International Organization
for
Chemical Sciences in Development

I O C D

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Chemical Sciences for Development: Potential and Prospects

This talk is divided 3 sections:

- First, I will make the case that the chemical sciences have been good for wealth and health– but only up to a point, and only for some.
- Second, I will tell you a little bit about the work of the International Organization for Chemical Sciences in Development
- Third, I will talk about some of the major challenges that the world now faces and the potential that the chemical sciences offer for meeting these challenges.

1. The chemical sciences have been good for wealth and health

So let's begin with the role of the chemical sciences. If we go back to ancient Egypt and Greece, we find evidence that the precursors of modern chemists, the alchemists, were already experimenting with matter and trying to transform it.

The alchemists had two major goals in their work: they were searching for the Philosopher's Stone, a substance that would transform base metals into precious ones like gold and silver; and they were also searching for an Elixir that would confer eternal life or eternal youth on the person who drank it. The alchemists were not very successful in their quest, but their efforts did occasional have some interesting results – as when, in the search for the Philosopher's Stone, the distillation of urine led to the discovery of phosphorus; or when Chinese alchemists blending substances to try to create the Elixir of Life invented gunpowder.

But if the alchemists were not successful in trying to create wealth or extend the human lifespan, in the modern age their scientific successors have been spectacularly successful and the chemical sciences have played a central role in this success.

Let's look overall at how human wealth has changed over time. This graph plots average global Gross Domestic Product per capita (Gross World Product/capita), expressed in constant dollars, over the last 2000 years (note that the time scale is not a liner one, to allow a more detailed focus on the more recent events). As you can see, global GDP per capita remained relatively unchanged for over the first three quarters of this whole period of two millennia, but then began to rise increasingly steeply. An important precursor to this rise was the Agricultural Revolution, which took place in the 17-19th centuries in Europe. 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:

- In 1800 Alessandro Volta established the beginnings of the field of electrochemistry, laying the foundations for the electrochemical industry, including the generation of electrical power, its storage in portable forms in batteries, and electrolysis processes that have provided many important industrial materials.
- Synthetic chemistry made important advances in the 1840s and 50s with work on the aniline dyes by August Hofmann and William Perkin. The scale-up and commercialization of synthesis processes led to major growth in organic chemicals industries in several European countries.
- Work by Pasteur in the 1860s founded the field of biochemistry and paved the way for the development of the biotechnology industry.

- Over the course of a century from the 1830s to the 1930s, work by several scientists created a new set of industries manufacturing materials such as rubbers, fibres, polymers and plastics.
- Studies by Felix Hoffman on aspirin and by Paul Ehrlich on antibiotics just before and after 1900 provided the basis for medicinal chemistry and gave rise to the modern pharmaceutical industry, whose sales now exceed a trillion dollars a year.
- William Herschel's work laid the foundations of spectroscopy in 1800, while the basis of chromatography was established a century later by Michael Tswett. The combination of powerful techniques for the separation and structure elucidation of chemical species provided the basis of a whole range of important analytical sciences with applications that include food, medicine and the environment.
- The second agricultural revolution had its origins in work in the early 20th century by Fritz Haber on nitrogen fixation and later by Paul Müller on the insecticidal properties of DDT. These were precursors to a wide range of agrochemical industry products.
- The demonstration by Michael Faraday of the first semiconductor effect in 1833 and work on transistors by William Shockley and a group of physicists and chemists at the Bell Laboratories in the late 1940s were important milestones in solid state chemistry. We are still seeing the expansion of information and communications technology industries based on this field today, with a host of applications of computer microchips that are transforming our lives.

Of course, this phenomenal rise in global GDP per capita during the last few centuries has not been evenly distributed around the world. If we look at a global map of income distribution, as measured by Gross Domestic Product per capita, we find that average country incomes vary by one to two orders of magnitude. It is convenient to classify countries according to whether they are high, middle or low-income. This is greatly preferable to using terminology such as 'developed' and 'developing' – especially at a time when China is the world's leading exporter of manufactured goods and already the second largest economy in the world – and I will use this terminology (LMIC for low- and middle-income countries; 'HIC' for high-income counties) in my talk.

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

Taiwan provides an example of a HIC country (with a current GDP/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/capita 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.

Turning now to 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? Well, 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 19th century. It then began to increase very rapidly and more than doubled during the 20th century. Over the past 150 years, average life expectancy at birth has increased by roughly 3 months per year.

So, what role ***might*** science and technology have played in this dramatic increase in average global life expectancies?

- As we have already seen in the case of economic development, an important precursor was the ***Agricultural Revolution*** which took place in the 17-19th centuries in Europe. This brought greatly increased efficiency of food production, simultaneously ensuring that people were generally better fed, as well as meaning that fewer of them were needed to work on the land.
- The field of ***immunization*** began in 1796 with the demonstration by Edward Jenner of using cowpox to inoculate against smallpox a first step on the road to the eventual eradication of smallpox as a disease of human beings in 1980.
- The technique of ***anaesthesia*** was initiated in the period 1830-50 with the demonstration of the anaesthetic effects of volatile liquids and gases like ether, chloroform and nitrous oxide. This was a

vastly important step for medicine, because it made possible advances in surgery and dentistry that were hitherto completely impractical.

- The era of ***public health*** dates from 1849-55, when John Snow demonstrated that cholera was caused by contaminated water in public water supplies such as the well in Broad Street in Soho, London.
- The foundations of ***biochemistry*** and of our understanding of fermentation and of the bacterial origin of infections were laid by the work of Louis Pasteur in 1860-64.
- The foundations of ***medicinal chemistry*** were laid at the end of the 19th and beginning of the 20th centuries with the creation by Felix Hoffman of aspirin, the first synthetic analgesic; and by Paul Ehrlich of the first antibiotics (which were organo-arsenic drugs for the treatment of syphilis).
- And the modern ***antibiotic era*** really took off a few years later with the discovery by Alexander Fleming of penicillin in 1928 and the introduction by Gerhard Domagk of the first sulfa drugs in 1935.
- The ***anti-cancer era*** began in the 1940s with the work of Louis Goodman and Alfred Gilman on nitrogen mustards 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 – although the real benefits could not become more generally available until the natural product cyclosporin was isolated in 1969 and its immunosuppressive properties were discovered in the 1970s and it first began to be applied clinically in 1980.
- ***Science-based' drug development*** began in the 1960s, with a more systematic and experiment-led approach to discovering compounds with specific kinds of biological activities.
- And the new era of ***gene-based medicine*** that we are now witnessing can trace its origins, among other things, to 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 this map shows, national average life expectancies for some countries, including Canada, now exceed 80 years, while for others, national average life expectancies can be less than half that - including for some of the poorest countries such as those in parts of Africa and Central Asia.

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). 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. This is an important indicator that wealth cannot be the only factor involved. Well, you may say, perhaps it is just that at a certain point you reach the natural lifespan of human beings?

If you plot a set of Preston curves for the last century covering different time periods, 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 buys more life in a later period.

Preston himself considered that improvements in health technology accounted for 75% to 90% of the increase in life expectancy, 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.

Ismail Serageldin, the Director the Library of Alexandria in Egypt, has commented that "developing countries cannot do without home-grown capacity for scientific research and technological know-how. Increasingly, he predicts, 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".

Of course, not all countries have made the same levels of investments in science, technology and innovation. This map illustrates variations between countries in R&D density, which is the number of researchers per 1 million population. Notably, again, it is some of the countries in Africa, Central Asia and South America that have some of the lowest densities of researchers. Not surprising, low rates of investment in R&D correlate with low levels of scientific capacity and output. Indeed, if you scale a map of the world according to scientific papers published by citizens of each country in 2001, it looks like this... which provides a rather striking illustration of a 'North-South divide'.

In fact, this picture is now changing quite rapidly and a number of low- and middle-income countries, including Brazil, China and India, have been investing increasingly in S&T and are beginning to show increasing outputs of scientific papers and patents. For example, a report just published in Nature in June 2014 illustrates the increase in the share of world publications coming from South America in the last couple of decades. Great increases have been seen in the numbers of papers coming from China, and the prediction is that citations of papers from China, which are rapidly increasing, will overtake those from the USA some time in the present decade.

So, I hope that this short history of the world in 12 slides has demonstrated my initial point, that the sciences – and in particular the chemical sciences – have been good for wealth and health, at least up to a point and for some.

2. International Organization for Chemical Sciences in Development

IOCD was founded at UNESCO at the beginning of the 1980s, at a time when a number of visionary people, including the Belgian chemist Pierre Crabbé, had a conviction that science and technology could be key factors in the development of countries and people and in reducing the growing gaps in prosperity and health that were visible between and within nations.

In the first phase of its work, through to the mid-1990s, IOCD established a series of working groups, conducting research projects in aspects of medicinal chemistry and the utilization of natural products. IOCD undertook research facilitation, including through creating some analytical service centres at universities in HICs – to support chemists in LMICs by provided spectra free of charge. IOCD also supported capacity building – which at the beginning was mainly at the level of the individual, through grants and assistance to engage in international research programmes.

Following Pierre Crabbé's untimely death in a traffic accident in 1987, IOCD appointed its second Executive Director, Robert Maybury, a chemist who had worked on science and development with UNESCO and the World Bank. The 1990s saw many changes in the development sphere, with on the one hand rising capacities for science in a number of countries but on the other hand a series of financial crisis and a severe 'donor fatigue' which meant that there was much less money available for development work. During the '90s IOCD moved into the second phase of its existence, developing new Working Groups and programmes but shifting its approach from running research projects to organizing meetings, seminars and workshops. The capacity building aspect also underwent substantial change, expanding its focus from the individual to institutional and working more with LMIC networks and on aspects of policy.

Robert Maybury was succeeded in 2010 by IOCD's 3rd Executive Director, Alain Krief, a Tunisian who moved to France, trained as an organic chemist and worked for a major part of his career at the University of Namur in Belgium. By the time Alain Krief took over, IOCD was approaching its 30th anniversary; but the world had changed greatly since IOCD was founded in 1981: economically, politically and socially. And the field of international development has changed. It has moved from 'international aid' to 'development cooperation'; from the Millennium Development Goals focusing on the plight of the poorest countries to global 'sustainable development goals' that are everyone's concern; and the whole concept of 'developing' has undergone a radical rethinking.

In the light of these changes, IOCD saw the need to develop a new strategy for the present decade (2011-2020). This
has three Strategic Priorities: Chemistry for better health; Chemistry for a better environment; Capacity building in chemistry education.

IOCD's strategy is to support ownership, partnership and capacity building for the use of the chemical sciences globally, but especially in and for the benefit of LMICs. Its approach involves fostering science applied to equitable global development. And its function is increasingly to serve as an umbrella, facilitator and promoter for programmes and funding for research, education and capacity building in the chemical sciences.

IOCD has been fortunate to attract some very prominent and brilliant scientists to its cause – including the first President, the Nobel Laureate Glen Seaborg; the current President, the Nobel Laureate Jean-Marie Lehn; and members of the Senior Advisory Council including the Nobel Laureates Norman Borlaug (father of the 'green revolution'), Roald Hoffmann, Sune Bergstrom, and a current member of our Council, Ryoji Noyori; as well as prominent scientists from LMICs and HICs, including the other current Council members CNR Rao, Koji Nakanishi, Ata Uh Rahman, Yitzak Apeloig, Berhanu Abegaz.

In developing its new Working Groups and Programmes. IOCD places great emphasis on recruiting a very diverse range of younger scientists, including women. We are very proud that among our newest recruits are Mohamed Chakar and Federico Rosei, who has established a new IOCD Working Group dealing with materials for energy.

3. Chemical sciences for development: Potential and prospects

So, coming to the third part of my talk, what are the new challenges that the chemical sciences for development face in a changing world? I have time only for a brief look at this, but what I want to stress overall is that the challenges are of three kinds: not just challenges for the specific science needed to solve particular problems, but also challenges in developing the capacity for science and in the governance of science – and in this third part of my talk I will be repeatedly stressing the importance of linkages between science and policy.

Some of the biggest science challenges we currently face can be summed up by two very simple statements:

1. There are **more** people and **limited** resources in the world; and
2. It's a **dirty** world and a **fake** world.

There are more people and limited resources

The world we inhabit has an increasing population, but limited resources. The global population passed the 7 billion mark in 2011 and according to the most likely fertility projections will probably reach 8 billion by 2025, 9 billion by mid-century and 10 billion by the end of this century. Most of this increase will take place in some of the poorest regions of the world. We are already experiencing the fact that the world's physical and biological resources are limited and even at present levels there are shortages of energy, foodstuffs, water and raw materials. As the population grows, there will be increasing demand for a wide range of physical and biological products and for methods of production and waste management that do not harm the environment. These are all areas where ingenuity and innovation in the chemical sciences can be harnessed globally for the benefit of the global population.

Because of limited time, I am only going to look briefly at a few of these topics today.

Energy

Coming here to the INRS-EMT Centre, I don't think I need to tell you about the kinds of research that are going on in the Energy field or about the potential of the chemical sciences to contribute to developing new methods of energy generation. So I just want to say a little bit about the context,

Most of the world's rapidly rising consumption of energy has involved the burning of fossil fuels (oil, coal, gas) and apart from the issue of atmospheric pollution, which I will come on to later, there is the challenge that these are finite resources that will be seriously depleted in the next century. And oil, of course, is not only a source of energy but also a feedstock for a vast array of petrochemicals that are used in many other industries. Most of the increase in demand for energy is coming from LMICs – especially the large populations in the Asian region.

So, taking a step back from the details of the science that needs to be undertaken to alleviate this global energy crisis that the world is facing, what are the broader science and policy goals that we need to have in place?

The overall goal needs to be to find ways of sustainable energy creation and use in a “low-C economy” that meets two central human needs:

- Energy security: reducing dependence on finite supplies of fossil fuels
- Environmental security: reducing emissions of greenhouse gases

The scientific challenges cover the fields of energy generation and storage; the transmission and transportation of energy; as well as energy for transportation.

The policy challenges involve: defining the goals and targets; creating enabling conditions and incentives for the science to be carried out and the goals to be met; and concurrently de-incentivizing non-sustainable and environmentally unfriendly energy sources.

And, as anyone who keeps an eye on local, national or international affairs will be aware, it is at the interface between the science and the policy domains that the biggest challenges are to be found. Just to mention two examples from my own local and national context – (1) wind turbines were initially greeted with great enthusiasm by many in the UK as a potentially major contributor to generating ‘green’ energy – but as soon as they began being built, local opposition groups began to object to them on the grounds that they are noisy, unsightly and kill birds. Similar reactions have been seen in many parts of Europe. (2) For many years nuclear energy was seen as a vital policy option and the UK invested heavily in building nuclear power plants. There was always a vocal, but not very influential, opposition to nuclear energy in the UK. But following the Chernobyl disaster in the Ukraine in 1986 and the Fukushima disaster in Japan in 2011, many European countries have down-regulated or suspended their nuclear programmes as a result of public pressure. Faced with a critical energy gap coming in a few years’ time, the UK has very recently changed policy again to re-start investment in a new generation of nuclear power stations.

These two examples serve to illustrate the critical importance of science being in tune with policies – and since these policies are made by politicians who pay a lot of attention to public opinion, it is critically important for scientists to engage with both politicians and the general public to ensure that the science they do is acceptable and that policies and opinions are informed by sound scientific evidence.

Food

Turning now to the question of food for the planet – there are issues about Quantity, Quality, Safety and the Sustainability of global food supplies.

The Green Revolution began with the work of Norman Borlaug in the 1960s. Through the development of high-yielding, resilient varieties of plants and application of modern agricultural production techniques, paying attention to soil chemistry, irrigation and the use of fertilizers and pest control agents, the Green Revolution ensured that the production of foodstuffs globally has more than kept pace with the increasing world population since the middle of the last century.

But as illustrated by this Figure, the global surplus of food as measured by total dietary energy supply is decreasing and on present trends the surplus will have disappeared by the middle of the century. Even under this scenario of a present global surplus, 1 billion people were under-nourished in 2009, while >30% of the food produced went to waste; and while the percentage of hungry people in LMICs has decreased for decades, the absolute number of hungry people in LMICs barely dipped during this period. And despite the central importance of agriculture to human welfare and this clearly recognized coming food crisis, agriculture R&D currently makes up only 5% of total global science R&D.

It has been estimated that global food demand will increase by 70% by 2050and global food output will need to double to keep pace with this. This would require an annual productivity increase of 1.75%, while the present trend is an increase of 1.4%, so the prediction is that the food gap will widen. The Food and Agriculture Organization has projected that even if doubling of world food production was achieved by 2050, nearly 300 million people would remain under-nourished. And at current rates of growth, this doubling is not going to happen.

And one of the reasons for this is the impact of global warming on agricultural productivity. As it happens, Canada is one of the few countries in the world that will see a net increase in agricultural productivity from global warming. Most regions, including where the large and growing populations in

LMICs reside, will see a net decrease, both in yields of important staple crops such as maize and in overall agricultural productivity.

There are numerous potential contributions that the chemical sciences can make to meeting these challenges. For example, genetic modifications can create new crop varieties that are resistant to pests and herbicides; and that can thrive in environmentally challenging conditions. But resistance is a property of people as well as of plants. There has been great resistance to GMCs in Europe, for example, where protest movements have labelled GMCs “Frankenstein foods” and have destroyed crop-growing experiments. And in Mexico, all experimental and commercial planting is currently on hold while a legal battle is settled involving activists, agrochemical companies and researchers.

So, the science and policy goals for global food must include: Sustainable production and consumption of food that provides adequate nutrition and does not harm health or the environment.

A very interesting movement that has emerged in the last couple of decades is the ‘One Health’ initiative. This is dedicated to improving the lives of all species—human and animal—through the integration of human medicine, veterinary medicine and environmental science and it sees all three of these as being intimately inter-related.

The initiative champions the need for a multi-disciplinary approach – and requires that science and policies in any one of these areas must take account of the other two.

And no-where is this need for an integrated approach to human and animal health and the environment more urgently required than in tackling the problem of antibiotic-resistant bacteria. I am grateful to Sally Davis, England’s Chief Medical Officer, for providing a number of the slides I am using on this topic.

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 even in 1928 the first examples of bacteria developing resistance to antibiotics were seen, and in his Nobel Prize acceptance speech in 1945 Fleming warned that this 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 could look back on a golden age when fewer than 7% of deaths were being caused by infections. It is estimated that on average antibiotics 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 – to the extent that many people, including politicians like the Prime Minister of the UK – are publically declaring that we are now facing a crisis.

There are at least 4 major factors driving this crisis in ARB:

- Antibiotic misuse: including over-prescribing in some countries and unregulated over-the-counter access to medicines in others. Failure to complete the necessary course of treatment with antibiotics also helps to select for resistant strains of bacteria.
- There is also massive veterinary use of antibiotics to maintain animal health, especially under modern factory farming conditions, and to promote animal growth – also a major factor in breeding resistant bacteria that cross into the human population.
- Environmental contamination – I will speak about this shortly.
- And we are also living in a period of a discovery void.

So, as I mentioned, many new antibiotics – and whole new classes of antibiotics – were discovered or synthesised during the 20th century. But we are now in a ‘discovery void’ – not a single new class of antibiotics has been discovered since 1987. And at least 3 major factors have contributed to this 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 new life science technologies, that have been heralded as the potential source of all kinds of new medicines, including antibiotics, have so far failed to yield new approaches in the treatment of bacterial diseases.
- 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 market size. 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, further disincentivising the market in an area where the economic returns are already poor.

So the present picture, as summarised in The Lancet Infectious Diseases journal in 2013, is that ""We stand 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 because any kind of surgical procedure will carry a high risk of infection.

On the science side, the challenge is not only to develop new classes of antibiotics. For example, there is a critical need for better tools to be able to recognize resistant organisms and diagnose their type. In 2014, the UK Government launched a new Longitude Prize, worth £10 million (over CDN$ 18 million) "to help solve one of the greatest issues of our time". Following a vote by the public, the challenge for the Longitude Prize will be, within 5 years, to create a cheap, accurate, rapid and easy-to-use point of care test kit for bacterial infections. These test kits will allow more targeted use of antibiotics, and an overall reduction in misdiagnosis and prescription and they will form a vital part of the toolkit for stewardship of antibiotics in the future.

A final word about limited resources: regarding materials. We are faced with the prospect that limited world supplies of many of the elements and natural will become a serious constraint during the 21st century. This presents a host of challenges – and opportunities – for the chemical sciences to create new materials with useful properties for a very wide range of applications. Crucial criteria for these new materials is that they should be low in carbon; have a low-energy footprint; and be environmentally friendly.

I don't have time to go into this area in any detail today, so let me just give you one example of an interesting new material that meets these sorts of criteria. It comes from the work of Takuzo Aida's group in Japan and offers the possibility of replacing plastics for many applications with novel hydrogels. In this work, a dendritic material with multiple arms, each ending in sticky guanidinium groups, was mixed with clay nanosheets with a dispersant in water, producing an aquamaterial that is 98% water and less than 0.4% organic components. This aquamaterial is transparent, non-flammable and environmentally friendly. It is easy to mould and similar to silicone rubber. It promises to have a very wide range of applications.

It's a dirty world and a fake world

- It's a dirty world: in which we are faced with increasing levels of contaminants in the environment, food and pharmaceuticals.
- It's a fake world: and it's especially worrying that counterfeit drugs are becoming increasingly available.

One extremely serious source of contamination of the environment is the emission of greenhouse gases into the atmosphere, which have been generating a significant increase in global temperature over the last century. Most of the main greenhouse gas, carbon dioxide, results from power generation. While the long term solution must be to stop burning fossil fuels, a lot of current attention is being given to the approach of capturing the CO_2 to prevent its release into the atmosphere. Increasingly, attention has turned to the possibility of utilization of the captured CO_2 in various ways. CO_2 is a reactive molecule that can be converted to a wide variety of products. However, many of the current utilizations result in the CO_2 eventually being recycled into the atmosphere: there is a challenge here for chemists to develop new applications of CO_2 that deliver valuable products and processes where the carbon remains permanently out of the atmosphere.

Another very important example of environmental contamination concerns pharmaceuticals. To take an example, a 2011 report in *Nature* discussed high levels of pharmaceutical ingredients in treated effluent from wastewater-treatment plants and in effluent downstream from pharmaceutical factories, with examples coming from India, the USA, and the European Union. It is important to recognise that there has been a systematic failure, at both national and global levels, to deal with these problems. As the Nature report observes: *"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." Equally importantly, however, we need to recognize that such regulations are meaningless without very rapid, accurate, sensitive and affordable analytical techniques: without these, it will be impossible to police and enforce regulations. There is a challenge here for chemists, biotechnologists and instrument makers to develop new analytical tools that can be applied at or close to the site of contamination and that will give reliable results that will hold up in courts of law.

A complementary area of very serious concern is the contamination of pharmaceutical products themselves, and also 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.
- In China, widespread adulteration of infant feeding formulas with melamine (trimer of cyanamide) caused serious harm on a large scale.
- And 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.

There are a number of important lessons to be drawn about drug and food safety in a globalized world:

- The problem is often only identified when large numbers of people or animals are affected and there are numerous deaths.
- Deliberate contamination may be widespread but escape detection in poorly regulated markets.
- Contaminated raw material may cross national boundaries and be used in more well-regulated markets.
- It is not clear that regulatory organizations have the capacity to deal with the problem.
- There is a need to develop cooperative programmes to detect and limit these global outbreaks.
- The relevant scientific communities need to develop proactive global approaches to this global problem.

The challenges with pharmaceuticals go much further than this – so let's look more broadly at this area. Prior to the 19th century, pharmacy was a cottage industry – locally based apothecaries would each make up their own remedies and the general public was at the mercy of practices for which there was little evidence and no regulation. During the 1800s, better science and better regulation began to transform this picture, ensuring that products sold to the public to treat their ill health were both effective and safe. The huge demands for products that are effective and safe has driven a massive amount of investment in science, both in the public and private sectors, with the result that the pharmaceuticals and biotechnology sector attracts the largest amounts of R&D investment of any sector in the world.

So the modern pharmaceutical industry presents a very different picture to the 19th century cottage industry from which it grew. Globally, it is now a vast industry with annual sales of c. US$ 1 trillion. The largest pharmaceutical and biotechnology companies employ over million highly trained people worldwide and invest tens of billions of dollars a year in R&D. Canada, as an example, has a significant share in this global picture.

But the global pharmaceutical industry faces some very considerable challenges in the 21st century and I would like to highlight a few of these here.

First, it's important to note that pharmaceuticals are moving East and South.

- ***Consumption*** is moving East and South: North America and Europe, together with Japan, dominate world pharmaceutical sales in terms of total sales. But in the recent period we have seen compound annual growth rates (CAGRs) of only 0-3 % in North America and Europe, while we have seen CAGRs of over 10% in Latin America and the Asia-Pacific region. These new, rapidly growing markets have been termed the 'pharmerging' markets and one of the leading pharmaceutical market research companies, IMS Health, has projected that pharmerging markets will drive c.65% of global pharma growth over the next several years.
- ***Production*** is moving East and South: At the end of the 20th century, 90% of the world's pharmaceutical production was concentrated in high-income countries and there was little or no production capacity in several regions, including Africa and parts of Asia and Latin America. But that picture has begun to change rapidly in the last decade and we are seeing more and more production moving to cheaper locations in LMICs – and especially, for example, to India and China.

Bangladesh also has a growing local pharmaceutical industry. Even in Africa, where production capacity is at its weakest, there are efforts under way to expand production. Of course, a major concern as new sites of production come on stream is how to ensure quality: this requires a combination of regulation and enforcement and relies heavily on the existence of national laws and effective policing; and the existence and effective operation of national drug control laboratories, which so far has been a very big challenge in Africa.

- ***Research*** is moving East and South: Pharmaceutical R&D is globalizing – including, expanding substantially in what have become known as "innovative developing counties" like India, China and Brazil.
    - Brazil enacted a new Patent Law in 1997 to encourage innovation and has made large increases in investments in R&D..
    - India has long been known as the "pharmacy of the developing world", producing cheap versions of known drugs for markets in low- and middle-income countries. More recently, Indian pharmaceutical companies have begun an intensive innovation drive to create new molecules.
    - China has invested heavily in R&D infrastructure and many multinational companies have been establishing operations there. They are now shifting their focus from late-stage drug development and R&D outsourcing to setting up a second wave of more fully integrated R&D capabilities.
    - As a region, Africa has the weakest capacities for drug development as well as drug production – but efforts to change this are now under way, with a commitment by the African Union to strengthen both pharmaceutical innovation and production and new initiatives such as the African Network for Drugs and Diagnostics Innovation.

While this geographical shift has been under way, there has also been a major scientific change in the nature of pharmaceuticals. A significant proportion of the new molecular entities registered as drugs in the last 20 years has been large biological molecules rather than small drug molecules and it is predicted that this proportion will increase significantly in the next few years. The new biologic drugs include a range of proteins, nucleic acids and carbohydrates with a variety of biological activities.

But registration of the new types of products is not straightforward: we are dealing here with molecules that are usually produced by biological processes rather than synthesis. They are often high molecular weight, fragile, and have complex structures that can vary in subtle ways that can be strongly influenced by the conditions of production.

Over 300 new biologic products have been approved by the US Food and Drug Administration (FDA) in the last dozen years. In 2012 the biologic drug market generated worldwide sales of US$ 169bn; predicted to rise to $220 billion by 2019 and because of the high expense of these drugs there is great demand for lower-cost biologics, driving interest in "generic" versions known as "biosimilars or "follow-on biologics".

A number of early biologics are now off-patent; but meanwhile the process by which generic versions can be registered is still being worked out. Thescience challenge is: when is a generic biologic equivalent to the original patented version?

- The European Union has a specially adapted approval procedure for "*similar biological medicinal products*." – demonstrates *"comparability*" of the *"similar"* product to an existing approved product
- In 2010 the USA introduced an abbreviated approval pathway for biological products shown to be "biosimilar to, or interchangeable with", an FDA licensed reference biological product.

There is obviously a need for greater harmonization in terms of the regulatory functions of these two prominent regions. But the underlying problem is at least in part scientific and is an analytical challenge – In the case of a complex biological molecule, how do you use analysis to ensure the functional identity of different batches or of successor biosimilars?

The present view is that there is no silver bullet:

- No one analytical technique is sufficient to properly characterize all the ways the structure of a follow-on can vary from that of the innovator product.
- There is consensus that multiple, orthogonal approaches to characterizing a follow-on biologic will be necessary.
- And it is highly likely that some form of clinical trial data will be required to establish that the follow-on product is safe.

So life is much more complicated for analysts dealing with biologic drugs and this may be an area where new science and new analytical approaches could have a very major impact.

Looking at the world of fake drugs, it's estimated that counterfeit drug sales were worth US$ 75 billion globally in 2011. Counterfeit medicines are estimated to constitute more than 10% of the global medicines market, with a range up to 50% in some low- and middle income countries. 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 active ingredients in US drugs come from overseas sources.

Of course, these types of fraud have been made very much easier by the use of the internet as a source of pharmaceutical products. A case in 2011 involving a Belgian man illustrates some of the typical global characteristics of these crimes. He was extradited from Costa Rica to the USA and convicted and jailed for 4 years. When we look at the details of the fraud, it involved production, marketing, supply and payment chains operating across several countries and making it very difficult for national enforcement agencies to catch and successfully prosecute the perpetrators. In this particular case, the Canadian accomplice escaped capture.

WHO assessments have 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. Sometimes the lack of effective treatment can potentially result in death. Examples include this fake treatment for malaria; this counterfeit of the anti-cancer drug Altuzan which was found being prescribed in the USA but had no active ingredient; and these counterfeit copies of Pfizer's statin product Lipitor.

It is clear that:

- The problem has reached a global dimension and needs a global approach.
- But in many places there is absence of, or weak, drug regulation

As the WHO stated 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 that hardly functions.

And alongside these regulatory challenges, there are clearly scientific challenges in how to detect counterfeit medicines in the field. There is no single approach to technologies to prevent/identify counterfeits: a combination of methods essential, especially as the dosage and packaging can become separated along the supply chain. It has been predicted that the world market for pharmaceutical anti-counterfeiting technology will rise to roughly US$1.2 billion in 2015.

So, let me conclude this section by pointing to some general conclusions.

First it is clear that there are major scientific challenges and opportunities to develop new chemistry products and processes and that these need to be safe, effective, affordable and sustainable.

Second, there are challenges for regulation and some of these challenges involve the need for better cooperation and harmonization among analysts; and better cooperation and harmonization between analysts in all fields and policy makers.

This communication between scientists and policy makers needs to embrace all the stages of dialogue, decision-making, regulation and enforcement. It needs to involve the different sectors such as pharmaceuticals, food and the environment; it needs to include policy makers and national, regional and global organizations. But one of the problems is that there is a huge number of these interested parties and stakeholders among these various scientific and policy communities. There are national and regional regulatory authorities, and scientific and professional bodies representing different subjects, techniques and categories of scientists, as well as civil society and industry bodies with a stake in the game.

So the question is, how to make some sense of this, and have a dialogue and a system of regulatory governance that is fit for purpose in the globalized world of the 21st century? Well, perhaps it's time that we saw the creation of a World Organization for Regulation of Food, the Environment and Drugs (WORFED)?

To conclude this presentation, I have talked about challenges in science, capacity for science and governance of science; and the need to have much more effective and productive communication between scientists and policy makers. In particular, there is need for:

- Policy-makers to develop evidence-informed policy and an understanding of the significance of research results;
- And for scientists to conduct policy-informed research and to develop their understanding of the significance of policy and practical constraints.

And there is a need for the collective development of a shared non-technical language and a shared understanding about issues – especially those concerning questions of 'certainty' and 'risk'. None of this is at all easy.