haves' and the 'have-nots' will be synonymous with the 'knows' and the 'know-nots'. And clearly, for the poorer countries, not acquiring and using new knowledge is not only a matter of economics – it is also a question of life and death. To put it simply – *"ignorance is fatal"*.[12]

I hope that this short history has demonstrated my initial point, that the chemical sciences have contributed to global progress – that is, they have been good for wealth and health, at least for some.

And the chemical sciences will go on being needed to meet the many new challenges that we are facing in the 21st century.

## 3. Meeting oncoming challenges

At the beginning of the 21st century, the world's countries agreed a set of Millennium Development Goals, with targets to be reached by 2015. Three of the eight goals (4,5,6) related directly to health, while all of the others had some implications for health.

While the world was working towards these goals over the next 15 years, there were also lots of criticisms levelled against them. Many low- and middle-income countries complained that they had not been sufficiently consulted and they the goals represented an agenda of the high-income countries rather than their own highest priorities. And many people globally felt that the goals were too narrowly focused and left out many other problems that the world faced.

So, since 2000 there have been many other efforts to delineate the challenges that the world is facing. To give a couple of examples:

The third Copenhagen Consensus[13] emerged from a meeting in 2012 of a panel of experts (all economists and including 4 Nobel Prize winners) and produced a list of 10 of the world's biggest challenges, with recommendations on how to tackle them: the results were published in a book entitled *"How to Spend $75 Billion To Make The World A Better Place"*.[14]

Specifically in the field of chemistry: about 10 years ago the Royal Society of Chemistry and American Chemical Society agreed to collaborate in meeting the coming global challenges. In 2009, the American Chemical Society published a major study on global challenges and how chemistry could contribute to solutions.[15] The report highlighted a number of priority areas and these converge with the issues in the Copenhagen Consensus.

In parallel, a report in 2009 by the RSC on 'chemistry for tomorrow's world' highlighted 7 priority areas where chemistry can contribute.

You will note that both the ACS and RSC reports referred to 'sustainability' as one of the big challenges – and indeed this has emerges as the most serious overarching challenge for the whole planet in recent decades.

The concept of 'sustainability' was first used in its current sense in a report entitled 'The Limits to Growth' published in 1972 by the Club of Rome (an influential international think-tank). It recognized the danger that the world was consuming resources at an increasing level that could not be supported in the future. In the 1980s the UN established a World Commission on Sustainable Development chaired by Gro Harlem Brundtland (who at various times was Prime Minister of Norway and Director-General of WHO). Their 1987 report defined Sustainable Development as "***Development that meets the needs of the present without compromising the ability of future generations to meet their own needs".*** The need for sustainability was further highlighted in the 1992 Earth Summit in Rio de Janeiro, and the 'Agenda 21' document from this conference was subsequently developed further as a manifesto for "socially inclusive and environmentally sustainable economic growth". And on the 20th anniversary of the Rio conference, 192 governments renewed their political commitment to sustainable development in a document entitled "The Future We Want".

Very importantly, this strand of meetings on sustainable development then combined with another UN strand of work that was looking at the progress of the Millennium Development Goals and considering what to replace them with in 2015. The result was that in September 2015 the world's leaders gathered in New York and agreed on the UN Sustainable Development Goals for 2030.These 17 SDGs differed from the earlier MDGs in having been developed by a much more inclusive process; in being much more comprehensive in their scope; and in placing sustainability at the very centre of attention. Health is now the subject of a single goal (3), with an extremely comprehensive aim to "Ensure healthy lives and promote well-being for all at all ages" – with one of the targets being to achieve Universal Health Coverage, consistent with the SDG intention of "leaving no-one behind".

If you take these and other similar lists and try to boil them down to the essentials, they reflect a combination of aspirations for progress and determination to deal with some looming crises. I see two major sets of inter-related crises that our planet is facing in the 21st century:

First, there is the area of health, where we see challenges due to the fact we have a growing world population that is increasingly urbanizing and ageing. There are challenges due to the emergence of new diseases[16],[17] and at the same time old diseases like TB that we thought we had conquered have re-emerged as major health problems. And the traditional model of drug development, which seemed to have served us so well in the last century and a half, is now failing in some important respects. And then there is a second area of crisis, which relates to the fact that we're seeing the prospect of serious shortages in many key resources, including food, water, energy and materials – and the environment itself is now understood to be another resource with finite limits.

And alongside these two sets of crises I see two further sets of issues that are cross-cutting:[18] it's a dirty world, in which pollution of land, sea and air is harming the entire biosphere; and it's a fake world, in which counterfeiting and adulteration are very widespread and, among other areas, affect food, medicine and the environment.

Obviously, there are many ways in which the chemical sciences can contribute to solutions to these problems. But as we start to look at the contributions that the chemical sciences can make, I want to emphasize that the nature of the challenges has three aspects: there are not just challenges for the specific science content needed to solve particular problems; but also for developing the capacity for science and in the governance of science.

About 3-4 years ago, a group of us associated with the International Organization for Chemical Sciences in Development began working and thinking together and writing a series of articles about the future of chemistry – especially in the context of sustainability. One of our articles, published in Nature Chemistry in 2015, discussed the need for chemistry to make pivotal contributions to help realize the ambitious Sustainable Development Goals, but to do so it needs a new orientation in its priorities, approaches and practices.

We followed this up with a paper in 2016 in which we proposed what this new orientation might be – which we called 'one-world chemistry' and which offers a framework for how to achieve this reform. The goals of OWC are that chemistry should focus on becoming – and being seen as – a science for the benefit of society – and that, in particular, it should aim to be recognized as a core 'sustainability' science and an ethical science. The approaches needed to achieve this would involve the adoption of systems thinking in education, research and practice, embracing the principles of sustainability, working across disciplines, improving the productivity of the interface with industry; and in all areas taking an ethical approach. The new orientations needed would involve aligning chemistry and its external relationships with these goals and approaches; and, very importantly, projecting this to the public and media. Overall, this would allow chemistry to deliver three complementary roles. The first two of these have traditionally been strong – creating new knowledge and translating that knowledge into useful applications; the third role would now be given much stronger emphasis that previously, to ensure that the chemical sciences are doing their best to help meet global challenges

So what does all this mean in practice? In the short time available I'm going to look at a couple of examples and to try to illustrate these points.

## Materials

Let's start with some simple chemistry of the organic halides. If we are learning about the synthesis of the alkyl halides, we would cover things like free radical and ionic substitution and addition reactions and we would consider the properties of the halogen elements and how these affect the physical and chemical properties of the organic halides. A broader chemistry literacy requires that we ask how these substances fit in the real world and what kinds of roles people play in determining their use. There are many examples that could be chosen of well-known applications of organic halides, including those listed here: let's briefly consider the case of refrigerants – and, in particular, of the fluorocarbons.

The thermal effects of gas expansion and of liquid evaporation provide textbook examples of the physical basis for refrigerators, but the search for the ideal chemicals to use as refrigerants has been a continuing challenge. Early refrigerants like ammonia were tried, but were found to be too toxic and corrosive for domestic use. This General Motors 'Monitor Top' domestic refrigerator from about 1927 used sulphur dioxide, but this was also corrosive and tended to leak, with results that were both smelly and very toxic. Methyl chloride was also tried, but was toxic and also extremely flammable.

Seeking less dangerous refrigerants, in 1928 Thomas Midgley, working at General Motors, improved the synthesis of chlorofluorocarbons (CFCs) such as $CF_2Cl_2$ (b.pt. -30$^oC$). This was patented by GM and developed by Kinetic Chemicals as 'Freon'. It was used in refrigerators from 1930; and by the 1960s members of this family of halogenated fluoroalkanes or 'halons' were also being widely used as propellants in aerosol cans and in fire-fighting as well as refrigeration, as they are non-flamable.

In 1957 James Lovelock invented the electron capture detector, which is extremely sensitive for the detection of halogenated compounds in gas chromatography. In the late 1960s, Lovelock was the first person to detect the widespread presence of CFCs in the atmosphere and it was subsequently shown that these chemically inert gases accumulate in the stratosphere and have very long lifetimes there.

Alarm bells rang in 1974, when Molina and Rowland (who subsequently shared the Nobel Prize) published their findings that the photolysis of atmospheric CFCs by sunlight releases chlorine atoms and these catalyse the breakdown of ozone. It's been shown that since the 1970s there's been a steady decline in atmospheric ozone. A particularly large annual springtime decrease in stratospheric ozone over the southern polar region was discovered in the mid-1980s by the British Antarctic Survey. This is the so-called 'ozone hole', which has continued to grow into the 21st century. [19,20,21]

Following the publication by Molina and Rowland, there was immediate public concern which focused both on the environmental damage itself and on the attendant increased risks of skin cancer. Here the interaction of chemistry, biology and environmental systems had reached a crisis point and public opinion demanded immediate, global action.

In 1977 the UN Environment Programme (UNEP) adopted a World Plan of Action on the Ozone Layer, which called for intensive international research and monitoring of the ozone layer; and in 1981 UNEP began work on drafting a global framework convention on stratospheric ozone protection. The Vienna Convention, [22] concluded in 1985, was a framework agreement in which States agreed to cooperate to understand the ozone problem, and to adopt "appropriate measures" to prevent activities that harm the ozone layer. The obligations were general, however, and contained no specific limits on chemicals that deplete the ozone layer. These came two years later, in 1987, as an addition to the Vienna Convention, when the Montreal Protocol on Substances that Deplete the Ozone Layer[23] was signed. This protocol required the rapid phasing out of CFCs and a slower phasing out by 2030 of hydrochlorofluorocarbons (HCFCs), which are less damaging to the ozone layer but are also very powerful greenhouse gases.

It was remarkable that international agreement should be reached so quickly on such a major and contentious issue. Richard Benedick, who headed the US delegation in the ozone negotiations, commented[24] that there was a need *"to bridge traditional scientific disciplines and examine the earth as an interrelated system of physical, chemical, and biological processes"*: a good example where systems thinking was central to understanding and responding to a global challenge that originated with chemistry.

Let's look at another example of the overall environmental challenge that the world now faces – which is with the levels of contaminants in environment, food & pharmaceuticals – and some of those contaminants are themselves pharmaceuticals. For example:

- In 2006, the Indian government banned use of the anti-inflammatory drug diclofenac for veterinary purposes after it brought vultures to the brink of extinction. Vultures were being poisoned after eating

the carcasses of cattle that had been treated with the drug. However, a study[25] reported in 2011 showed that the ban was widely being ignored and numbers of the Asian vulture had continued to decline after 2006.
- Another report in 2011 in *Nature*[26] discussed high levels of pharmaceutical ingredients in treated effluent from wastewater-treatment plants and in effluent downstream from pharmaceutical factories, with examples coming from the European Union, India and the USA. Evidence of the environmental impact included the effect on fish and the appearance of very high levels of intersex characteristics.

Environmental contamination with pharmaceutical ingredients is very widespread – and it's important to recognise that there has been a systemic failure, at both national and global levels, to deal with these problems. As the Nature report observes, contrary to what many people believe: *"The USA and Europe do not have regulations limiting the concentrations of pharmaceuticals released into the aquatic environment in either municipal wastewater or in effluent from manufacturing facilities."* So there is a need for better regulation – and equally importantly, such regulations and their enforcement are meaningless without very good analytical techniques. The whole system of environmental protection, monitoring and enforcement needs improving in this area.

A complementary area of very serious concern is the contamination of pharmaceutical products themselves, and also of foodstuffs, with harmful ingredients. Just to take a couple of representative examples:
- Illegal use of diethylene glycol in various pharmacy products has caused hundreds of deaths across several countries in recent years.[27] The Nigerian case in 2009 was traced to deliberate fraud by a chemical dealer in Lagos supplying diethylene glycol instead of glycerine.[28,29]
- In China, widespread adulteration of infant feeding formulas with melamine (a trimer of cyanamide, added to boost the measured nitrogen content) caused serious harm on a large scale.[30,31,32]
- In the UK, an example of deliberate contamination of a pharmaceutical product occurred in 2011, when a man was prosecuted and subsequently jailed for adulterating packages of the painkiller Nurofen Plus.[33,34]

And of course, if we look at contamination of foodstuffs more broadly, beyond pharmaceuticals, in 2013 there was a scandal in the UK and a dozen other countries across Europe, when foods advertised as containing beef were found on analysis to contain as much as 100% horse meat instead.

A paper by Brown & Brown in 2010 overviewed the global picture and looked at lessons that could be learned. Regarding the Extent of problem, they concluded that
- Toxic results from contaminated food and drugs are often only identified when there are large numbers of cases and numerous deaths;
- Deliberate contamination may be widespread, but it is likely to escape detection in poorly regulated markets; and
- Contaminated materials from poorly regulated places may cross national boundaries and end up in numerous products, including in more well-regulated markets.

The review also looked at the capacity for solutions and concluded that
- It is not clear that regulatory organizations have the capacity to identify significant contaminations, despite their best efforts. And therefore
- The [relevant scientific] communities, in cooperation with regulatory agencies, should develop cooperative programmes designed to detect and limit these global outbreaks. But,
- while addressing regional or national outbreaks remains an important role for regulatory agencies, the [relevant scientific] communities must develop proactive global approaches. This is a global problem and needs global solutions.

Clearly, the chemical sciences can play a major role in tackling these adulteration challenges, but this requires that scientists engage in an organized way with one another and with the public, with legal systems and with policy makers for this to be effective.

And then there is the massive problem of counterfeit drugs. This is a global business worth many tens (if not hundreds) of billion dollars a year. Counterfeit medicines are estimated to constitute more than 10% of the global medicines market, with a range up to 50% in some LMICs. It remains a big challenge even in well-regulated pharmaceutical markets like that in the USA, because c. 40% of drugs in USA are imported and c. 80% of the active ingredients in US drugs come from external sources. About 10% of all counterfeit seizures made by US customs in 2014 were counterfeit medicines.[35]

Of course, these types of fraud have been made very much easier by the use of the internet as a source of pharmaceutical products and globally a high proportion of all drugs sold on the internet are counterfeit.

WHO has shown that a very wide range of drug types are involved, and a whole range of faults from little or no active ingredients to substitution with potentially harmful substances.[36] The lack of effective treatment can result in death.[37] Examples include fake treatments for malaria; it is estimated that every year hundreds of thousands of people die as a result of counterfeit malaria medications – and a study in NIgeria in 2011 showed that close to 2/3 of all antimalarials available were counterfeit.[38]

While such problems are a lot more common in low- and middle-income countries, they are also found in high-income countries:

- In March 2008, the US FDA recalled batches of heparin, a widely used injectable anticoagulant. It was found that the bulk ingredient, which had been manufactured in China, had been mixed with a much cheaper material made from chondroitin sulphate. The FDA received 785 reports of serious injuries and at least 81 deaths were believed to be associated with this fraud.[39]
- In 2012, a counterfeit of the anti-cancer drug Altuzan was found being prescribed in the USA which had no active ingredient – a Turkish man was jailed for this fraud in 2014. [40,41,42]

It is clear that the problem is also one with global proportions and needs a global approach; but in many places there is absence of, or weak, drug regulation. As the World Health Organization stated[43] in 1984: *"every country, regardless of its stage of development, should consider investment in an independent national drug quality control laboratory".* But: at present, of 191 WHO member states, only about a fifth have well developed drug regulation. Of remainder, about half implement some drug regulation while another 30% either have no drug regulation in place or a very limited capacity.[44] The world market for pharmaceutical anti-counterfeiting technology was estimated to be worth around US$3.4 billion in 2015 and is growing rapidly.[45] It's predicted that the combined pharmaceutical and food anti-counterfeiting market may exceed US$ 160 billion by 2020.

So, looking across the whole problem related to contaminants in the environment, food and drugs, some general conclusions are:

- There are major scientific challenges and opportunities; and the public and policy makers need to understand the problems and support the systemic solutions required. This presents challenges for developing both the science and the appropriate science literacy.
- And there are also challenges for regulation, which is failing to deal fully with issues that have global dimensions and require systematic solutions on a global scale. And developing these solutions also gives rise to a need to develop appropriate capacities for science literacy, communication and diplomacy.

I will now turn to what many people see as the biggest single challenge to global health in the 21st century – Antibiotic Resistant Bacteria (ARB).[46] In the early 20th century, before antibiotics came into use, infections caused around 43% of all deaths. Fleming's discovery of penicillin in 1928 began to change that dramatically – but Fleming was among the first to warn that development by bacteria of resistance to antibiotics was going to be a serious problem. But many new antibiotics were discovered or synthesised during the 20th century and by the end of this period we enjoyed a golden age when fewer than 7% of deaths were being caused by infections. WHO estimates that, on average, antibiotics and vaccines add 20 years to each person's life.

However, during this period ARB has been growing and spreading and is now causing serious health problems and serious economic loss in every part of the world. For example, ARBs cause the majority of the 100,000 deaths a year from infections acquired in hospitals in the USA and result in additional health care costs amounting to tens of billions of dollars. At least 4 major factors are driving this crisis in ARB:

- Antibiotic misuse
- Massive veterinary use of antibiotics, especially to promote animal growth (banned in Europe since 2006 and from 1 Jan 2017 in USA)
- Environmental contamination
- We are also living in a period of a discovery void.

Many new antibiotics – and whole new classes of antibiotics – were discovered or synthesised during the 20th century, so that chemistry provided a steady pipeline of new drugs as the old ones gradually lost their effectiveness against the evolving strains of bacteria. But we then entered a 'discovery void', where not a single new class of antibiotics was discovered in the period 1987-2014.

And at least 3 major factors have contributed to this discovery void:

- The first of these is a failure in science. Some people argue that the *"low-hanging fruit has all been picked"*; and meanwhile the promising new life science technologies have so far failed to yield new classes of antimicrobials.
- A second factor is a failure in the market system that drives the investment in creating new medicines. On one hand, drugs for chronic diseases offer a far greater potential return on investment for pharmaceutical companies; and on the other hand it has been the case for many years that any new antibiotic discovered is likely to be reserved for use as a last-resort treatment, which greatly reduces the size of the market and the profit to be made. This has been summed up as a *"systemic global market failure"*.
- And there are also regulatory burdens – it has become increasingly difficult over time to get new drugs, including new antibiotics, registered. This acts as a further disincentive to the market in an area where the economic returns are already poor.

Some better news came in 2015, with the discovery of a new antibiotic named teixobactin, which is in a new peptide class and for which Gram-positive organisms appear to show no resistance. The discovery of this natural product followed a breakthrough in developing a new way of screening for antibiotic activity in bacteria that cannot be cultured in the laboratory. Of course, it will take several years before we know whether teixobactin will make it into the clinic. But it's also notable that this promising candidate drug did not come from industry but from research that was publicly funded and the patent is held by an early-stage biotech company. There are still a range of systems issues that need to be sorted out if the world is going to get better at discovering and developing new antibiotics.

And the extent of this systems thinking needed becomes more evident if we look at the way that the determinants of AMR cut across the whole spectrum of human, animal and environmental factors. Antibiotics enter these highly interconnected systems at many different points and it will clearly not be possible to reduce the evolutionary pressures that lead to resistance without simultaneously tackling all these systems together.

So the picture summarised[47] in *The Lancet Infectious Diseases* journal in 2013 was that "*we are at the dawn of a post-antibiotic era"*. And as we look towards the middle of the century, we are faced with the prospect that without action, infection-related mortality may return to pre-antibiotic levels. If this happens, the whole practice of medicine will have to change and any kind of surgical procedure will carry a high risk of infection. As we saw on an earlier chart, ARBs already cause the majority of the 100,000 deaths a year from hospital-acquired infections in the USA alone.

On the science side, there is a critical need for better tools to be able to recognize resistant organisms and diagnose their type. Then there is the challenge to develop new classes of antibiotics.[48] In 2016, the US government nearly doubled the federal funding to combat AMR to US$ 1.2 billion. The EU has launched its own Action Plan on AMR and has established a public-private partnership with the European pharmaceutical industry called the 'Innovative Medicines Initiative', one of whose areas of work is to develop new antibiotics.

It is evident that there is need for a coordinated global effort to counter antibiotic resistance:

- ➢ May 2015 World Health Assembly: Global action plan on antimicrobial resistance (AMR)
  - ✓ governments all committed by May 2017 to put in place a national action plan on antimicrobial resistance, aligned with the global action plan
- ➢ USA+EU: Trans Atlantic Taskforce on Antimicrobial Resistance
- ➢ WHO, UN's Food and Agriculture Organization and World Organisation for Animal Health collaborating closely

## 4. The chemical sciences and health

The last area I want to talk about today is to look at the application of the 'one-world chemistry' approach to the field of 'the chemical sciences and health'. I've made two overall points so far in my talk, namely that

- The chemical sciences have been good for health; but that,
- Faced with the oncoming global challenges, even greater efforts are required

I now want to argue third point, which is that, at present

- The chemical sciences are not able to function optimally in helping to deliver SDG 3: *"Ensure healthy lives and promote well-being for all at all ages"* and *"leave no-one behind"*

Our group thinks that there are three systemic fragmentations which are responsible for this weakness and in fact, I've been exemplifying what these are throughout my talk. They are fragmentations:
1. In the science discipline
2. In the functioning of the related industry
3. In the regulatory systems

So, let's take a look at the picture. The chemical sciences support health through multiple channels.
- They support education, research and practice in 'the chemical sciences for health'.
- They support pharmaceutical and other health science industries; and also agriculture & fisheries
- and they provide the basis for monitoring, protection, preservation and cleaning of the environment

Together, these activities provide us with
- Safe, effective, affordable pharmaceutical products: drugs, vaccines, drug delivery systems, etc; and they also provide other medical products and devices: anaesthetics, prosthetics, diagnostics, medical imaging;
- they contribute to our access to safe, nutritious food from production, processing and preservation;
- and they enable us to be able to work for good quality of land, water, air, and the global ecosystem

And there are regulatory systems that are intended to oversee each of these three areas which are so vital for our overall health

Together, these activities have a central contribution to make to the overall ambition of sustainable development that supports healthy people, animals and planet.

But we are arguing that there are **fragmentations in three critical areas** – highlighted here. Let's look at each of them in turn, briefly.

### 1. Compartmentalization in the science discipline

The discipline of chemistry itself is highly compartmentalised, with a host of sub-disciplines that often work in silos in departments that are structurally divided. And the same is true for the adjacent biological sciences – and for the sub-disciplines that are constantly developing at the interfaces. The same is true at the interfaces with the adjacent materials sciences.

And amidst all these compartments and silos, the reality is that 'the chemical sciences and health', or 'chemistry and health', does not exist as a recognised subject.

We propose that 'the chemical sciences and health' should be created as a recognised discipline, in order to provide:
- an overall vision on which learning, research and practice can build
- a comprehensive platform of knowledge and skills on which to build, across the whole spectrum of education, research and practice; and promoting the
- convergence of diverse knowledge streams and harnessing these to strengthen innovation and synergy.

### 2. Dis-integration in the pharmaceutical industry

The pharmaceutical industry is in the process of moving: shifting its locus to the East and South: production, consumption and R&D are all increasingly taking place in, especially, China and India.
Paradoxically, two other movements have also been taking place:
- One has been a massive consolidation tendency of mergers and acquisitions that began in the 1990s. This has led to a concentration of the production and sales of pharmaceuticals being in the hands of a relatively small number of giant companies;
- and at the same time, the industry has been undergoing a dis-integration – a shift from 'vertical' to 'horizontal' structures, including the separation of discovery research from development.

The various functions of the pharmaceutical industry were traditionally all located within the same company, but these vertically integrated supply chains are breaking apart into component activities that can be outsourced. There are now numerous stages at which outside agents are taking over specific functions and we are increasingly seeing alliances, licensing agreements and joint ventures along the whole value chain, The separation of research, development and manufacturing is reshaping the character of R&D around the world – and it is not at all clear that this is for the better in the long term. As one recent, detailed study put it: mergers may have achieved cost reductions and addressed short-run pipeline problems, but so far there is little evidence they have increased long-term R&D performance or outcomes. And there is a persistent problem with R&D productivity.

There has been a lot said in the last few years about whether innovation in the pharmaceutical industry is declining. The number of new molecular entities registered as drugs has certainly fallen back from the peak seen in the 1990s. At the same time, R&D costs have been rising steeply for many years and the overall productivity of investments in pharmaceutical R&D has therefore been diminishing very substantially in countries like the USA. Leaders of the pharmaceutical industry itself have noted that its very survival in its current form is in great jeopardy; and that the impact of mergers and acquisitions on R&D has been devastating.

The pharmaceutical industry located in high-income countries has been/is:
- Concentrating increasingly in the hands of a few mega-players, focusing on high-profit ‘blockbuster’ drugs
- Dis-integrating from ‘vertical’ to ‘horizontal’/outsourced

And in order to feed the emptying drug pipelines, they have been
- Buying intellectual property rather than creating it (and buying and ‘absorbing’ the innovative small companies that create the candidates)
- Experiencing a shift to the East and South in production, consumption and R&D

Well, the question is: Does it actually matter where and how the science gets done, as long as new products are created to meet the world’s growing health needs? Analysts differ:
- Some: the metamorphosis has had ‘mixed results’
- Some: it has not been to the advantage of people’s health
  - decline in numbers of new drug entities coming into use annually
  - narrowing of focus on block-buster drugs while ‘diseases of the poor’ neglected
  - may be a shift in job opportunities in the relevant sciences accompanying the geographic relocation of pharmaceutical R&D to South and East Asia;
  - and this may decrease the popularity of these sciences in Europe and North America, weakening their traditionally strong capacities in research for health

It’s interesting to look at the report issued last year by the Association of British Pharmaceutical Industries on ‘The changing UK drug discovery landscape’. This notes that more organisations, particularly large firms, reported a greater increase in their global discovery investment than that in the UK. This could suggest that whilst areas of the landscape may be thriving, overall the UK may be proportionally losing out globally.

And they conclude that the UK needs to consider how it can best U its position as a central player in the global landscape.

So, it seems that the model needs revisiting, since the world needs
- more drugs and other health products at more affordable prices for more diseases and conditions; and
- a system that enables achievement of the SDG goals of health and health equity for all, based on the principle of ‘leave no-one behind’.

But it’s clear that finding solution(s) will not be straightforward, because the current trends are
- driven by economic forces that do not originate in the pharmaceutical sector itself, but in functioning of economic reward and innovation systems at national and global levels.

If the high-income countries with traditionally strong pharmaceutical development capacities wish to retain their industries and their leadership roles in the field, they need to play close attention to systemic elements involved and bolster critical ones, including:
- ensuring strong, robust and well-designed education programmes, including relating to the chemical sciences, that create a pool of talent with skills honed in conducting inter-disciplinary and trans-disciplinary research
- well-funded academic centres that can create new leads to health products
- innovation hubs that foster early-stage drug development

- national innovation systems and innovation financing that encourage the growth of independent middle-size companies that have options beyond buy-out when they create promising candidate products and high-value new licensed drugs

We can argue that all of these things are being done to some extent at present. But the comments by the ABPI and others suggest that they are not yet being done sufficiently to arrest and reverse the trends that are happening.

### 3. Disconnections in the regulatory sector

It's a dirty world and a fake world – affects pharmaceuticals, food and the environment
Need for more effective regulation

- Licencing
- Quality of products procured
- Quality of products in circulation
- Counterfeits
- Contamination of environment
- Contamination of foodstuffs

Regulation = Laws + policing + criminal justice system

- Analytical science feeds into all three
  - Sets position for what is possible
  - Sets practical framework for timescale and cost of what is detectable
  - Sets limits of what is 'provable' and therefore enforceable by courts

Dialogue essential: between scientists, policy makers, legal system, public, media

- ➢ Non-technical language
- ➢ Communication about 'certainty' and about 'risk'

So what is needed is communication that creates productive dialogue, leading to decision-making and effective regulation and enforcement. This process needs to involve people working in the diverse but, as we have just seen, interconnected fields of pharmaceuticals, food and the environment as well as policy-makers and people from an array of national, regional and global organizations.

But there are quite a lot of these. There are diverse organizations that represent groups of professional analysts and different analytical techniques; and there are national and occasionally regional bodies involved in the regulation of registration, quality and enforcement. So, with such a complex array of actors, how is the world going to be able to create a coherent dialogue, reconcile different views and make sense of the field?

Well, perhaps it's time to consider whether we need a World Organization for Regulation of Food, the Environment and Drugs – a truly global solution to a global problem?

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