40

1978
2018

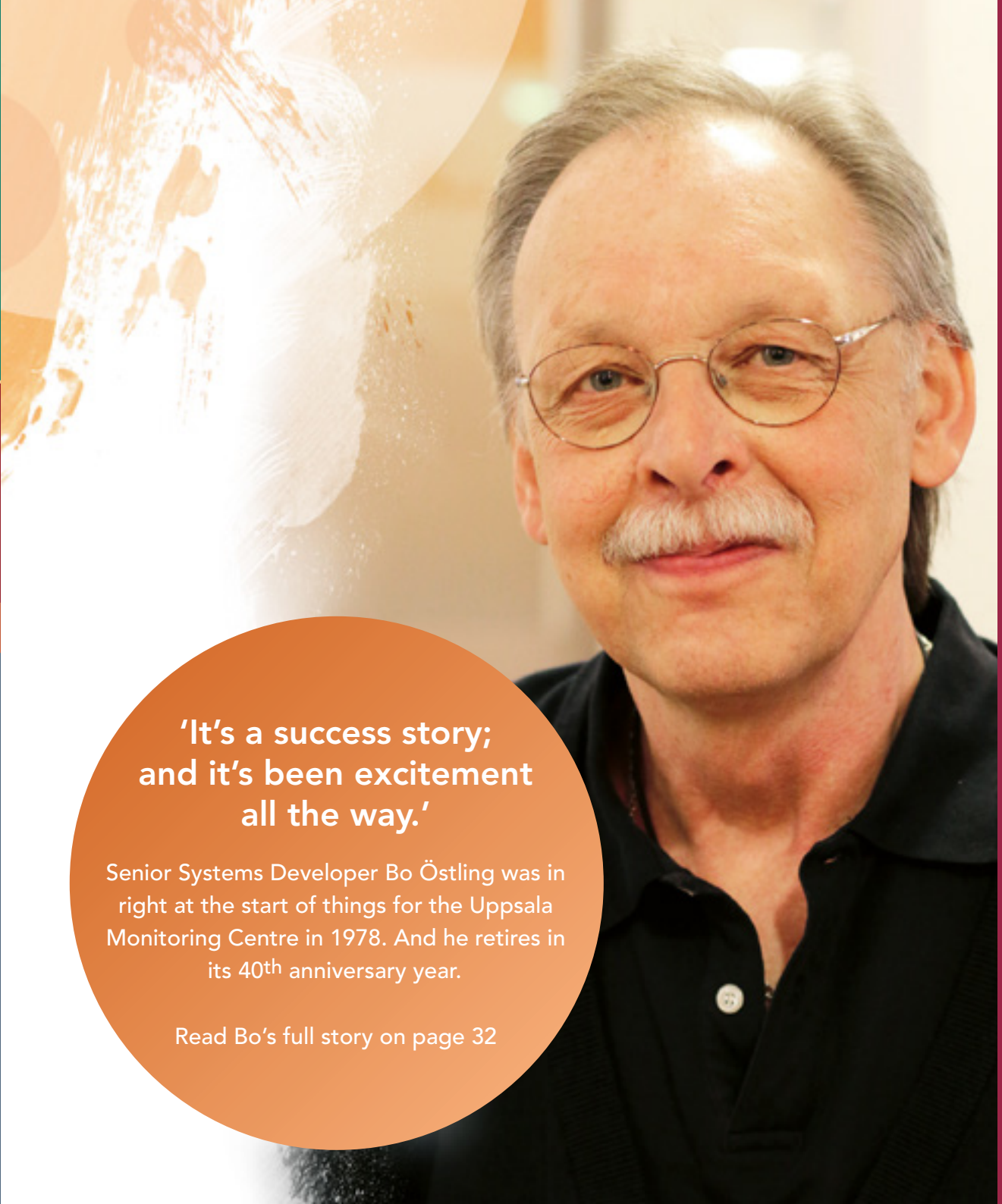
MAKING MEDICINES SAFER

Uppsala Monitoring Centre – 40 years of pioneering pharmacovigilance

safer medicines – safer use – safer patients

Uppsala Monitoring Centre

WHO Collaborating Centre for International Drug Monitoring



‘It’s a success story; and it’s been excitement all the way.’

Senior Systems Developer Bo Östling was in right at the start of things for the Uppsala Monitoring Centre in 1978. And he retires in its 40th anniversary year.

Read Bo’s full story on page 32

MAKING MEDICINES SAFER

Uppsala Monitoring Centre – 40 years of pioneering pharmacovigilance

Making Medicines Safer marks Uppsala Monitoring Centre's pioneering first 40 years, through the words of some of those who've contributed to and benefited from its success. These diverse faces and voices are all members of the Centre's global family.

Watch the short film that accompanies this publication at www.youtube.com/c/UppsalaMonitoringCentre

Published by Uppsala Monitoring Centre
(a not-for-profit foundation and the WHO Collaborating Centre for International Drug Monitoring)
Box 1051
SE-751 40 Uppsala, Sweden

Tel: +46 18 65 60 60
Email: info@who-umc.org
Internet: www.who-umc.org

Uppsala Monitoring Centre

WHO Collaborating Centre for International Drug Monitoring

ISBN 978-91-639-7587-5

Designed and typeset by Vajer [wire], Sweden
Text set principally in Mercury and Avenir

Printed and bound at Åtta.45, Järfälla, Sweden

NORDIC ECOLABEL
3041 0001
PRINTED MATTER

Inside

Page

UMC, the world, health, technology and space…

Only a few aspects of human existence achieve the same level of international cooperation as the World Health Organization's Programme for International Drug Monitoring. UMC's 40-year story also closely tracks the beginning and development of the digital age.

So this celebration highlights important milestones in the wider world – in health, technology, space travel and climate change, alongside UMC's key growth points and achievements.

Look out for these icons: WHO Programme membership Associate membership Health Technology Space Climate

UMC 1978–2018

Uppsala Monitoring Centre (UMC) in Sweden exists to help make the world a better place. Created in 1978 as the Collaborating Centre for the World Health Organization's (WHO) Programme for International Drug Monitoring, its work potentially affects nearly every person on earth. The Centre's success in building a global family and culture of patient safety is a forty-year story of positive, international cooperation.

Per Manell and colleague in Geneva, 1978.

Working as an independent, not-for-profit foundation with day-to-day responsibility for the WHO Programme for International Drug Monitoring, UMC's multi-disciplinary team is dedicated to promoting the safer use of medicines for patients everywhere, through the science of pharmacovigilance. 2018 also marks WHO's 70th anniversary, and 50 years since the start of the WHO Programme. Membership now comprises 130 full member countries and 26 associate nations, representing more than 95 per cent of the world's population.

Across every continent, pharmacovigilance centres are on constant alert for adverse drug reactions and other harmful effects of medicines. While each country responds to problems in its own territory, UMC takes a unique, supra-national view of emerging patterns and problems. The Centre issues signals of new concerns, which might not be evident from a single country's data.

Over the years, the WHO Programme and UMC have provided leadership, developed norms and set standards in data management, training, international collaboration and the protection of patients. Pharmacovigilance is now embedded as an essential element of modern public health and patient care all over the world.

Most people use medicines at some point in their lives, so they need to understand what they are taking and the risks involved. With around half a million medicinal products on the worldwide market, there's an almost infinite number of ways in which harm can arise from treatments themselves or from interactions between them, as well as from dietary, environmental and genetic factors. Poor quality and fake medicines are also constant threats in many parts of the world.

Pioneering pharmacovigilance for patient safety

Since 1978, UMC has supported the international WHO pharmacovigilance network and provided useful information about adverse effects for the world's citizens, patients, clinicians, regulators, scientists and pharmaceutical professionals. Rooted in the international outcry after the tragic birth defects caused in Western countries by thalidomide in the 1960s, UMC has grown from small beginnings to become the vital world epicentre of medicines safety. The Centre is constantly watching for signals of adverse effects, to help keep clinicians and patients informed and support wise therapeutic decisions.

The quest for improved safety has and seeks no end

UMC's story so far spans moments of inspiration and breakthrough, and periods of struggle and conflict, directed and performed by a strong cast of diverse characters. And its growth traces the parallel journey of information and communication technologies; from the realm of science fiction to the everyday essentials of modern life in many countries.

The quest for improved safety has and seeks no end. It's a dynamic discipline that's constantly evolving to meet the challenges of new science and treatments, growing markets and changes to the way medicines are produced, distributed and used.

World-class science

UMC provides ground-breaking analysis of the WHO global database of individual case safety reports, *VigiBase*. This scrutiny helps to detect problems and support rapid local action to prevent and limit harm. The Centre also maintains *WHODrug* – the world-leading WHO Drug Dictionary of medicinal products and their ingredients.

Pessimists may doubt if it's possible to prevent multi-national, commercial interests from overriding the welfare and rights of individuals, especially in countries with low and middle incomes or less-developed healthcare systems. But the success of WHO's international pharmacovigilance programme shows it can be done, and done well.

With the global population set to reach 11 billion by 2100, humanity needs a joined-up, international framework for safer medicines and patient safety now more than ever. UMC will continue building and supporting this community. And reading this book makes you part of it

A global system for safer use of medicines

UMC's continuous scientific research and development of analytical tools and methods maintains a constant worldwide watch for the adverse effects of medicines. And its outreach, training and public information campaigns help to build awareness and capacity in every member country.

This diagram gives a simplified overview of how local and global pharmacovigilance systems work together to support patient safety across the world. The critical medicines safety decisions and communications for member countries of the WHO Programme for International Drug Monitoring are made locally, but they may be prompted or informed by the global perspective of UMC's data and communication. Almost all countries use the Centre's tools and resources in their systems, with electronic health records and other sources of patient data also playing an increasingly important role.

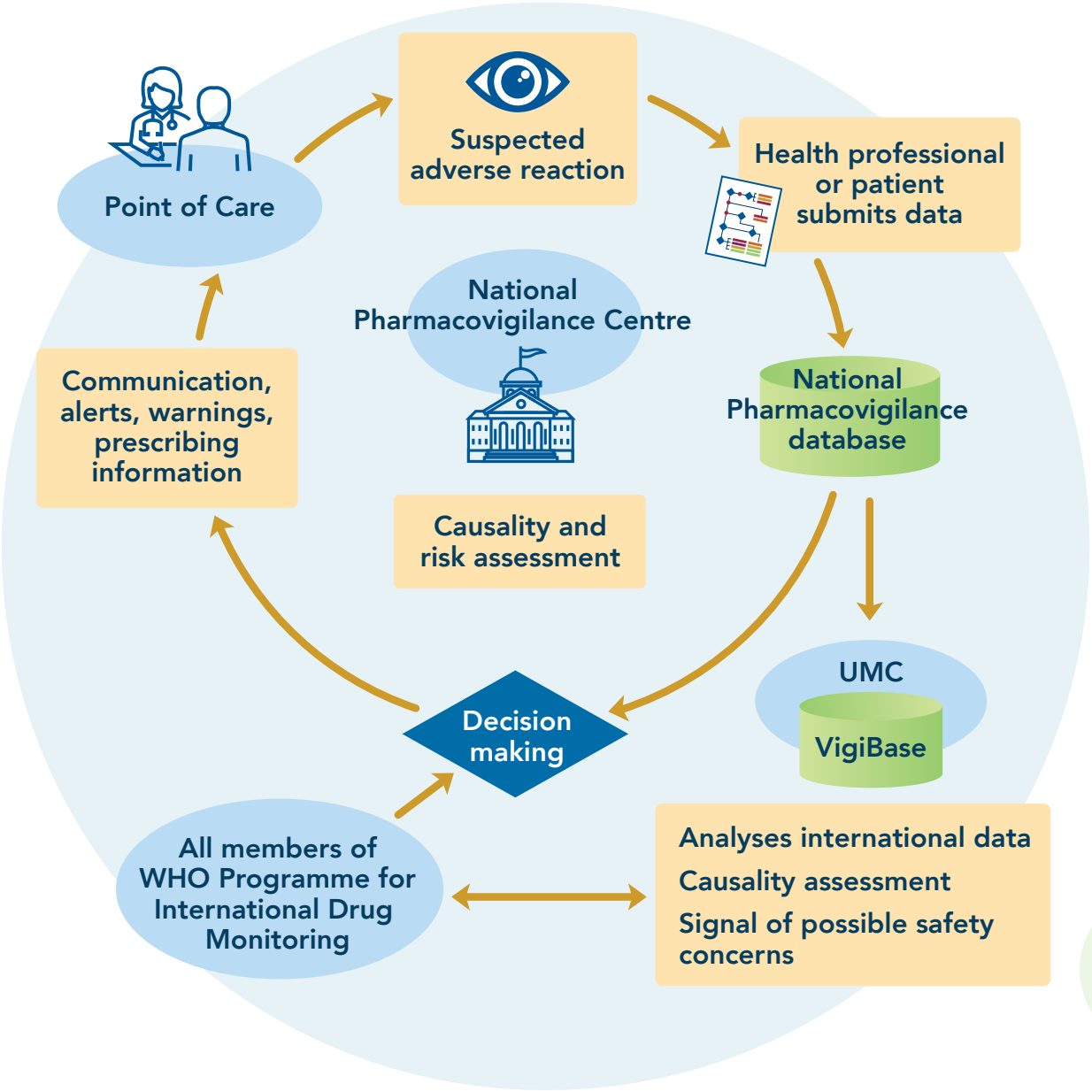
Pharmacovigilance begins and ends at the point of care and the therapeutic experience of patients. At every stage, communication plays a crucial role – from accurately reporting suspected adverse effects and assessing causality and risk, to delivering information for patients and health professionals that is wise and useful.

Pharmacovigilance

'The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems.' ●

World Health Organization

A simplified overview of the local and global pharmacovigilance systems



A global family

Ask people involved in patient and medicines safety across the world what UMC means to them, and they talk about its success in building and nurturing a truly global pharmacovigilance family. It's taken time, determination and visionary leadership, but the steady spread of WHO Programme membership and numbers of individual case safety reports in the Centre's VigiBase system speak for themselves.

The many and the few

Most of UMC's work starts with individual reports of suspected harm caused by medicines – pinpointing occasions where sometimes a very small number of people have experienced real harm, or even died, because of an adverse reaction to medicine. This highly qualitative approach (often only brought to light by analysing and comparing people's personal stories of illness) can sit uneasily alongside the quantitative, sister science of pharmacoepidemiology – studying the effects of treatments in whole *populations*.

1968
10 member countries,
world population 3.5 billion

2018
130 member countries,
26 associates,
world population 7.6 billion

This larger-scale methodology informs the traditional model of public health – concentrating on norms that deliver the greatest and most cost-effective benefit for most people. It's about what happens to the majority, whereas pharmacovigilance is concerned with rarer effects that *don't* happen to the majority.

In some instances, only a small number of people can be affected, but if the evidence is strong and the impact is severe, then these are signals of which the world needs to take note. UMC's analysis helps to inform the tough decisions that regulators need to make, when concerns about safety of medicines come to light.

Death or serious injury to a few people may not justify limiting or withdrawing a medicine that benefits millions of people, and which has taken years of costly development to bring to the market. Pharmacovigilance shines the light of ethical conscience on this sort of decision by finding out *why* some people experience adverse effects, and how this can be avoided or minimised in the future

Death or serious injury to a few people may not justify limiting or withdrawing a medicine that benefits millions

VigiBase individual case safety reports 1978–2018

1978
115,000

1995
1.5 million

2004
3 million

2010
5 million

2014
10 million

2018
16.8 million

Inspiration, innovation, integrity

Organisations are only as strong as the values they stand for and the way they live up to them. Three core principles underpin and inform everything that UMC does, and drive its commitment to inspire, engage and transform. These values decorate an entire wall in the Centre, and are at the front of every staff member's mind as they go about their work to make the world a better, safer place. They're also the words people from all over the world use to describe their contact with UMC and experience of its work.

Inspiring…

People – practice – standards – growth – improvement – education – training – collaboration – friendships

and innovating…

Ideas – technology – methods – tools – analysis – products – communication

with integrity…

Honest – true – open – complete – transparent – determined – focused – ambitious

…and a Swedish twist

Sweden's fourth largest city, Uppsala is steeped in history. Twelve Swedish kings were crowned there, and it has Scandinavia's oldest university, founded in 1477. This was the academic home of Prof Carl Linnaeus (1707-1778), the father of modern, scientific taxonomy. A botanist, zoologist and physician, he developed the system of classifying and naming organisms, which remains the basis of all natural science today.

Linnaeus is also considered one of the founders of modern ecology, and he rests beneath the twin spires of Uppsala's magnificent 13th century Lutheran cathedral; his remains are still the type specimen for our Homo sapiens species. Right opposite is the world's second oldest anatomical theatre, inside what is now the Gustavianum Museum.

This exceptional scientific and medical heritage combines with a national working culture that favours flat, non-hierarchical organisations and a willingness to debate and argue openly in pursuit of consensus. Swedish working relationships are

Ralph Edwards
(see page 36) on Sweden:

'Sweden's image is of a stable, social democratic country with high standards of humanity and technology. This has really helped UMC to reach out and relate to other countries.'

less formal and authoritarian than in many other countries. This aids good communication and fosters an atmosphere in which people are allowed to make mistakes and so encouraged to use their initiative. Scandinavian communalism can take time, patience and effort, but when it's done right, everyone benefits

Risk, benefit and harm

What is life about if not risk? We all take – and accept without thinking – significant risks everyday. We do this because the likelihood of harm is low, and the benefits are great. Driving, air travel, eating and drinking can all fall into this category. No medicine is 100 per cent safe, and patient outcomes depend on a dazzlingly long and complex chain of interactions and choices, with hazards lurking in every link. UMC keeps watch on this ever-changing landscape to support wise therapeutic decisions.

What risk means

Living is not a safe occupation. While we all *know* this, our *perceptions* of risk and attitudes towards it vary according to our individual psychology, circumstances, experiences, culture and language. Most people expect medicines that are authorised for use to be safe, when in fact they usually present a low, but real, probability of harm in the context of the conditions they treat and their expected benefits. Someone with a serious disease is more likely to accept a potential adverse effect than someone with a minor illness, for whom any harm may seem a much greater burden.

There is increasing public and political pressure to reduce or – the impossible dream – to eliminate risk. But pharmacology and healthcare are complex and uncertain pursuits, and clinicians are fallible. So the goal of pharmacovigilance is to provide the knowledge to use medicines wisely and well, to reduce harm and achieve an acceptable level of safety. Even when this happens, there will still be rare, unavoidable, unlucky or even negligent instances when treatments cause harm or even death. And that's when quality, individual case safety reports really count. This is the heart of UMC's scientific territory.

Deciding if the risks of a medicine outweigh its benefits will never be black and white. It's about dealing with uncertainty – trying to find the best balance between warning too early, which could cause unnecessary panic or the withdrawal of useful medicines; and too late, causing avoidable harm.

Effectiveness

Governments, agencies, officials and professionals have a duty to protect the populations they serve from harm. But authorities often have to make decisions on the basis of uncertain or incomplete information, and their actions can be skewed by ideology, faith, tradition or the pressure of events.

Good pharmacovigilance helps to inform a better understanding of the real-world safety and effectiveness of medicines compared to the relatively

Patient safety is a constantly moving target

small-scale testing within clinical trials. Alongside larger epidemiological studies, it also illuminates absolute, relative and attributable risks to identify how likely and serious adverse effects are, compared to people not exposed to the treatment.

Interaction

Patient safety is a constantly moving target of almost infinite variation and complexity. There is growing evidence that the ways individuals react to medicines vary not just by age, sex, environment and genetic differences, but also by tiny disparities in diet, lifestyle and interaction with other substances that we touch, breath or ingest. Even the same person taking the same medicine for the same disease can react differently at different times.

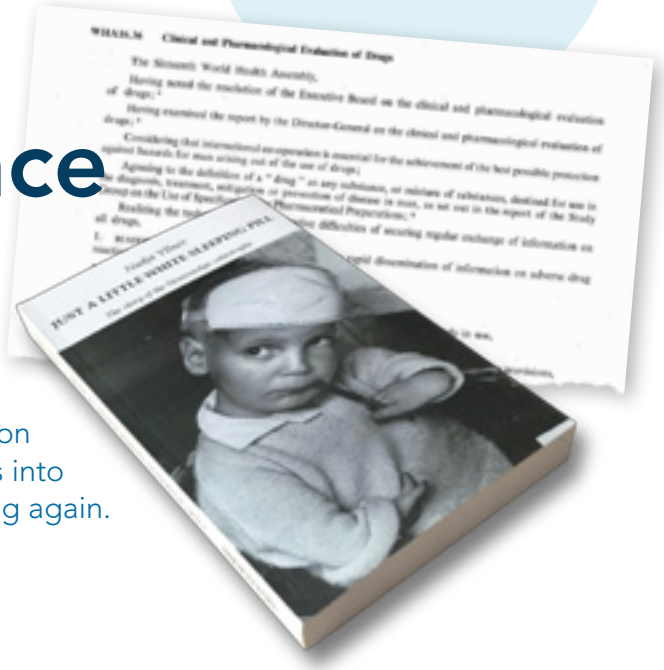
The Canadian pharmacovigilance pioneer Ed Napke (see page 28) sees the human body as a living test tube, into which we pour all kinds of chemicals from all kinds of sources. These may react with one another, and in some cases cause harm.

Dr Napke also believes that, at best, *'we walk into the future backwards'* – trying to make sense of current and future challenges with minds encumbered by old knowledge that can compromise new thinking.

Communication and controversy

Issues around the safety of medicines are often debated by journalists and others with little real knowledge of statistics, scientific method or medical practice. And poor communications from officials and scientists, or the perception of secrecy can stand in the way of open debate. The priorities of manufacturers, regulators, doctors and patients are not always aligned, so this can also contribute to misunderstandings and controversies

Origins of pharmacovigilance



The shocking birth defects caused by the sedative and morning sickness drug thalidomide in the late 1950s and early 1960s woke the world up to the potential post-marketing dangers and side effects of officially tested and approved medicines. The impact on thousands of families galvanised global health leaders into action to reduce the risk of similar problems happening again.

The thalidomide tragedy

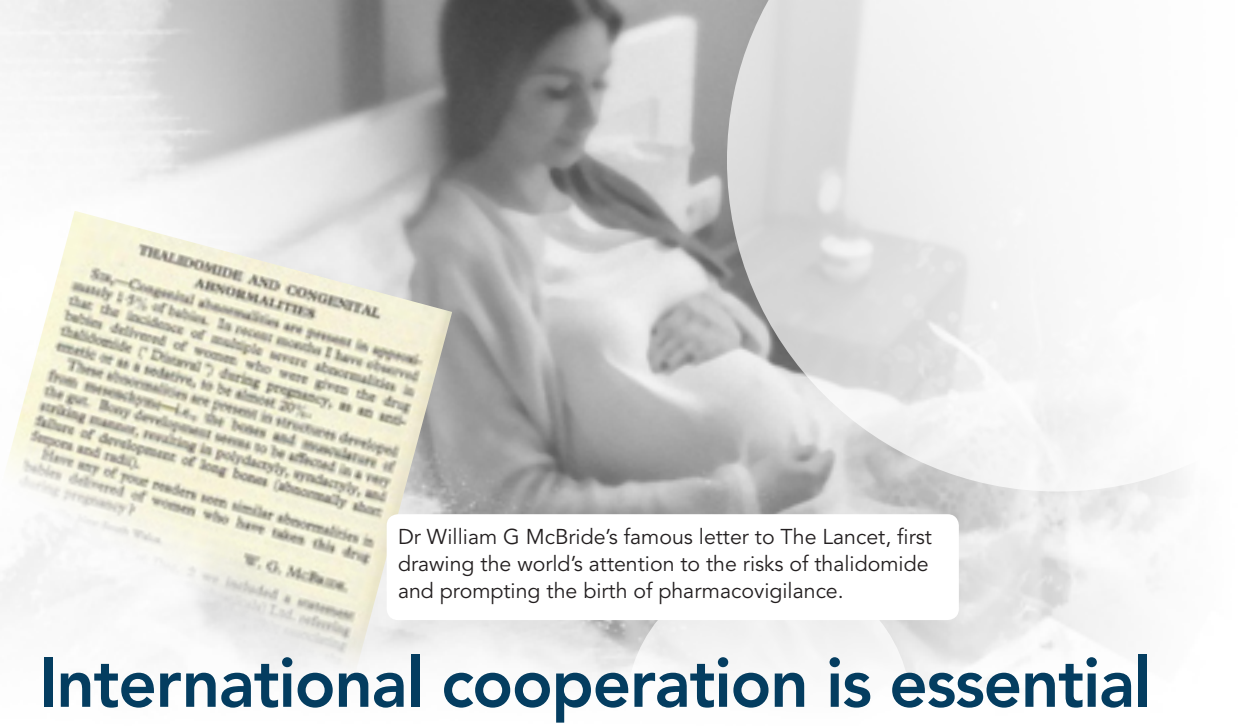
In the late 1950s and early 1960s, around 10,000 babies were affected by birth defects caused by their mothers' use of thalidomide – prescribed to aid sleep and reduce nausea for pregnant women. Serious limb abnormalities were a particularly visible hallmark of the problems caused by this *'little white sleeping pill.'*

Once the drug was withdrawn from sale, people quite reasonably asked why so many children had been born with these problems before something was done. The episode also highlighted the shortcomings of unregulated drug markets and testing being left almost entirely in the hands of pharmaceutical manufacturers.

The tragedy of thalidomide triggered action by governments to regulate medicines, and highlighted the need for proper, international monitoring and reporting to identify adverse effects, especially rare ones. Since that time, thalidomide has been used to treat leprosy and some cancers, but the risks remain the same. These are likely to be well managed in sophisticated cancer clinics, where most of the treated patients are older people. But the safeguards are not equal for women of child-bearing age receiving treatment in environments where the regulations and warnings may be less well understood.

Above all, thalidomide proved that we could not just wait until drug safety crises occurred – and that systems were needed to reduce the risk of similar problems escalating or happening at all. So in Geneva in May 1963, the Sixteenth World Health Assembly passed resolution 16.36 on the Clinical and Pharmacological Evaluation of Drugs.

This landmark declaration said that *'international cooperation is essential to achieve best possible protection against hazards arising out of the use of drugs,'* and reaffirmed *'the need for rapid dissemination of information on adverse drug reactions.'* WHO member states were encouraged to *'arrange for systematic collection of data on*



Dr William G McBride's famous letter to The Lancet, first drawing the world's attention to the risks of thalidomide and prompting the birth of pharmacovigilance.

International cooperation is essential

serious adverse drug reactions,' and to *'continue seeking international acceptance of principles and requirements applicable to the toxicological, pharmacological and clinical evaluation of drugs.'*

This is how modern pharmacovigilance came into being.

Systematic responses

While certainly the best known, thalidomide was not the only influential example of adverse reactions to medicines that forced the pace of change. In the early 1970s, practolol (a treatment for angina and hypertension) led to a syndrome that affected patients' bowels, eyes and skin. The effects were serious, but slow to emerge (averaging almost two years in the most harmful cases).

The experience of practolol further sharpened the science by demonstrating that some adverse effects could not be predicted from clinical trials, and that spontaneous reporting on its own was not enough to secure post-marketing safety. So this led to some countries creating a new approach to systematically observe the users of new medicines, through nationwide prescription event monitoring (PEM) programmes.

These programmes, in the UK and New Zealand, illustrated the need for patients to be properly informed about possible side effects and how to recognise and minimise them. So patient information leaflets became more common and comprehensive, then compulsory in the European Union during the 1990s. Post-marketing studies by manufacturers, plus national guidelines and international standards followed – to create the global safety framework that operates today

Early years, 1968–1977

Five years after the World Health Assembly's resolution, ten countries came together as founder members of the WHO Programme for International Drug Monitoring. These first pharmacovigilance pioneers started work in the city of Alexandria, near Washington DC in the USA, before the Programme moved to WHO's headquarters in Geneva, Switzerland.

Founding members

Australia, Canada, Czechoslovakia, Federal Republic of Germany, Ireland, Netherlands, New Zealand, Sweden, United Kingdom, USA

Early gains

1968

- Format agreed for collection of international data
- Adverse drug reaction terminology and drug dictionary established

First successful heart transplant
Hong Kong flu pandemic

1969

- First definition of adverse drug reaction
- Clioquinol Subacute myelo-optic neuropathy (SMON) reported in Japan, highlighting possible ethnic susceptibility

First computer communications via ARPANET
First humans on the moon

1970

Cholera epidemic in Turkey
Apollo 13 flight
First Earth Day celebrated

1971

- WHO Programme centre moved to Geneva
- Scientific basis of future disproportionality analysis published
- First regular format reports produced

Denmark, Norway
First microprocessor
Mariner 9 spacecraft orbits Mars

1972

- *The Role of National Centres* WHO technical report published

Japan, Poland
300 people affected by Thalidomide offered £11.85 million compensation
First digital watch, video game and handheld scientific calculator

1973

Israel
First use of genetic engineering, barcodes and optical fibres

1974

Finland
Smallpox epidemic in India
First word processor

1975

- Oral contraceptives and venous thromboembolism – acceptance of the importance of epidemiological findings
- Practolol oculo-muco-cutaneous syndrome – belatedly recognised as a new and unexpected adverse effect

Bulgaria, Italy
First microcomputer and supercomputer, video recorder and digital camera
US and Russian spacecraft linked up

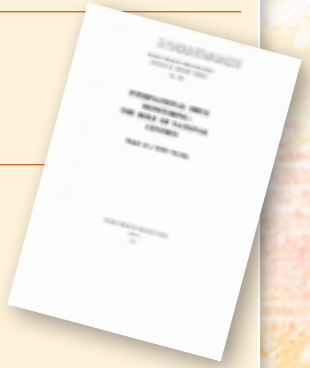
1976

Romania
Ebola epidemic in Sudan
First laser and ink jet printers
Viking I and II spacecraft landed on Mars

1977

- Intensive Medicines Monitoring Programme (IMMP) founded in New Zealand

Belgium
First MRI scan
First integrated personal computer
Voyager I and II launched to explore outer solar system



1978, Sweden steps in

Ten years into the Programme for International Drug Monitoring, WHO decided on a change in direction and priorities – to concentrate its resources onto increasing access to medicines and healthcare in developing countries. With so many nations striving to even obtain essential medicines, safety monitoring seemed like a luxury to some.

This switch of funding threatened to stall advances in the fledgling science of pharmacovigilance, until the Swedish Government and its regulatory authority stepped in to take over responsibility for the Programme – and the Foundation WHO Collaborating Centre for International Drug Monitoring in Uppsala was born

Per Manell (Sweden) and Peter Heslop (WHO), Geneva, 1978.

1978

- First baby born from in vitro fertilization
- First mobile phone and computer bulletin board
- Sweden first country to ban aerosol sprays

1979

- Start of China's one child per family policy
- Anthrax epidemic in Russia
- First spreadsheet, personal music player and commercial cellular network

UMC's early Chairs

Åke Liljestrand

Åke Liljestrand (1917-2000) was Head of the Drug Division of the National Board of Health and Welfare – the precursor of the Swedish Medical Products Agency. He played an important role in persuading the Swedish Government to take on responsibility for the WHO Programme. When the new Collaborating Centre was opened in 1978, he became its first chair and acting director.

Åke also chaired the European Society for the Study of Toxicity and was a member of the WHO Expert Committee for Drug Evaluation. Quiet and modest by nature, he also had a tough streak, and fought hard for his views in scientific discussions

Kjell Strandberg

From 1983, Prof Liljestrand's successor as chair and acting director was the new Head of the Drug Division of the National Board of Health and Welfare (and later Director General of the Swedish Medical Products Agency), Kjell Strandberg. He provided medical support to help establish the Centre in its early years, and was an effective figurehead in representing and promoting UMC and its work in its early years

Pioneers – the politician

The passionate, driving force behind Sweden's decision to host the WHO Programme in Uppsala was Liberal People's Party Member of Parliament, Dr Barbro Westerholm. Still an active politician in her eighties, Barbro has remained an energetic advocate for patient and medicines safety, and close friend of UMC ever since.

Barbro Westerholm

'At the frontier of safety'

An early pioneer of pharmacoepidemiology and pharmacovigilance, Barbro worked on the early stages of the WHO Programme for International Drug Monitoring and the WHO Drug Dictionary (now WHODrug). She did extensive research into the side effects of oral contraceptives, and as general director of the Swedish National Board of Health and Welfare, she had homosexuality dropped from the list of mental health diseases in 1979. First elected to the Riksdag in 1988, she was awarded the Nordic Public Health Prize in 2009 for her work to fight discrimination against older people.

Personal and political

'I never had any thought of becoming a politician, but it's been a fantastic way to raise and promote really important issues. As a low-paid PhD student, I took the opportunity to join the National Board in 1965 to work with WHO and other countries following the catastrophe with thalidomide.

I felt very close to this, because I'd been given a packet of the drug when I was expecting my second child – but decided not to take it. I soon realised that I could help more patients by working for better medicines safety than as a doctor in a clinic.

A tightknit family

We started off in a very small way, with a phone-based system that involved reporting details of suspected adverse effects by phone. WHO head-quarters would then alert other countries using the same drug. A tightknit network grew out of this – a family of individuals united around safety concerns, with a commitment to educate, communicate, develop methodologies and listen to other countries' needs. Even now, if one of us has got a problem in front of us, we know we can pick up the phone to each other.

Even in today's digital age, personal contacts like these are so important. You need to know you're working with people you can trust, who will give you good advice and won't let information leak out and cause unnecessary panic. I think those early relationships laid the foundation for UMC's values of inspiration, innovation and integrity.

You need to know you're working with people you can trust

Per Manell (see page 30) on Barbro Westerholm:

'Barbro helped to create Sweden's scientific platform for safety. She was an early player in building confidence that – if a drug is approved in Sweden – it can be safely used.'

Sweden's decision to step in and take over running of the WHO Programme was part of a campaign by all five Nordic countries. We had already committed to 'Health for All by the year 2000', so this gave us the chance to boost our reputation of being at the frontier of safety. The Government's financial backing and help with premises came together with the qualified staff we recruited, to set UMC on its way.

Looking ahead

Pharmacogenetics is going to play a big part in future patient safety – finding new ways to pinpoint people who are most vulnerable to risk and harm. This is especially important for our growing population of older people, and differences between men and women. It will demand even closer collaboration across global pharmacovigilance, and making more use of direct reports by patients.

In a hundred years, I'm sure we'll know much more about who should take what medicines, so that we can do the very best for patients. We need to keep safety at the forefront of health debates, and keep on highlighting the benefits and risks.'

Pioneers – the pharmacists

A small group of young and enthusiastic pharmacists provided technical support for the WHO Programme after its transfer to Sweden. This was an onerous task, performed in a cost-efficient way thanks to the skilful application of the most advanced database management technology available at the time. The Centre's four decades of success, and pivotal role at the heart of global patient safety rest on the foundations of this pioneering team's early work.

Cecilia Biriell, Marie Lindquist and Sten Olsson

Cecilia Biriell

'Totally amazing growth'

Cecilia Biriell joined UMC in 1978 after working at a research laboratory in the UK. She played an important role in developing the WHO Adverse Reaction Terminology, and maintaining contact with and support for new Programme members and reporting countries, especially in Africa.

A loyal and gifted manager with an exceptional eye for detail, Cecilia also helped to create the Centre's early administrative systems. She retired from UMC in 2015 and went on to volunteer as treasurer for Pharmacists without Borders Sweden.

Simple beginnings

'Thinking back, the technology we had when UMC first started was totally different. We were using typewriters to send letters, and our facilities were so simple. But one of the main reasons for moving the WHO database to Sweden was the modern facilities created by Per Manell (see page 30) and his colleagues at the Uppsala University Computing Centre.

We didn't really know where to start, and progress was very slow for the first ten years. We had just a few scientists and consultants working here. But

Kenneth Hartigan-Go (see page 78) on Cecilia Biriell:

‘Cecilia is one of the icons of UMC and pharmacovigilance‘

We didn’t really know where to start

things really started to pick up from the mid ‘90s, and we’ve seen totally amazing growth since then – in the numbers of Programme member countries, the numbers of reports in our database and the numbers of people working at UMC.

Ambition to succeed

I don’t think WHO ever expected us to do so much – it seemed we were just required to maintain the database as it was. But the signals we published in the British Medical Journal (in 1989 about diltiazem and depression, and then in 1992 on cisapride and abnormal heart rhythms) were real breakthroughs.

The annual meetings of national centres, and the outreach work we’ve done by travelling to so many other countries have been incredibly significant. This has enabled us to show health ministers that pharmacovigilance is really important and has given local experts the back-up they need to develop systems.’

Sten Olsson

'The most sensitive method we have'

Sten Olsson was plucked from his PhD studies at the Uppsala University Department of Toxicology to help establish the new monitoring centre following transfer of operational responsibility for the WHO Programme from Geneva in 1978. He went on to become UMC's tireless, globetrotting ambassador – personally supporting pharmacovigilance development and training in almost 70 countries across five continents.

Sten holds honorary and guest positions at universities in China and India, and has been President of the International Society of Pharmacovigilance (ISOP) since 2016. He is currently playing a lead role in PROFORMA – a five-year project funded by The European & Developing Countries Clinical Trials Partnership (EDCTP) to accelerate the development of new and improved treatments for poverty-related infectious diseases in sub-Saharan Africa.

A great opportunity

'When a colleague told me about the chance to join the new Centre in Uppsala, and I was offered the job, it was too good an opportunity to miss. In offering to take over management of the international drug monitoring programme, the Swedish Government felt that there had been too much investment made and too much data collected, and it would be a great pity to lose all that.

It quickly became obvious that there was a big gulf between our ambitions at UMC and the expectation that we would simply continue to manage and maintain the system. We wanted to continue developing and take things much further. To start with, there was also a fair amount of confusion, criticism and conflict between member countries about why and how they should share data with us. Some nations even stopped reporting for a while, until we'd proved ourselves.

UMC staff and international colleagues with Prof Ralph Edwards, then Chair of the UMC Advisory Group, Dubrovnik, 1985.

Proving our worth

Even now, academic researchers continue to question the validity of spontaneous, individual observations and reports. And there's even still an underlying concern about linking medicines to doing harm.

Causality can often be difficult to prove in particular case safety reports, and of course there are no control groups as such – but this is the most sensitive method we have for detecting rare and serious effects. The vast majority of regulatory decisions are made on the basis of direct experience of clinicians and patients.

To address these doubts in the early days of UMC, we commissioned an independent review of our approach and systems, conducted by Professor Jim Crooks from Scotland. As part of this review, the US Food & Drug Administration's representative, Dr Judith Jones, made a very powerful and telling case for harmonising global reports. So we have a lot to thank her for.

Causality can often be difficult to prove

John McEwen (see page 80) on Sten Olsson:

'Sten is a very good scientist, teacher and speaker. He's made a very important contribution to the confidence of countries developing new systems for medicines safety.'

In the mid 1980s, we also worked closely with Dr Ron Meyboom and his colleagues from the Dutch national centre. They were brilliant at analysing signals, and were – rightly – convinced that our database contained lots more valuable information that was not being analysed and utilised.

Going global

From the early 1990s, we started to get more invitations to visit other parts of the world and talk about patient safety – for example, Peru and Tunisia. And this was the foundation of the annual training courses we started in 1993. These attracted still more interest from low- and middle-income nations, and have really made a big difference. It's great to see that many of the people who attended that first course are still working in and leading global pharmacovigilance. The yearly courses remain a vital part of sustaining scientific progress.

Important as the early years I spent at UMC were, I feel that the projects I've been involved in over the last decade have been even more significant. I'm especially proud to have helped bring China and India into the Programme. I've also worked on situation analysis to support new safety systems in low-income countries, the Monitoring Medicines project and WHO Global Vaccine Safety Initiative and pharmacovigilance indicators.'

Pioneers – the thinkers

UMC's early systems drew extensively on the ground-breaking work by the head of Canada's drug regulatory authority Ed Napke, and Swedish pharmacist Per Manell. The fundamental principles of their paper-based and early, integrated computer databases to detect signals of adverse effects to medicines remain the foundation of UMC's modern, web-based tools and methods. And Scottish statistician David Finney led the way in analysing the significance of spontaneously reported adverse reactions.

Ed Napke

'Healthy bodies are cheaper'

Ed Napke is one of the true pioneers of world pharmacovigilance. Born in Lebanon, he became involved in the science 'by accident', but went on to create Canada's first adverse reaction reporting system and was instrumental in driving through new laws on smoking, child-proof packaging, poison control and a wide range of environmental legislation.

Dr Napke did ground-breaking research to show that many adverse effects from medicines are not related to active ingredients, and can be triggered by excipient components, or the almost infinite range of potential interactions resulting from people's diet, gender, age, lifestyle, genetics, location and other variables.

An unexpected challenge

'My introduction to pharmacovigilance happened when I was on my way to San Francisco to do some aviation research. I met a friend of mine who asked if I could join the Canada Food & Drug Directorate to help implement new regulations in the wake of the problems with thalidomide. I agreed to take on this challenge, with a budget of just Can$100,000, which had to be split across ten teaching hospitals!

At first, there was little real science to what I was doing, and I encountered quite a lot of resistance. But the colour-coded, paper-based 'pigeon hole' system we created gave birth to something brand new – the idea of spotting and acting on patterns of adverse effects and disproportionate incidences of harm.

There are whole extra layers we still need to explore and understand

UMC – then, now and next

Since it started in 1978, UMC has been a great ally in developing these fundamental, concepts into the advanced systems in use today. In hindsight, it was a good move to create UMC – the Swedish Government was willing to put in resources, and the WHO Programme urgently needed a sponsor and leader.

The Centre's work has helped to mitigate the sometimes limited value of pre-market clinical trials. But I think there are whole extra layers we still need to explore and understand, and there's still plenty of scope for UMC to take some further giant steps.

Being in my 90s, I'm especially interested in medication for ageing populations, and the potential for more personalised medicines tailored to the individual. We must also return to the idea of preventing disease through good nutrition and exercise. Healthy bodies are cheaper, so we simply need to help people live better lives, with less fear. And I think that's a hopeful message for the future.'

Per Manell

'The well of the world's knowledge'

Pharmacist Per Manell helped to create the world's first computer relational database for adverse drug effects, and he recruited UMC's first staff members to put it into practice. His career saw the rapid development of technology – from punch-cards to modern, online systems.

Per worked for many years at Sweden's drug regulatory agency, the National Board for Health and Welfare, and was on the spot when responsibility for management of the WHO Programme transferred from Geneva to Uppsala.

Well placed to help

'When WHO decided to shift its priorities to supporting access to healthcare in developing countries, Sweden was well-placed to take over the drug monitoring programme. Apart from the Government's support and a strong scientific base, we had the key advantage of already having developed an early database in collaboration with the University of Uppsala's Computing Centre, UDAC.

We called this system MIMER – after the mythical Norse God Mimer, who guarded the well of all the world's knowledge! We adapted the database for the National Board of Health and Welfare to create SWEDIS – a system that was capable of giving an immediate answer to the questions we asked. This may not seem remarkable now, but in the 1970s, it was something really special.

To transfer WHO's existing, offline data to our database, we travelled to Building L at Geneva to collect it on magnetic tapes. There was quite an atmosphere there among staff whose jobs were no longer needed. But this was progress, and I'm pleased to say that the relationship with WHO headquarters has improved a lot since then.

Companies soon came to recognise the value of what we were doing

We continued to innovate – by first putting reports for member countries onto microfiche, and then being the first people to ever store an entire database onto a CD-ROM. Reactions to what we were doing from the pharmaceutical industry were mixed at first, but companies soon came to recognise the value of what we were doing.

Open to all

For all its success, I'd like to see UMC make its data even more widely available to the public for anyone to use, and give more feedback to the countries that provide it. When anyone can share their experience on social media, the Centre needs to show its expertise to keep pharmacovigilance as an even more active part of healthcare.

UMC is a highly professional scientific centre with an excellent reputation. It's the best place on earth at doing what it does, so that needs to be shared.'

David Finney

David Finney is Professor Emeritus of Statistics at the University of Edinburgh, who reached the age of 100 in 2017. He is a pioneer in the development of systematic monitoring of drugs to detect adverse reactions. While on an academic sabbatical in the US, Prof Finney helped to report concerns about the adverse effects of thalidomide (see page 16) to WHO.

During the 1960s, Prof Finney played a key part in giving advice to the UK's fledgling system for safety of medicines and to WHO's work to create an international system of pharmacovigilance. He also helped to set up the independent Drug Safety Research Unit in the UK, and was a founding member of the World Cultural Council (an international organisation based in Mexico, which exists to promote cultural values, goodwill and philanthropy).

David was a prolific author of scientific papers on statistical methodology, the role of health professionals and drug safety regulation. UMC published an anthology of his Writings On Pharmacovigilance in 2002

Pioneers – the data man

Bo Östling

Starting with a huge IBM computer in 1978, and working with fellow expert Bill Dagérus, Bo Östling had clear ideas right from the beginning about how the global database for adverse drug reactions should work. He's maintained UMC's systems ever since; charting an unbroken line of technological development to the advanced, web-based tools used by the Centre now.

Bo is the only person still employed at UMC to witness and support its development right from the first day to the 40th anniversary. His personal journey tracks the revolution in information technology and the Centre's own growth from tiny beginnings to becoming the global hub of medicines safety.

Where it started

'I was working at the Uppsala University Data Centre, when the WHO database needed to be transferred from headquarters in Geneva to UMC. My colleague Bill Dagérus had already set up the Swedish Drug Information System (SWEDIS), which was useful when creating the international version (INTDIS). The data was brought from Geneva on magnetic tapes, which we loaded into the new system. And that's how our database was born.

We've taken the system through several generations with changes in programming languages and operating systems since then, but the essentials remain the same. The WHO Drug Dictionary was a by-product of the database, since we needed to give each medicine a unique number to store and search against the reports of adverse reactions. It's a nice feeling that we've been able to realise the Dictionary's potential as a commercial product to support UMC's growth over the last four decades.

Technology will continue to change rapidly

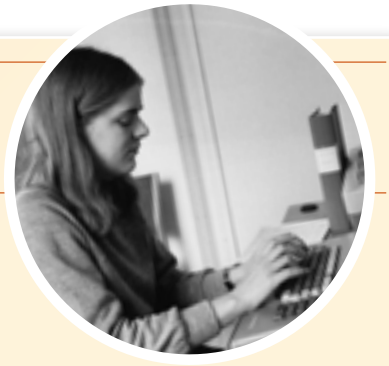
I started here using paper as output media, then moved through microfiche to hard disk storage and now cloud-based systems – always using coding methods to solve problems. I think that technology will continue to change rapidly, and the new EU regulations on data protection mean that UMC will have to keep on adapting.

What next

I'm going to do some different things in my retirement: spending more time with my grandchildren and brewing beer, growing vegetables, spices and flowers, watercolour painting, making tapestry, weaving and woodworking. But UMC and its people will always be in my thoughts – there are so many bright people here doing so many good things. It's a success story; and it's been excitement all the way.'

1980s – gathering momentum

UMC's second decade saw further growth in the WHO Programme, as new national pharmacovigilance centres began to spring up and make their presence felt. There were also important advances in data sharing and signal communication that laid the foundation for future technological breakthroughs.



1980

- Drug Safety Research Unit founded in UK
- WHO Programme meeting – London, UK

First fax machine and domestic camcorder

1981

- Computerised drug dictionary made available outside WHO programme
- WHO Programme meeting – Uppsala, Sweden

Artificially produced insulin launched
IBM computer and MS-DOS launched
First Space Shuttle mission

1982

- Benoxaprofen adverse effects triggered need for rapid alert system between agencies
- First Adverse Reaction Newsletter published with summaries from national centres
- Coding agreed for all medicinal products to Anatomical Therapeutic Chemical (ATC) classification
- WHO Programme meeting – Ancona, Italy

First artificial human heart implant
First CD player, computer freeware and use of emoticons
Vanera 13 spacecraft lands on Venus

1983

- WHO Programme meeting – Brussels, Belgium

First consumer mobile phones
Microsoft Word and Internet Protocol launched

1984

- WHO Programme meeting – Washington DC, USA
  - Spain, Thailand
  - HIV/AIDS virus identified
  - DNA profiling developed
  - Apple Macintosh computer and computer diskettes launched

1985

- High background incidence recognised as a problem in analysing gastrointestinal bleeding caused by non-steroidal anti-inflammatory drugs (NSAIDs)
- *SIGNAL* – regular dissemination of new safety signals derived from database
- International expert panel set up for intensive review of signal data
- WHO Programme meeting – Dubrovnik, Yugoslavia
  - Blood tests for AIDS approved in USA
  - Windows operating system and Nintendo entertainment system launched

1986

- WHO Programme meeting – Paris, France
  - France
  - Human Genome Project launched
  - First triple transplant operation (heart, lung and liver) and Nicotene patch
  - First laptop computer and use of email
  - Mir space station launched

1987

- WHO Programme meeting – Canberra, Australia
  - Turkey
  - AZT AIDS drug and Prozac anti-depressant launched
  - First disposable contact lenses

1988

- UMC 10th anniversary
- WHO Programme meeting – Uppsala, Sweden
  - Crack cocaine appears
  - First computer virus spread by internet

1989

- Fenoterol controversially linked to deaths in asthma in case-control studies
- First UMC studies published in the *British Medical Journal*
- WHO Programme meeting – Geneva, Switzerland
  - Microsoft Office suite and Nintendo Game Boy launched
  - First Global Positioning System satellites

Pioneers – the directors

UMC has had just two, full-time directors in its four decades at the forefront of global pharmacovigilance. The successful, symbiotic professional relationship between Prof Ralph Edwards and Dr Marie Lindquist grew into a similarly strong and interdependent, personal partnership. Their skills complement each other well and have helped to take UMC from its small beginning to the global scientific force it is today.

Ralph Edwards

'Let patients tell their stories'

UMC's first full-time director, British-born Professor Ralph 'Rafe' Edwards, arrived in September 1990. He set about revolutionising the Centre's work and relationships through his broad medical expertise, potent influencing skills and driving commitment to greater patient safety. Ralph's tenure saw UMC become a leading scientific and professional body and gain financial independence. The Centre's staff grew from just four people when he arrived, to 55 when he stepped down in 2009.

With his qualifications and experience in internal medicine, clinical pharmacology and toxicology gained from working in the UK, Zimbabwe and New Zealand, Ralph brought a unique mix of practical skills, energy and capabilities to UMC, together with a global network of contacts.

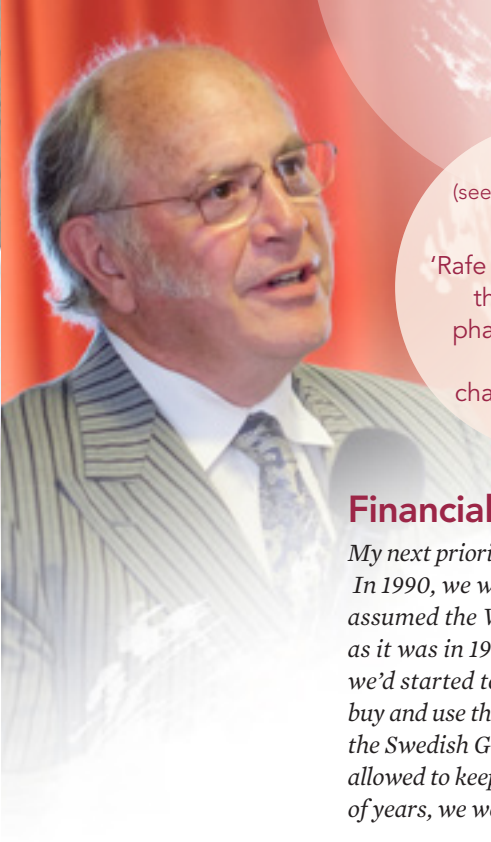
In need of direction

'Before my appointment, there had been a longstanding disagreement between WHO and the Swedish Government about creating a full-time director post.And when I arrived, there was some genuine concern about the Centre's activities and effectiveness. It was definitely in need of more direction.

At first, it felt as if I was trying to serve three different masters – WHO, the Swedish Government and the growing number of national pharmacovigilance centres. So I made the very firm decision that the national centres were our main responsibility. Until then, safety of medicines had been principally a clinical discipline – a diagnostic, decision-making process. But UMC's emphasis on methods, tools and data brought a larger set of scientific techniques to bear on critical problems.

It meant that we were able to put patients and the science first, and avoid being pressured into changing our advice where signals didn't fit with political policy or expediency. Perverting science is a very dangerous thing – and if it's good science it's right – even if results are not always interpreted correctly.

This goes to the heart of UMC's approach – we let patients tell their stories. We analyse the reasons for clusters of adverse effects, then formulate a hypothesis and search for evidence to support it. We were working with 'big data' long before it became a catchphrase, which enabled us to look for risk factors that might be more frequently associated with those who suffer adverse outcomes from medicines.



Ambrose Isah (see page 91) on Ralph Edwards:

'Rafe practically crafted the discipline of pharmacovigilance. He's a really charismatic leader'

People come together, learn from each other and become friends for life

Financial independence

My next priority was to sort out the Centre's finances In 1990, we were still working to a contract that assumed the WHO Programme continued to operate as it was in 1971, which just wasn't feasible. Because we'd started to get increasing numbers of requests to buy and use the WHO Drug Dictionary, we persuaded the Swedish Government and WHO that we should be allowed to keep and use this income. So within a couple of years, we were able to make UMC self-funding.

The training courses we started in 1993 were a direct response to what national centres said they wanted. Right from that first course, they've always been wonderful occasions – where people come together, learn from each other and become friends for life. Pharmacovigilance can be a lonely job, so it's helpful to have this mutual support.

UMC's special offer

I like to think that our approach offers something truly distinctive for public health. UMC always focuses on the individual patient and what's best for them. This is the core of every physician's role – and it often involves difficult dilemmas to balance the chances of benefits with risks of harm. This is why we've got to keep on finding out more about how individual genetics, exposures, characteristics and circumstances shape different people's outcomes. UMC also offers cooperation, because patients will always lose out if data and decisions are not transparent.

I applaud the numerous patient groups that have developed over the past decade, and the work they do to analyse data and share people's stories. I think there's a growing role for UMC to help coordinate all these sources of information and communicate the results to the public. Building pharmacovigilance into the basic education of all healthcare staff is still in its infancy, so that's another priority for the future.

Future challenges

I think pharmacovigilance practice should also extend more into connected areas like poisoning, clinical errors, medical devices and therapeutic outcomes in general. It's estimated that up to half of all adverse effects of medicines are related to some form of mistake – perhaps prescribing the wrong drug, confusing two similarly named medicines or even parents giving their children the incorrect dose. These are difficult situations, so we need to do more to understand why such errors happen and how similar problems occur with other therapies.

I'm confident that UMC has helped to make the world a better, safer place. It's been very successful in getting out to developing countries to help establish centres that take responsibility for medicines safety. Even if the numbers of reports from some member nations remain relatively low, it's immensely valuable to know that there's someone looking out for patients in most countries.

There is still a huge amount to be done if we're going to find the patients at risk before they have problems, and be able to prevent them.'

Marie Lindquist

'Behind every number is a human being'

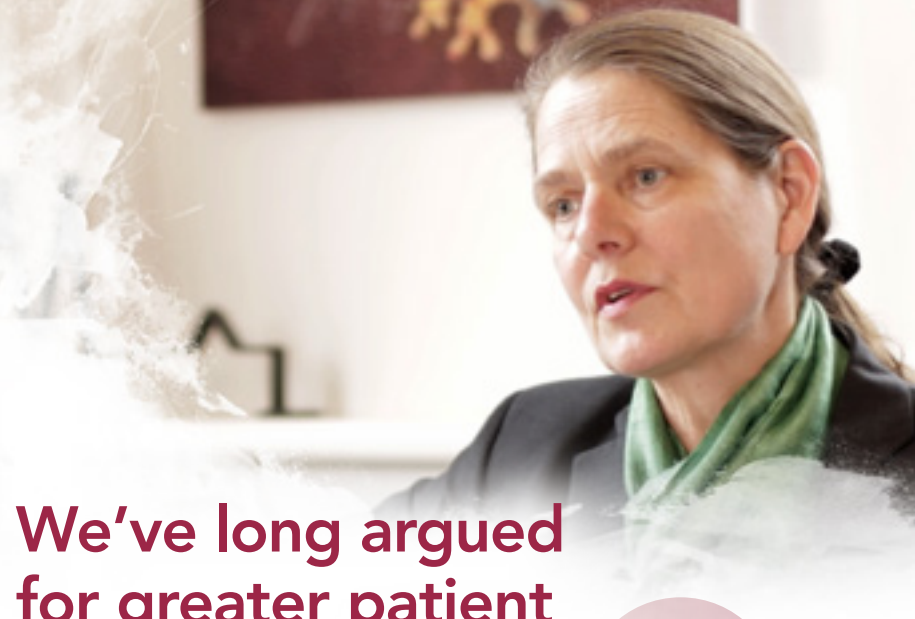
Marie Lindquist has dedicated her working life to the development of pharmacovigilance. She studied Pharmacy at Uppsala University, and served as Research and Development Manager, General Manager and then Deputy Director before becoming UMC's second full-time Director in 2009. During her nine years at the helm, UMC has doubled its staff and more than doubled its income.

Marie joined UMC not long after finishing her MSc in 1979. Her broad intellect and inquisitive mind saw her continuously seeking out new challenges within the expanding organisation. She has made critical contributions to UMC's developmental work on signal detection and data mining, and gained a PhD in medical science from Nijmegen University, Netherlands. Marie also spent a year in the Swedish national pharmacovigilance centre, learning from the noted physician-epidemiologist, Beje Wiholm.

Marie's experiences and ability to learn on the job gave her a solid platform to become and succeed as the leader of a dynamic organisation, operating in a challenging environment where political, diplomatic, and business skills are just as important as scientific expertise.

Taking on the challenge

'I first saw the advertisement for a pharmacist job at the WHO Collaborating Centre on the notice board in the office building it shared with the Medical Products Agency. I was very attracted by the idea of working internationally.



We've long argued for greater patient participation

Later on, having had leadership roles in data management, research, IT and implementing the first routine signal detection process for pharmacovigilance, I felt I had the interests, skills and determination needed to take on the challenge of leading this unique organisation. I get inspiration from being with thoughtful people who have courage, integrity and a sense of humour, and who share the desire to do something important and useful for this world.

Key achievements

It has been fantastic to see UMC changing the face of pharmacovigilance. We've proved that it's possible to find signals in the international database, and have set and implemented the research agenda for pharmacovigilance. Signal detection and hypothesis testing using longitudinal data sources and patient-generated data, pattern recognition and benefit/risk analysis are all part of UMC's work.

The Centre has ensured the sustainability and expansion of the WHO Programme by turning the WHO Drug Dictionary into a commercially available product and the medicinal product dictionary of choice for the international pharmaceutical industry.

We have demonstrated the importance of good communications, and long argued for greater patient participation in the safety of medicines. Our approach is based on openness and transparency, in both the data itself and decision making.

We have expanded the global pharmacovigilance family and served the WHO Programme for 40 years; providing knowledge transfer, networking opportunities and capacity building in all parts of the world. What defines us as an organisation is that we are here to serve people and humanity. Protecting patients from harm is our real raison d'être. And when we talk about data, we never forget that behind every number is a human being.

I'm proud of what we do here and how we do it. And I'm tremendously excited about what lies ahead. UMC is here for good, and to do good.'

Lembit Rägo (see page 50) on Marie Lindquist:

'Marie is a wonderful scientist and has been a very successful director. She's done a great, great job.'

Symbols of pharmacovigilance

Ralph Edwards' talents aren't confined to science and leadership – he is also a gifted and enthusiastic amateur artist. With Marie Lindquist, he designed UMC's logo, which evokes Uppsala's two principal landmarks of the castle and cathedral. And he used a canvas given to him by staff on his retirement to create a painting that's rich in symbolism about the pursuit of truth and health through pharmacovigilance.

It greets visitors by hanging just inside the entrance of UMC, next to the list of WHO Programme members

Across the continents – Europe

UMC's early work and systems translated readily to the political, healthcare and regulatory environments in different parts of Europe. Boosted by creation of the European Medicines Agency (EMA) in 1995, scrutiny and standards for patient safety have developed rapidly on the doorstep of WHO and UMC.

Peter Arlett

'Good at getting out there'

Head of the EMA's Pharmacovigilance and Epidemiology Department, Peter Arlett has played a major role in defining the vision for the management of marketed medicines in the EU, transforming safety monitoring and designing and implementing medicines legislation for better public health. He sees UMC as helping to set the worldwide agenda for technical standards, data integrity and guidelines, and highlights its work in training and building capacity in resource-poor countries.

After five years' experience at the sharp end of hospital medicine in the UK National Health Service, Dr Arlett joined the Medicines and Healthcare Products Regulatory Authority (MHRA) in 1997, and then the European Commission in 2003. At EMA since 2008, he coordinates safety of medicines across the EU and is a member of the WHO Advisory Committee on the Safety of Medicinal Products (ACSoMP).

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Getting out there

'UMC delivers a core part of WHO's mission. The team is very good at getting out there – jumping on planes to go anywhere in the world, and working with the other WHO Collaborating Centres to spread the use of its methods and tools for global pharmacovigilance.

The Centre is at its excellent best when delivering on its core purpose to collect reports, detect and share signals from its database. UMC has done outstanding work on statistical algorithms and produced significant research into pharmacovigilance methods, including ground-breaking collaborative work such as the EU PROTECT project.

Going further

I'd like UMC to do more to make its pharmacovigilance tools more widely available to governments, industry and everyone who can benefit from using them. This would help to extend pharmacovigilance further beyond the skills of individuals to become truly systematised.

UMC delivers a core part of WHO's mission

We're going to see rapid changes in technology, with much greater use of big data and information drawn from real world sources like insurance, dispensing and electronic health records. UMC will remain a vital service provider, especially in supporting local action in countries where the infrastructure for healthcare is still developing. And I think WHODrug will continue as a world-leading product.' ●

Collaboration not competition

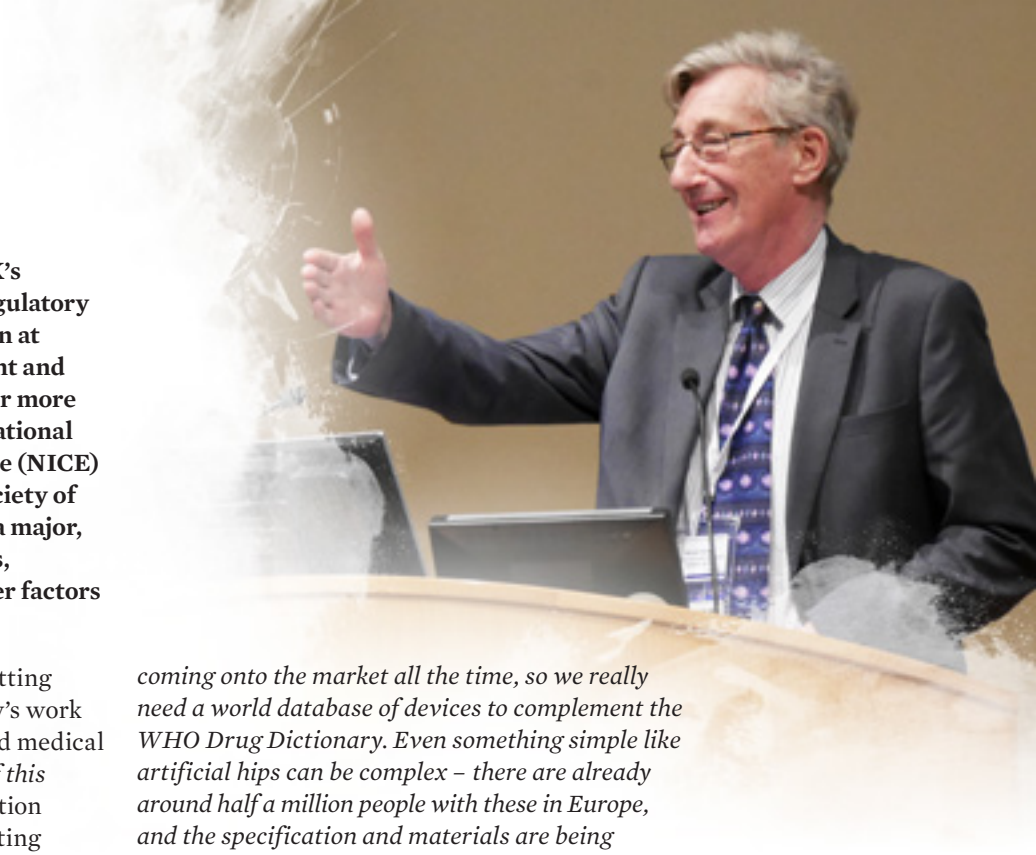
Europe is one part of the world where international cooperation on patient safety has taken on another dimension – particularly through the EMA (currently based in London but soon to move to Amsterdam), and the harmonising work of the EU Commission.

Basic principles relating to citizens' healthcare are enshrined in the EU's Charter of Fundamental Rights, which provides that 'everyone has the right of access to preventive health care and the right to benefit from medical treatment,' It also stipulates 'a high level of human health protection in all the Union's policies and activities.'

As with the role of the FDA in the United States, when large-scale, state-funded programmes also take up the challenge of pharmacovigilance, there's the potential for overlap, duplication or even outright competition with the WHO Programme. But thankfully, the atmosphere is more about collaboration. The scope and challenge of modern medicines safety is so vast and ever-changing that there's room for all players to do what they do best, and support each other's efforts ●

Sir Michael Rawlins

'The world is changing'



Sir Michael Rawlins has chaired the UK's Medicines and Healthcare Products Regulatory Agency (MHRA) since 2014. He has been at the forefront of innovation, development and leadership in the public health sector for more than 30 years. The founding Chair of National Institute for Health and Care Excellence (NICE) and formerly President of the Royal Society of Medicine, he also chairs UK Biobank – a major, long-term project to study how genetics, nutrition, lifestyle, medication and other factors affect the development of disease.

Sir Michael leads the MHRA board in setting strategy to guide and oversee the Agency's work as an effective regulator of medicines and medical devices across the UK. He sees *'the joy of this job'* as being able to witness the organisation delivering innovative science and protecting public health.

Growth and coordination

'UMC has played an important role in growing and coordinating global activity on pharmacovigilance. The Centre has done this very effectively, by collecting and communicating information and collaborating on worldwide research. I have huge respect for the Centre and its people – they've done a fantastic job. Pharmacovigilance was traditionally an activity confined to high-income countries, but that's no longer true – thanks in no small part to UMC.

A changing world

The world is changing though, so we need to change with it. Medical devices haven't had enough attention yet, and are an issue that's rising fast up the agenda. There are so many different products coming onto the market all the time, so we really need a world database of devices to complement the WHO Drug Dictionary. Even something simple like artificial hips can be complex – there are already around half a million people with these in Europe, and the specification and materials are being constantly tweaked.

We need to make sure that less-developed countries don't get left behind

Artificial intelligence and nano-technology are going to play a big part in future healthcare, so we need to make sure that less developed countries don't get left behind, or that we underestimate the contribution they can make to how the science develops. We're going to see medicines and treatments designed specifically for different parts of the world, so pharmacovigilance has to continue recognising the varying needs and specialisms of each country.'

Niamh Arthur

'A long and fruitful relationship'

Niamh Arthur is Pharmacovigilance Manager for the Health Products Regulatory Authority (HPRA) in Ireland. She helped to develop the national pharmacovigilance system and is responsible for managing vigilance systems for blood, tissues, cells and organs. The HPRA also covers medical devices, cosmetics, controlled drugs and veterinary medicines. Niamh has served on UMC's Board as a WHO representative, and on the Advisory Committee for Safety of Medicinal Products (ACSoMP).

Niamh's work involves coordinating all reporting activity by patients, healthcare professionals and industry, including processing reports of adverse effects for submission to the EMA (and from there to WHO). She believes in selling the message of pharmacovigilance through education and campaigns, to persuade people of the importance and benefits of reporting, to counter negative perceptions that pharmacovigilance *'costs money and brings bad news'*.

Part of something big

'Ireland is extremely proud to have been one of the founding members of the WHO Programme. Back in 1968, my predecessors saw the opportunity for a relatively small country to be part of something much bigger – and that's how it's worked out.

I've had a long and fruitful relationship with UMC and WHO – working closely with the teams to help evolve and develop systems. The Centre has been ahead of the game in terms of transparency and access to data, and its culture of communalism not competition has kept a clear focus on patients' needs and their stories. UMC has shown an exceptional ability to engage and communicate sometimes complex information and important safety messages in an understandable way.

Worldwide political instability, population growth and changes in the use of medicines will test UMC's agility

WHO and UMC have different but complementary roles, so there have inevitably been challenges in the Centre's relationship with WHO headquarters. But I've always been impressed at how these have been managed in positive and mutually respectful way. This has supported both organisations and allowed UMC's talented staff to carry on being creative and productive.

On the horizon

There are many challenges for patient safety on the horizon. Herbal, complementary and over-the-counter medicines are increasingly used alongside complex and diverse conventional treatments. And there's also been a massive jump in the volumes and speed of data. There are ever-increasing expectations about accountability and levels of public scrutiny that seek clear and unambiguous recommendations and don't welcome uncertainty. So we're all going to have to work very hard to respond to these pressures, while maintaining trust.

Worldwide political instability, population growth and changes in the use of medicines will test UMC's agility. It's a unique organisation, which has remained loyal to its core values through its evolution and development. UMC has a huge legacy that needs to be protected and carefully managed into the future.'

Ronald Meyboom

'A huge contribution'

Ronald Meyboom is senior researcher for the Department of Pharmacoepidemiology and Clinical Pharmacology at Universiteit Utrecht in the Netherlands. He played a big part during the 1990s and early 2000s in developing UMC's international approach to education, and its delivery throughout the world. A kind, gifted and intuitive clinician, Ronald's PhD thesis on signal detection remains the basis of the Centre's analytical methods.

Dr Meyboom's academic research includes work on intranasal corticosteroids as a cause of neuropsychiatric disturbances and acute hypersensitivity reactions induced by herbal medicines. He believes that whatever technologies and tools come into use in future pharmacovigilance, the original function of spontaneous monitoring – to detect new and unexpected drug-related problems – is likely to continue in some form.

Bruno Stricker, Cecilia Biriell and Ronald Meyboom, Uppsala, 1980s.

A balanced approach

'UMC has been centrally involved in all three aspects of pharmacovigilance: collecting and analysing spontaneous reports, applying science to identify the best evidence of harmful effects and supporting the legal and regulatory framework for public health. The key thing is to balance all three so that they form a positive, cyclical feedback system.

Our science has to avoid what Max Weber called 'the iron cage' – the tendency for traditions, values, instincts and emotions to be crowded out by pure functional efficiency and bureaucracy. We need the sort of safety disciplines that every physician and patient can take into account as a thoroughly embedded part of everyday healthcare.

UMC has made a huge contribution to helping us stay alert to the risks of seeing this purely as a social system based on laws, rules, risks, controls and compliance. It may seem straightforward, but using people's individual medical histories is complex and difficult; scientifically, technically and ethically. So interpreting this sort of data is often ambiguous and uncertain.

Too often, pharmacovigilance findings are regarded as bad news

The basic aim of pharmacovigilance is to increase knowledge, enabling a better use of medicines. But too often, pharmacovigilance findings are regarded as bad news, or as something negative. Different parties have different interests and priorities, so news about a medicine can cause tension or trouble. To be effective, patient safety agencies need to be scientifically and financially independent – and that (alongside its tremendous methodological and technical work) is one of the things that UMC does so well.'

Success in... *The Netherlands*

International collaboration brings big benefits

In 2016, a team from UMC travelled to the town of 's-Hertogenbosch – home of the Netherlands WHO Collaborating Centre, Lareb. Their trip mirrored a visit by Dutch staff to Uppsala 30 years previously. The objective of the visit was to bring colleagues together to assess a list of adverse reaction reports filed by patients. The study aimed to identify both new signals and new details of known adverse effects that would be most relevant to patients' concerns.

Effects characterised as non-serious in clinical trials can be much more severe in real-world use

Over four days, the teams examined more than 200 medicine and side-effect combinations in VigiBase. The patient narratives this revealed led to eight new signals being communicated to national pharmacovigilance centres in the WHO Programme. The details from personal accounts yielded important information about the severity of problems, as well as their impact on people's quality of life.

The first new signal focused on dapaglifozin (a class of oral medications used to treat type 2 diabetes). Itching was already known as a common, non-serious adverse reaction for these types of drugs, but the patient reports showed that in some cases, this could be so severe as to stop people using the medicine, so risking other health effects.

A second signal concerned dry eyes caused by amitriptyline (a medicine used to relieve chronic pain from arthritis and related conditions, plus improve sleep and help with anxiety or depression resulting from pain). The product labelling and patient information leaflet mentioned 'anticholinergic effects' – a term that healthcare providers would be likely to link to dry eyes, but few patients would understand. So the information needed updating to make this explicit.

This face-to-face collaboration between UMC and another WHO Collaborating Centre broke new ground by adjusting traditional statistical methodologies to prioritise data combinations included in a significant proportion of patient reports, cross-referenced to a thorough review of product and patient information.

The signals showed that some effects characterised as non-serious in clinical trials can be much more severe in real-world use, impacting on patients' lives so much that they stop taking the medicine and expose themselves to other risks.

Conceived in Sweden, undertaken in the Netherlands and relevant to the whole world, this partnership project highlights how subtle and complicated medicines safety can be – and how relatively small improvements can help to safeguard millions of patients from harm ●

1990s – data and methods take hold

The birth of the internet transformed UMC's capability to handle, analyse and search aggregated individual case safety reports to detect signals of harm. As the Centre took big strides in developing scientific methodology, it became possible to focus more on rare reactions and events often overlooked by research concentrating on large groups or whole populations. UMC successfully thrust information technology skills, training and high-quality communications into the spotlight of global pharmacovigilance. Meanwhile, the WHO Programme continued to grow – but not without challenges.

1990

- International Council for Harmonisation (ICH) founded by the USA, EU and Japan, to harmonise medicines regulation
- UMC's first full-time Director, Ralph Edwards, appointed
- WHO Programme meeting – Geneva, Switzerland

  Greece, Hungary, Iceland, Indonesia, Malaysia
  First web page and in-car satellite navigation
  Ulysses space probe launched to orbit the Sun

1991

- Online WHO database search programme launched for national centres
- Definitions of adverse event, side effect and causality agreed
- WHO Programme meeting – Barcelona, Spain

  Austria
  Cholera epidemic in South America
  First web browser and Linux operating system launched

1992

- 1 million reports in VigiBase
- WHO Programme meeting – Ottawa, Canada

  Croatia, Czech Republic, Republic of Korea, Morocco, South Africa
  DNA fingerprinting invented
  First videophone

1993

- Windows-based programme launched for database searches
- 1st international training course, Uppsala, Sweden
- WHO Programme meeting – Geneva, Switzerland

Portugal, Singapore, Slovakia, United Republic of Tanzania, Tunisia
14 million people worldwide infected with AIDS/HIV
First human embryo cloning
Pentium processor launched

1994

- Denominator data methodology developed to calculate ADR reporting rates
- WHO Programme meeting – Berlin, Germany

Argentina, Cuba
Pakistan
First genetically modified foods and digital television service
Java programming language launched

1995

- UMC name and brand launched
- WHO Programme meeting – Bangkok, Thailand

Oman, Philippines, Venezuela
DVDs, Windows 95, JavaScript and eBay launched
Space Shuttle docked with Mir Space Station

1996

- Benefit/harm methodology developed
- Launch of Uppsala Reports quarterly magazine
- WHO Programme meeting – Lisbon, Portugal

Chile, Costa Rica, Switzerland
Meningitis epidemic in West Africa
First mammal, Dolly the sheep, cloned
10 million internet users worldwide

1997

- Oral contraceptive 'pill scare' demonstrated the need for good communications practice and consequence evaluation
- Data mining tool developed for automated signal detection in large data sets
- WHO Programme meeting – Geneva, Switzerland

Weight loss drug Fen-phen withdrawn from the market
Microsoft becomes world's most valuable company
Kyoto climate change protocol agreed

1998

- *Erice Report* promotes the importance of pharmacovigilance communications
- Online discussion group launched for national centres
- WHO Programme meeting – Tokyo, Japan
- UMC 20th anniversary

Estonia, India, Islamic Republic of Iran, Russian Federation, Zimbabwe
Viagra went on sale in USA
Google and Apple iMac computer launched
Construction of International Space Station began

1999

- WHO Programme meeting – Ankara, Turkey

Fiji, Mexico, Vietnam
First breakthroughs in stem cell research
First BlackBerry device released

Pioneers – the Programme managers

The rapidly-expanding WHO Programme and development of advanced tools at UMC demanded high-level political skills, careful diplomacy and clear-minded determination. The job of establishing the right combination of WHO's global reach and UMC's technical excellence fell to some eminent physicians.

Martijn ten Ham

Dutchman Martijn ten Ham (1938-2010) was Chief of the Drug Safety Unit at WHO from 1990 to 1999. A cheerful and enthusiastic pharmacologist with a strong grasp of policy in all aspects of medicine, he had a particular interest in the ethics of pharmacovigilance.

Martijn's gentle, humorous and collaborative style helped to create a positive working relationship between UMC and WHO – letting the Centre provide the technical expertise, while he supported the annual Programme meetings and did pioneering work on the issue of counterfeit medicine.

A dedicated motorcyclist, during his time working at the Netherlands' National Institute of Public Health, Martijn once rode to the offices of a pharmaceutical company to deliver the licence cancellation for a problematic product, triumphantly in person

Lembit Rägo

'A substantial impact'

Now Secretary-General of the Council for International Organizations of Medical Sciences (CIOMS) in Geneva, Switzerland, Lembit Rägo was formerly Head of Regulation for Medicines and Health Technologies at WHO. He helped to found the regulatory system in his native Estonia and was the State Agency of Medicines' first Director General there. He has also served as a UMC Board member and strongly supported the Centre's strategy of financial independence.

Prof Rägo has clear views about the importance of good communication and the need to tailor pharmacovigilance systems to match the uniqueness of each country, its culture, customs and population. He thinks that the needs of patient safety will always far outweigh the resources available, and that professionals can always do more and better.

Prevention and education

'I discovered for myself in Estonia that creating and building up a regulatory system is not so easy! It was a hard task to persuade medical authorities and pharmaceutical companies of the importance of both spontaneous reporting and structured monitoring. Too many adverse effects are down to irrational use of medicines or errors in dosage, so we need to channel effort onto prevention and better education of clinicians and patients.

UMC has been amazingly successful in doing this – working internationally and being right on the frontline of scientific innovation. The Centre has had a substantial impact through its work on methods and promoting the value of patients' views, reporting and input to the whole life cycle of medicines.

There's a real synergy between WHO and UMC

There's a real synergy between WHO and UMC, which is an exceptional collaborating centre and a major force in global pharmacovigilance. It sits on a gold mine of information in its database, so I'd like to see it go further to make that more available in the public domain.

A new role

As direct patient reporting and the use of longitudinal electronic health records increases, UMC needs to redefine and carve out a new role. As an innovative enabler, I believe it can be a significant player in helping to integrate all forms of information and medical treatments into global pharmacovigilance.'

Mary Couper

'Committed, bright and dedicated'

Mary Couper managed the WHO Programme for ten years up to 2009. She's proud of the interdependent working relationship built up between the Organization's headquarters and UMC during her tenure, and the supportive, family atmosphere that helped to drive innovation and spread pharmacovigilance to all parts of the world.

Dr Couper highlights the development of information technology as being at the heart of this successful synergy, plus UMC's outreach work to provide training and help new member countries to develop their national pharmacovigilance centres.

Growth and credibility

'The rapid growth in Programme membership and numbers of reports on UMC's database show just how effective the joint work between WHO and the Centre in Uppsala has been. While my team managed the Programme, UMC actually did it, and was always coming up with something new. We simply didn't have the expertise to do everything required in Geneva, but the WHO name has given UMC the credibility and backing to take education and best practice out into the world.

We can never do enough

Some people perceived UMC as being overly commercial, with the risk of becoming too close to the pharmaceutical industry, but I think this financial independence has been essential. And generating revenue hasn't altered the friendly, open way in which UMC goes about its work. The Centre's staff have proved themselves to be committed, bright and dedicated.

Communicate, communicate, communicate

In an era when priorities are increasingly dictated by big philanthropic and corporate donors, the job of keeping medicines safety in the public and professional eye is harder and more important than ever. So UMC's work to keep on communicating and raising awareness of locally tailored pharmacovigilance as an integrated part of public health remains vital. In fact, we can never do enough on this – and we're lucky that UMC is so good at it!'

Across the continents – USA and Canada

The United States hosted the WHO Programme in its early years, and remains the largest single source of individual case safety reports for VigiBase. The highly-developed, insurance-based healthcare systems, giant pharmaceutical sector and influence of the Food and Drug Administration and Bill and Melinda Gates Foundation make North America the world's predominant medicine superpower.

Gerald Dal Pan

'Their instincts are good'

Gerald Dal Pan has been the Director of the US Food & Drug Administration (FDA) Office of Surveillance and Epidemiology (formerly known as the Office of Drug Safety) since 2005. He originally qualified in internal medicine and neurology, and has also worked in the pharmaceutical industry and clinical research and statistics.

Dr Dal Pan represents the FDA at the annual meetings of national centres, so he is in close and regular contact with the UMC team and his pharmacovigilance counterparts from across the world.

A long history

'As one of the founding members of the WHO Programme in 1968, the US has a long history of working with UMC. There's nothing quite like it – the Centre has been a critical driving force in developing pharmacovigilance, especially in low- and middle-income countries. And it has done cutting-edge research into mathematical algorithms, informatics, data-mining and natural language processing.

But I'm pleased to say that UMC has never forgotten that its work is all about patients and the people using its systems across the world. The team has invested a lot of time in building and maintaining relationships, and engaging with all the national

UMC has never forgotten that its work is all about patients

centres. The Centre is a first-class organisation with impressive scientific credentials that produces data to the quality and standards its public health mission needs.

UMC and WHO

As a WHO collaborating centre, the relationship between UMC and headquarters feels seamless. They are both part of the global endeavour to detect and trigger action on signals from anywhere in the world. Initiatives like Take & Tell have been crucial in reaching out to encourage reporting of adverse effects by patients.

Pharmacovigilance was born into a paper-based world where people wrote to each other. And now it's moving into uncharted territory as we explore how social media and other technologies will change things. There are no conclusions yet about the real utility of digital tools or their limits in supporting post-market drug safety.

But UMC has already proved itself as a world leader in leveraging mobile technology, and I can see them moving much farther into the use of big data and real-world evidence. I hope they will follow their instincts on this – because their instincts are good.'

Murray 'Mac' Lumpkin

'The way the world does business'

Mac Lumpkin is a Deputy Director for Integrated Delivery and the Lead for Global Regulatory Systems Initiatives at the Bill and Melinda Gates Foundation. The Foundation focuses on helping to address neglected diseases in low-income countries. Launched in 2000, it's one of the world's largest private foundations and is a principal WHO funder.

Dr Lumpkin was previously Deputy Director of the Center for Drug Evaluation and Research at the US Food and Drug Administration (FDA). He was also the FDA's Deputy Commissioner for International Programs, and represented the Agency on the Council for International Organizations of Medical Sciences working group on drug safety.

Championing patient safety

'I've been engaged with UMC for the last 30 years, and I think there are two main strands to what it's achieved in establishing pharmacovigilance as a collaborative, global undertaking. The early work on reporting highlighted the sorts of rare and serious side effects that couldn't be detected in clinical trials. This has expanded enormously through the new definitions, methodologies, systems and approaches the Centre has developed.

The face and voice of training and development

The second vital aspect is how UMC has driven and championed patient safety in low-income countries. It has been the face and voice of training and development; acting as the coordinating hub, to keep safety at the forefront of global regulatory science so that it's now become part of the way the world does business.

People often forget that national regulatory authorities are not created or funded to be international health systems development institutions. So that's why UMC's global view and commercial self-sufficiency are so crucial. The WHO Drug Dictionary is a uniquely valuable resource, which UMC have kept on extending and improving to match new circumstances.

Relationships matter

Detecting and analysing adverse effects of medicines are of course just the beginning – the big challenges thereafter are how to communicate and manage those risks. I think this all comes down to positive, international relations – nothing successful happens without this; and that's something UMC and its leaders have always understood and promoted strongly.

The Centre also correctly believes that patients have to remain our prime focus. People who experience illness and treatments are capable of giving really good and useful information – so we have to make sure that they play an ever greater part in systems that allow us to get to the truth.'

Barton Cobert

'No-one touches UMC'

Fellow of the American College of Physicians and pharmacovigilance consultant Barton Cobert was formerly the Head of Global Drug Safety for the United States-based pharmaceutical company Schering-Plough. He sees UMC's success in promoting the safety of medicines in low- and middle-income countries as a major achievement.

Certified in Internal Medicine and Gastroenterology, Dr Cobert has chaired and served on various International Conference on Harmonisation (ICH) working groups, and is on the editorial board of the journal Expert Opinion in Drug Safety. He is a dual US and French citizen.

Anything is possible

'When it comes to working with developing countries to create and implement local approaches to medicines safety, no-one touches UMC. The Centre's training has been invaluable, and it's thanks in part to UMC that India and China are now so involved in global pharmacovigilance. The team has shown that anything is possible.

We're now entering a new era

The Centre can't do everything or fix the whole world, so I think it's been wise to choose its priorities carefully and concentrate on where it can have most impact. The WHO Drug Dictionary and VigiBase are the big deals – there was nothing like these when I worked in industry, and UMC always provided a good service.

Changing the game

We're now entering a new era, in which organisations and bureaucracy will be joined by new players. Big data and artificial intelligence are going to change the game. This is fine for countries that can afford and adapt to it – so in the United States, the Food and Drug Administration will be able to scrutinise patient data on 350 million people. But in some countries, the big challenge will continue to be getting the right medicines to the right people. I think UMC will continue to be a leader in this new world.'

Success in... *the USA*

The lessons of Vioxx

Delays in detecting the adverse effects of Vioxx (a painkiller commonly prescribed to patients with osteoarthritis) highlighted the need for more urgent studies and tighter regulation to respond to safety concerns. The drug's possible re-introduction in the US will test how well lessons about benefits and risks have been learned.

Making sound medicines safety decisions is rarely easy

Vioxx (a brand name for rofecoxib) was licensed by the FDA in 1999 as an effective, safer alternative to non-steroidal anti-inflammatory drugs. By 2003, millions of people were taking the drug, and it had generated more than $2.5 billion in sales. But reports gradually emerged that its chemical structure affected blood platelets responsible for bloodclotting, leading to an increased risk of heart attacks and strokes.

Concerns about adverse effects were first raised at the WHO programme's meeting in Tunis in 2000 by the Lareb Centre in the Netherlands – with a signal detected from VigiBase and their own data. There was ongoing pharmacovigilance monitoring throughout 2001 and 2002. The drug was withdrawn in 2004, by which time hundreds of people had experienced cardiovascular problems linked to its use.

Reasons for delay

The difficulty with establishing a clear, causal link between Vioxx and these problems was that, since heart attacks and strokes are common events anyway, it took a long time to prove that some of these were caused by patients' use of the treatment. The case was therefore not a failure of regulation itself, nor an issue of data collection or the quality of studies performed. It was a complex decision-making and communication challenge, which exposed some shortcomings in the way marketing and research interpreted the evidence used to inform patient care.

Making sound medicines safety decisions is rarely easy, but Vioxx showed that it's made harder by a lack of clear goals on the benefits and risks that are acceptable for patients. The case also highlighted the risks of decisions being driven by legal and bureaucratic concerns, and pharmaceutical industry and regulatory structures being overwhelmed by data. This resulted in protracted analysis of data and disagreements over interpretation creating some difficult and controversial communication issues between the various stakeholders trying to make sense of the data.

Shaking up regulation

The problems with Vioxx shook up regulation in the US and brought new urgency to carrying out proper, scientific studies at the first hint of serious problems. The episode demonstrated that regulators need adequate resources to do these studies, and that it's unhelpful for the manufacturers to take all the punishment (and therefore potentially become defensive), when decisions are shared with regulators. It also highlighted how the media can divert attention from medicines safety due to its narrow focus on what makes a newsworthy story.

In early 2018, plans were announced to bring Vioxx back to the market – to ease the severe joint pain caused by haemophilia. Given its history, this poses another difficult decision and communications challenge. It's likely that, if the drug is licensed once again, this will be subject to many of the measures triggered by the effects connected to its first generation. These include routine collection of safety data that's independently arbitrated, systematic post-market surveillance and including potential 'off-label' use of the drug for other symptoms and conditions.

In the spirit of wise therapeutic decisions, doctors should also adopt strategies that restrict access to a drug with known safety risks, and where possible consider steering patients towards alternative therapies that may be safer and equally effective


REGULATION OF VIOXX: SUCCESS OR FAILURE?

Insights and Challenges

2000s – going global

UMC grew steadily in the first decade of the new century, driving the WHO Programme's rapid expansion, especially in lower- and middle-income countries throughout Africa, Asia and South America. This bigger and far-flung community made communications ever more important, and proved that Western-style pharmacovigilance can't just be exported and plugged into very different settings. Meanwhile, data science and analytical methods continued to take huge strides forward, with UMC's methods and work featuring in several leading journals and academic theses worldwide.

2000

- WHO/UMC guidelines for setting up and running PV centres published
- WHO Programme meeting – Tunis, Tunisia
  - Cyprus, Former Yugoslav Republic of Macedonia, Serbia, Sri Lanka
  - First draft of Human Genome completed
  - Millennium bug fears and burst of Dot Com investment bubble

2001

- 5th international training course, Uppsala, Sweden
- WHO Programme meeting – Dunedin, New Zealand
  - Armenia, Brazil, Egypt, Ghana, Uruguay
  - First contraceptive patch
  - Wikipedia and Apple iPod launched

2002

- New database launched to allow more detailed storage, retrieval and analysis
- WHO Programme meeting – Amsterdam, Netherlands
- *Viewpoint* plain language guide to pharmacovigilance published
  - Guatemala, Jordan, Latvia, Peru, Ukraine
  - Bahrain
  - 40 million people infected with AIDS/HIV worldwide
  - 'Miss B' granted right to die in landmark UK legal case

2003

- Data mining tools launched for unsupervised pattern recognition
- UMC's Expecting The Worst crisis management guide published
- WHO Programme meeting – New Delhi, India
- Viewpoint published in French and Spanish
- UMC's first PhD theses published by Marie Lindquist and Andrew Bate

Kyrgyzstan, Republic of Moldova
Human Genome Project completed
SARS disease Asian bird flu outbreaks
Apple iTunes launched

2004

- WHO Programme meeting – Dublin, Ireland

Colombia, Malta, Nigeria
Georgia
Facebook launched
First privately funded spaceflight

2005

- Enhanced WHO Drug Dictionary launched
- Pilot of data mining longitudinal patient records
- Automated screening for suspected duplicates in VigiBase
- WHO Programme meeting – Geneva, Switzerland

Brunei Darussalam, Lithuania, Mozambique
Mongolia
Live8 and Make Poverty History white wristband campaign
YouTube and Xbox 360 launched

2006

- VigiFlow web-based report management tool launched
- Web-based WHO Drug Dictionary browser launched
- WHO Programme meeting – Liège, Belgium

Belarus, Nepal, Uzbekistan
Algeria
Twitter and Nintendo Wii launched
New Horizons space probe launched to explore Pluto

2007

- Erice Manifesto published on reform of safety communication
- WHO Programme meeting – Buenos Aires, Argentina

Suriname, Togo, Uganda
Zanzibar
Apple iPhone launched

2008

- MedDRA tool launched in VigiBase
- VigiMine launched with data mining algorithms and disproportionality analysis
- Methods for longitudinal database observation and signal detection published
- 10th international training course, Uppsala, Sweden
- WHO Programme meeting – Uppsala, Sweden
- UMC 30th anniversary

Andorra, Barbados, Ethiopia, Kazakhstan, Namibia, Sierra Leone, Sudan

Anguilla, Antigua & Barbuda, British Virgin Islands, Dominica, Grenada, Montserrat, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines

Large Hadron Collider opened at CERN

First hydrogen cell-powered car

2009

- PaniFlow and CemFlow web-based reporting and monitoring tools
- Monitoring Medicines and PROTECT collaborative projects started
- UMC-Africa office opened in Ghana as part of WHO Global Outreach
- Marie Lindquist appointed as UMC's second Director
- WHO Programme meeting – Rabat, Morocco

Botswana, Madagascar, Montenegro, Saudi Arabia, Senegal

Guinea-Bissau

Global pandemic of H1N1 swine flu virus

UN Copenhagen Climate Change Conference

The WHO connection

UMC supports WHO's mission to direct and coordinate international health for the United Nations, to build a better, healthier future for people all over the world. A growing world population and changing patterns of global need and funding make WHO's job more necessary and complex every year.

Alongside UMC, international pharmacovigilance is delivered by four, partner WHO Collaborating Centres – in Morocco, the Netherlands, Norway and India (see page 64). Pioneering work was also done in Sub-Saharan Africa by the former Collaborating Centre in Ghana, under the leadership of Professor Alex Dodoo.

Clive Ondari

'Unleashing the power of numbers'

Clive Ondari is WHO's Coordinator for Safety and Vigilance, and previously led the work on Medicines Access and Rational Use. Before joining WHO, Clive worked for the Government of Kenya, and was Technical Officer for the Kenya National Drug Policy Programme from 1997 to 2000.

Dr Ondari started his career in academia and regulatory affairs. He was Associate Professor and Head of Department at the University of Nairobi and Chairman of the Pharmacy Board (Committee on Registration of Medicines) for over ten years.

Financial sustainability

'I think UMC's greatest achievements are the scientific leadership it's provided on behalf of WHO, and the astounding growth it's driven in expanding the WHO Programme, working with partner centres and collecting data for analysis. These are not small accomplishments.

The Centre's commercial independence has been borne out of necessity – and I view it as a plus. The priorities for WHO's resources have shifted over the years, so while we've continued to offer support via nominations to UMC's Board, we could not fund its work. The Centre has proved that it's possible to be financially sustainable, so the big issue is how resources are used and reflected in its accountabilities.

Building future capacity

Having created national centres and systems in so many countries in all parts of the world, the next generation of pharmacovigilance is going to need

a completely different configuration. One that promotes local approaches to data analysis and is targeted more closely on the particular mix of diseases and medicines used in each region.

This demands even more active and systematic engagement with member countries, with UMC remaining the critical repository of global safety data. The team needs to continue unleashing the power of numbers, so that they can say: "Yes, we've seen this effect, and yes it's a real concern," when a new signal emerges.

The big issue is how resources are used

UMC has been truly instrumental in reaching out to build international capacity for patient safety. It's been an adaptive formidable force in overcoming political, diplomatic and managerial challenges. The growth in direct patient reporting is going to be a game-changer, which will bring new challenges in how to ensure quality from ever larger amounts of data. I'd like to see the Centre dedicate even more attention to developing innovative ways to meet these emerging needs.'

Shanthi Pal

'Robust scientific support'

WHO's Group Lead for Medicines Safety since 2010, Shanthi Pal is responsible for the policy that underpins the WHO Programme for International Drug Monitoring, and the day-to-day relationship with UMC. Originally from Southern India, Dr Pal is a WHO-nominated member of the Centre's Board.

Previously a WHO technical officer, Shanthi emphasises the 'very special arrangement' between the Geneva headquarters and UMC's operations as the lead technical partner for drug safety.

A unique relationship

'While WHO has other partners and collaborating centres, UMC is the only one of its kind – created and run thanks to the original agreement with the Swedish Government. It has done great work to build such a mammoth database, and made a singular contribution in developing simple, affordable tools to an international standard. VigiFlow and other systems have helped low- and middle-income countries to engage with and become part of the global community for pharmacovigilance.

I'm confident that we can achieve another surge in activity as more and more countries get access to improved tools and are able to leapfrog straight to the next level, incorporating smart technology and electronic health records.

Convincing sceptics

We still face political and scientific barriers in making medicines safety more present in public health programmes, especially those for Malaria, Tuberculosis and HIV/AIDS. Spontaneous reporting is often dismissed as too basic, voluntary and limited compared to large-scale studies that focus on collective benefit. So we have to keep on working on other methods to become relevant to these programmes. We need to be more interesting to ministries and donors, and be able to persuade them how we're best placed to help.

It can take a big scare to make people realise they need a proper safety net

Sadly, it can take a big scare to make people realise they need a proper safety net. I think the answer lies in more advocacy and using new medicines to lever greater influence. This is where UMC's robust scientific support is needed.

At the sharp end

Global pharmacovigilance is an intense environment – most things need doing yesterday, and if you're lucky you'll find that out tomorrow! This can put real pressure on UMC and its people, so I think the Centre needs to plan for this by keeping a slice of its capacity ready for the unexpected. Epidemics like Ebola don't tell us that they're coming, but we know that they will.

I've been privileged to work alongside many of UMC's brave foot-soldiers of patient safety. They're happy, committed, hardworking and humble people of whom I'm very fond. It's critical for these individuals to stay in the spotlight of UMC's work; doing even more to get patients on board and complete the loop with manufacturers and regulators in a proactive way.

Debate around the UMC board table can sometimes be feisty – but that's how it should be. What we do is important, and that's why we're all so passionate about it.'

Partner collaborating centres

UMC is one of five (previously six) official WHO Collaborating Centres, which concentrate on different aspects of medicines safety across the world.

Monica Plöen

'It's a big family'

UMC's Head of Pharmacovigilance Collaborations Monica Plöen plays a pivotal role in linking the Centre's work with WHO headquarters and projecting its impact out to the 156 member and associate nations. She loves the feeling of being part of an established, international endeavour that benefits the whole world.

Part of UMC's team since 1992, Monica's role involves coordinating collaborations with external stakeholders to support member countries, and building capacity to boost local analysis and action in response to the adverse effects of medicines.

A special place

'The world has evolved in so many ways since 1978, and UMC has been an important player in creating the new science around patient safety. It hasn't all been straight-line progress – the study methods we've used haven't always worked perfectly; but that's how scientists learn and make advances.

The Centre is able to attract and keep good people, and use WHO's reach to inspire and mobilise passionate, gifted people in every part of the world. It's great when we're able to make big breakthroughs, but the little points of progress we see every day are just as important. UMC is a special place – my grandmother used to very proudly tell all her neighbours about the work I do here!

Global healthcare is not just about access to medicines

The WHO Programme's steady growth shows that global healthcare is not just about access to medicines and their supply – you need to have pharmacovigilance built in as well. And that has to prove both better patient outcomes and the cost savings and benefits that go with them.'

Across the continents – Latin America and the Caribbean

Many human diseases can be treated with prescription drugs derived from nature. And the rainforests and other ecosystems of this region provide most of these. The continent is the world's medicine chest. Its extraordinary topographical, climatic and ethnic diversity present a microcosm of global pharmacovigilance. It's a part of the world where professionals and processes need to cater for the extremes.

Luisa Valdivieso

'Fantastic friendships'

Luisa Valdivieso is a Professor of the Faculty of Pharmacy at Universidad Central de Venezuela in Caracas, which is home to the CEFARVI pharmacovigilance centre. She is also an adviser to her country's national centre, Instituto Nacional de Higiene Rafael Rangel. She's positive about the role that UMC and WHO have played in helping to promote patient safety across South America, and confident about how technology and relationships will continue to yield results.

Luisa's contact with UMC dates back to the training course she attended in 1998, and she has remained in close contact with the Centre ever since. She has also taken in part in training events in Argentina and Italy, and assisted with almost all the annual WHO Programme meetings since 1999.

Amazing leaders

'UMC has helped the whole world discover and understand what pharmacovigilance is about. The team's training courses have done a wonderful job in helping to create a safety culture, by raising awareness with doctors, journalists and the public. And with reporting side effects now made much easier by mobile phone, we're starting to see the impact of this work.

We need to keep on raising awareness among professionals and patients

I've met some amazing leaders and classmates at UMC, and gained fantastic friendships from attending the national centres meetings and working alongside such gifted people. My national centre has also has a very good relationship with WHO headquarters. Together, we've been able to tailor and apply pharmacovigilance to the social, economic and genetic differences that exist in different parts of South America.

We need to keep on raising awareness among professionals and patients, so that people don't prescribe or take medicines so readily, without knowing the potential risks. Drugs should be used rationally and responsibly, so that's why we need UMC to keep on doing what it does so well.

On guard for problems

In Venezuela, access to proper medicines is still the biggest problem, but experience from Argentina, Colombia, Mexico and Peru shows how this can be overcome. And we must also be on guard for the problems of counterfeit and substandard medicines.

I love the team at UMC and I am so grateful to have met so many great people. They've really helped me like friends – and human relations like these are essential to the whole human condition!'

Mónica Tarapués

'A whole world picture'

Mónica Tarapués lectures in Basic and Clinical Pharmacology at Universidad Central del Ecuador and Universidad San Francisco de Quito. As part of her doctoral studies, she completed a three-month internship at UMC in 2014, and believes passionately in the Centre's hands-on, international approach to spreading learning and best practice for patient safety.

Ecuador became a full member of the WHO Programme in 2017, after five years as an associate member. Dr Tarapués has worked alongside UMC staff to deliver training courses to professionals in Peru and Panama.

The whole world

'During my time working at UMC, I was able to see the whole world of pharmacovigilance. The internship gave me a much clearer understanding of the complete science beyond just a national or regional view. I also got to see exactly how data is collected and used at the Centre. I think WHO found the perfect place for technology to thrive in Uppsala.

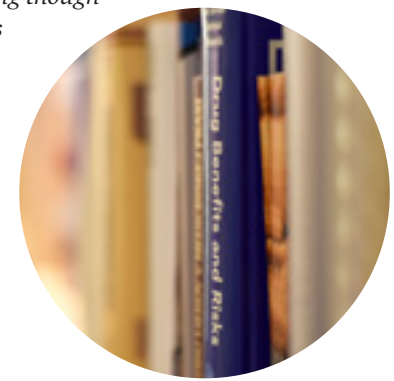
Education is the most important thing

The information methods and technological tools are brilliant, but it's essential to actually visit national centres too, and build up the personal connections that secure good pharmacovigilance. It's so helpful to have staff who speak local languages, who have the ability to explain what they do, how and why.

Close links

UMC always seems to be looking ahead and its working style really reflects the 'inspire – engage – transform' slogan. There's a close link with WHO headquarters in Geneva and also with the Pan American Health Organization – it's encouraging to see how we can all fit together. UMC maintains a whole world picture, and it feels like a big family.

Education is the most important thing though – we need to make sure that doctors understand and start talking about the potential harm medicines can cause as well as their benefits, right from when they are students.'



Success in… *Chile*

Swift action on the risks of intravenous medication

In January 2016, a hospital in Chile's capital, Santiago, and another regional hospital alerted the Institute of Public Health about adverse effects linked to use of metronidazole (an antibiotic commonly used to treat bacterial and parasitic infections of the skin, mouth and genitals). The drug comes in tablet, liquid, gel, cream and suppository forms, and can also be given by injection.

The manufacturer of the product withdrew the suspicious batch of metronidazole from sale

The suspected adverse reactions involved patients experiencing chills, fever, chest pain, low blood oxygen and increased heart rate, plus abdominal pain, nausea, vomiting, diarrhoea, rashes and dermatitis. Of 37 reports received from the hospitals over the preceding year, 12 were for people receiving the same dosage (nine women and three men), and all were associated with the drug being given intravenously. Two of the cases were considered serious.

A review of the medicine's technical information showed that these side effects were not included in the brochures approved by the Food and Drug Administration and European Medicines Agency. Only the data sheets used by Health Canada referred to the potential side effects. This prompted a search of UMC's global database, which revealed 390 cases of suspected adverse reactions to metronidazole worldwide.

Equipped with this global evidence, in May 2016 the Institute of Public Health issued a pharmacovigilance guidance note to all heath professionals Chile, alerting them to the possible risks for patients receiving the drug intravenously. The note advised physicians to administer the treatment slowly over 30-60 minutes, and to avoid mixing it with any other medicine or equipment containing aluminium (such as needles and cannulae).

The guidance, which also reminded professionals of the importance of reporting suspected adverse effects, was published on the Instituto de Salud Publica website in June 2016, replicated in the Bulletin of the Buenos Aires Pharmaceutical Surveillance Network in Argentina, and presented as a poster at the Congress on The Rational Use of Medicines in Brazil in 2017.

In response and as a precaution, the manufacturer of the product withdrew the suspicious batch of metronidazole from sale.

This case highlights how careful reporting and monitoring can detect and prevent harm quickly and across a whole continent. The 12 serious cases identified in Chile were put into context by the larger sample found in VigiBase, which enabled the regulatory authority to communicate the risks in a swift, clear and impactful way.

The Institute's ability to act with such speed and success is also, in part, down to Chile's strong investment in staff development, which has seen members of its team regularly attending the UMC international training courses since 2011. It's a perfect example of global pharmacovigilance in action, and the international benefits of the WHO Programme ●

Making it pay

UMC has been able to grow and survive thanks to the far-sighted decision to make it commercially independent and self-supporting. With baseline programme funding from the Swedish government having ceased in 2000, all the Centre's operating income now comes from sales of and subscriptions to the WHO Drug Dictionary, WHODrug, and other technical products and services. It's an approach that can create tensions and misconceptions, but one that's essential for the future of global pharmacovigilance and patient safety.

Mats Persson

'The cornerstone of medicine safety'

Mats Persson retired as UMC's Head of Global Sales and Customer Relations in 2015, after almost 20 years developing the Centre's commercial independence through sales of the WHO Drug Dictionary. His sharp business mind saw revenue double in his first year, and he is immensely proud of having been part of an organisation that's lived up to its values.

Mats studied Industrial Marketing at Uppsala University, then worked for two American pharmaceutical companies before joining the Swedish Association of the Pharmaceutical Industry. After seeing UMC's advertisement for someone to help sell their products, he was so sure that he could make a success of it, that he didn't worry about taking a 40 per cent pay cut to join the Centre's staff.

Win, win, win

'Right from the start, it was clear to me that UMC's blend of science and public affairs had to be paid for – we couldn't rely on government funding from Sweden or anywhere else. When Marie Lindquist first showed the WHO Drug Dictionary to drug companies at a conference, it became clear that it solved a huge problem for them. So they were very interested in buying it, and at that moment, UMC's future was created.

The Dictionary has become a de-facto global standard as the cornerstone of medicines safety. All of the profits are reinvested into the WHO Programme, so it's a win, win, win product, which connects UMC closely to the pharmaceutical industry while staying both independent and aligned to WHO's commitment to the people of the world.

Barton Cobert (see page 55) on Mats Persson:

'Mats is sharp, funny, reliable and a pleasure to deal with. He was always even-tempered, honest, charming and effective.'

Science in the lead

I think UMC is defined as much by what it's not as what it is. The centre isn't a drug manufacturer, a government agency or part of the United Nations; it's something specific and special. UMC is driven by science not politics, and patients are the stake-holders. It's an organisation that's prepared to stick its neck out and adapt its approach to different countries and markets.

An organisation that's prepared to stick its neck out

In today's open societies plagued by fake news and misinformation, the world needs honest, independent players like UMC more than ever. A single bad news story has the potential to kill off a drug and rob millions of its benefits, so the analysis and reporting that goes on in Uppsala will continue to be very important.

My time at UMC was the most exciting part of my business career, so I will always feel part of it.'

Progress from pain

As proof of the maxim that success rarely travels in straight lines, and the risks associated with becoming more commercial, UMC's early ventures into income generation led to some bureaucratic and legal issues. In part, these related to the Centre being responsible separately to national centres, the Swedish Government and WHO. This resulted in a change of the entire Board in 1998, to introduce new members with more economic and management skills. The silver lining of this change was that the new Board turned out to be highly effective, and helped UMC on its journey to being financially stable and self-sufficient.

The Swedish Ministry of Social Affairs insisted on the Board changes following a review of structural options for UMC as a revenue-generating entity. The possible choice of becoming a sub-department of an academic institution was discounted by UMC's Director, so a new and independent Foundation Board was created, with half the members appointed by WHO and the other half by the Swedish Government. The Government appointees were required to act with 'undivided responsibility' according to the Swedish Foundation Act.

UMC benefited from the financial and legal skills offered by the new Board members, which helped to set the Centre firmly on its feet as a not-for-profit foundation where surpluses can only be used to develop and support the WHO Programme.

This period was disruptive and painful for UMC, but was also an important development that ultimately secured its future sustainability

2010s – the family keeps growing

UMC's pre-eminence in global patient safety has enabled it to keep on growing and extending its reach to every part of the world. New countries continue to join or become associate members of the WHO Programme, and developments in both medical science and artificial intelligence put the Centre on the brink of an exciting and radically different future.

2010

- First clinical findings from patient records screening published
- Method to detect drug dependence from individual case safety reports launched
- Fuzzy text algorithm developed to spot adverse reactions in free text
- Standardised Drug Groupings launched
- Chinese drug dictionary and Japanese cross-reference tool launched
- WHO Programme meeting – Accra, Ghana
  - Burkina Faso, Cameroon, Democratic Republic of Congo, Côte d'Ivoire, Iraq, Kenya, Slovenia, Zambia
  - Bosnia and Herzegovina, Burundi
  - Apple iPad launched
  - First Space X flight

2011

- First substantial case study reports from India
- Reporting and knowledge transfer agreement signed with SFDA in China
- Collaboration on drug dictionaries agreed with FDA in USA
- VigiLyze search and analysis tool launched
- Web-based collaboration portal set up with groups for Vigimed, VigiFlow, CemFlow and VigiLyze
- WHO Programme meeting – Dubrovnik, Croatia
  - Benin, Mali
  - Albania, Gambia
  - First synthetic organ transplant

2012

- Signals made publicly available in WHO Pharmaceuticals Newsletter
- VigiFlow patient reporting module launched
- First direct use of VigiFlow by a pharmaceutical company
- WHO Programme meeting – Brasilia, Brazil
  - Cambodia, Cabo Verde, Eritrea, Jamaica, Niger
  - Syrian Arab Republic
  - Instagram launched for Android devices
  - Curiosity Rover landed on Mars

2013

- Pilot of EU-funded cohort event monitoring system
- Duplicate detection and free-text algorithms tested as part of IMI-Protect
- Medication error guidelines developed
- UMC's Expecting the Worst Japanese edition published
- 15th international training course, Uppsala, Sweden
- WHO Programme meeting – Rome, Italy
  - Angola, Bolivia, Guinea, Liberia, Rwanda, United Arab Emirates
  - Qatar
  - Micro-video application Vine released by Twitter

2014

- Cluster algorithm developed to identify spikes in reporting
- WHO Programme meeting – Tianjin, China
  - Bangladesh, Bhutan, Mauritius
  - Ebola epidemic in West Africa
  - Rosetta space probe landed on Agilkia comet

2015

- WHO pharmacovigilance indicators published
- Take & Tell awareness campaign launched
- Public access to aggregated data enabled through VigiAccess
- UMC's Expecting the Worst Chinese edition published
- VigiLyze 2.0 launched with disproportionality analysis tool
- First Asia-Pacific regional training course, Mysuru, India
- WHO Programme meeting – New Delhi, India
  - Lao People's Democratic Republic, Swaziland
  - Tajikistan
  - UN Paris Climate Accord

2016

- Patient reporting app launched as part of EU-funded WEB-RADR project
- Algorithms developed to identify signals in social media
- WHO Programme meeting – Muscat, Oman
  - Afghanistan, Maldives, Panama
  - Haiti, Malawi
  - Zika virus outbreak in South America

2017

- WHODrug Global bundle launched
- Pilot of Annie & Mac comic book in ten countries
- WHO Programme meeting – Kampala, Uganda
  - Ecuador, El Salvador

2018

- Focus on global capacity building
- 20th international training course, Uppsala, Sweden
- WHO 70th, WHO Programme 50th and UMC 40th anniversaries
- WHO Programme meeting – Geneva, Switzerland
  - Azerbaijan, Chad, Papua New Guinea, Paraguay
  - First monkey clones created with somatic cell nuclear transfer
  - First Space X earth orbit mission

Across the continents – Asia and The Pacific

Bringing the world's two most populous countries, China and India, into the WHO Programme was a vital milestone in the development of worldwide patient safety. The distinctive medicinal and healthcare heritage of these and other Asian and Pacific nations, plus technological leadership and the particular impact of climate change make the region a hot-spot for advanced pharmacovigilance.

A vital programme that's of great value to the whole world

Krishan Chandra Singhal

'A humanitarian approach'

Founder of the Society of Pharmacovigilance, India (SoPI) in 1999, Prof Singhal has served as vice chancellor of NIMS University in Jaipur and has a hospital in Aligarh, northern India named after him. He traces patient safety practice back over two millennia as part of Ayurveda, the 'science of life' that is world's oldest surviving medical system.

'K.C.' first encountered UMC's work at a seminar in New Delhi in 1983 – an experience that inspired him to start a national project of the Indian Council of Medical Research, with 13 centres across the country. He then went on to share his expertise with others at the annual courses in Uppsala and translate WHODrug into Hindi.

Strong connections

'There was very little understanding of adverse drug reaction reporting in India when I first started working in this field, so the strong connections I've had – and continue to have – with UMC have been tremendously important.

With such a vast and growing population, physicians in India were often too busy to pay attention to reporting adverse effects of the medicines they prescribed, and that's still a problem in many other developing countries. But the centres we created have helped to change this and develop the concept of clinical pharmacy.

UMC has succeeded in involving large parts of the world in medicines safety and helping individuals to strengthen their skills. Without its support and close coordination with WHO, we wouldn't be where we are in India now. UMC takes a humanitarian approach and delivers a vital programme that's of great value to the whole world.

On-the-spot expertise

The challenge now is to continue developing pharmacovigilance in ways that really work for each country – using the on-the-spot knowledge of professionals who really know and understand local populations. People and relationships are the keys to effective patient safety.'

Intensive Medicines Monitoring Programme

The Intensive Medicines Monitoring Programme (IMMP) was established in New Zealand in 1977 to enhance monitoring for previously unrecognised adverse effects connected to new medicines. It involved studying prescription data and event information; and was a pioneering example of cohort event monitoring methodology.

High response rates from prescribers and high-quality event information, spontaneous reports, prescription returns and links to other databases helped to identify and analyse signals that other approaches might miss. Key early IMMP successes included detecting problems with amnesia and arrhythmia due to sibutramine, and psychiatric and visual disturbances arising from the anti-inflammatory drugs celecoxib and rofecoxib.

IMMP highlighted the importance of rapid communication to prescribers about the risks of new medications. New Zealand's relatively small population enabled a longitudinal approach to data analysis, including cases where therapy was stopped or changed. The programme has made a significant contribution to in-depth epidemiological studies

Gurumurthy Parthasarathi

'Perseverance and hope'

Gurumurthy Parthasarathi is the Dean, Global Engagement, at JSS Academy of Higher Education & Research in Mysuru, Southern India. He has played a leading role in developing the Pharmacovigilance Programme of India and was a Theme Leader for pharmacovigilance and drug use evaluation of the BRICS Medicines Alliance (covering Brazil, Russia, India, China and South Africa).

Dr Parthasarathi qualified in Clinical Pharmacy at the University of South Australia in Adelaide. Since returning to India in 1997, his research has focused on promoting the quality and safe use of medicines in the region. In collaboration with UMC, he has helped to establish an annual Asia-Pacific region pharmacovigilance training programme, hosted in India.

Appreciating the wider aspects

'My connection with UMC goes back almost 20 years, when I was invited and awarded a Fellowship to join the 1999 international training course in Uppsala. It was so helpful and interesting to interact with people from all around the world, and appreciate the wider aspects of pharmacovigilance, which I was less familiar with. I discovered that medicines safety is much more than a patient-focused activity by seeing the Centre's work on WHODrug, genomics and regulatory issues.

Able to show people what's big about it

This gave me lots of ideas I was able to take back to India and use to build connections between my own hospital and others. It helped us look into how adverse effects impact on patients' adherence to treatments and the cost implications of problems with medication. Some health professionals asked what was so big about reporting side effects, so our research was able to show people what's big about it and why pharmacovigilance is so important.

A flagship programme

We work in a small but powerful and expanding global community that's dedicated to the safer use of medicines. It's always helpful to learn from other people's experience, and it's clear that there's much to explore in both the similarities and differences between countries.

The Asia-Pacific training course was made possible by the wonderful work UMC had already done on capacity building in this part of the world. As personal beneficiaries of this, I and some other national leaders wanted to offer a new model for regional training that could be a flagship programme of collaboration.

Since we ran the first course in 2015, I'm pleased to say that the course has evolved really well, and for the latest event we received 93 applications for the 32 available places. We've listened carefully to feedback, and I'm delighted that we've been able to deliver on people's expectations. The courses offer wonderful opportunities to build contacts and network with peers, plus fun and social activities. I know these are all things that participants value and treasure.'

Kenneth Hartigan-Go

'An integral part of the right thing to do'

School Head at the Asian Institute of Management (Stephen Zuellig Graduate School of Development Management) in Makati, Philippines, Kenneth Hartigan-Go sees WHO and UMC as the 'yin and yang' of global healthcare – an interdependent relationship that helps to make safety of medicines part of everyone's business. He believes that long-term coaching and support of pharmacovigilance specialists is vital for the future.

Dr Hartigan-Go founded the Adverse Drug Reaction Monitoring Program for the Philippines Government and served two periods as Director of the country's Food and Drug Administration between 1999 and 2014. He was also an executive committee member of the International Society of Pharmacovigilance (ISoP).

Saving lives

'UMC has created the worldwide community of pharmacovigilance – increasing membership of the WHO Programme and giving invaluable advice to drug regulators. The Centre has been remarkably effective with the resources available to it, and should be very proud of its achievements.

Drug intelligence is similar in some ways to counter-terrorism – you don't get rewarded for preventing risks, but are criticised if you miss an opportunity to avoid harm. We can never be sure how many of course, but UMC's work has definitely saved lives. There's no real money to be made out of pharmacovigilance, but it needs to be built into all public health qualifications, policy, industry and government. It's an integral part of the right thing to do.

New generations

'The priority now is to develop local champions in every country and look after the next generation of pharmacovigilance specialists. Training is crucial of course, but we need to follow people's careers and mentor them over the longer term.

UMC's work has definitely saved lives

Big data is also going to be important, but is has to be the right data, collected and used in the right way. And we're always going to need human intelligence and intuition to bring context to the data. Zero risk is impossible, and our work isn't about the drugs, it's about individual patients and their real lives.' ●

Yang Wei

'Remarkable results'

Pharmacovigilance in China is managed by the National Food and Drug Administration (CFDA), which operates the Center for Drug Re-evaluation and the National Center for Adverse Drug Reaction Monitoring (NCADRM), in Beijing. Dr Yang Wei directs the country's spontaneous reporting system, which connects the centres in the capital with 34 provincial offices and more than 400 municipal bases.

A WHO Programme member since 1998, staff from China's national centre have worked closely with UMC to develop training, education, standard medical terms, signal detection and analysis. Since 2013, CFDA has submitted almost a million individual case safety reports to VigiBase.

Setting a good example

'UMC has made a major impact on developing methods for pharmacovigilance research, as well as helping member states to establish and grow their systems. The Centre has achieved remarkable results through its methods for data mining and signal detection. These have proven to be good examples for other countries as they create their own signal detection frameworks. Good communication and exchange of knowledge about these techniques among Programme members is very important and needs to develop further.

We use the VigiFlow, VigiBase, VigiLyze and vigiRank systems provided by UMC to collect information about the adverse effects of medicines, analyse data and detect signals. These methods and tools not only help countries to establish local pharmacovigilance, they also provide valuable reference information, which has greatly promoted global patient safety.

Helping member states to establish and grow their systems

International exchange

There are huge economic, social and cultural differences between countries around the world, but UMC has done a great work to promote, coordinate and harmonise the development of pharmacovigilance among member states. The annual meeting of national centres functions as a platform for exchange and communication among Programme members.

UMC's rigorous scientific work and strong work ethic has made a big impression on us. We've received a huge amount of help and support to advance safety of medicines in China. Communication has always been good between us.

Accurate and efficient

Economic globalisation and the Internet mean that drug manufacture and use is also now global. Improved access to medicines brings greater challenges in assessing drug risks and protecting public health. We need to be more scientific, accurate and efficient in monitoring medicines safety. So I hope that UMC will continue to conduct in-depth research on methodologies and provide further guidance and help.'

John McEwen

'An array of great staff and volunteers'

John McEwen worked for the Department of Health in Australia as Medical Officer and Secretary to the Australian Adverse Drug Reaction Committee (ADRAC). He then led the medical staff at the government-owned vaccine manufacturer, before serving in various roles with his country's Therapeutic Goods Administration (TGA) in Canberra. He remains a part-time adviser there and was awarded the Australian Public Service Medal for his outstanding contribution to promoting patient safety.

Dr McEwen chaired UMC's Advisory Group in the mid-1980s, and played a significant role in developing pharmacovigilance in other parts of the region, including Singapore, Hong Kong and Vanuatu.

A crucial principle

'I first visited Uppsala in 1979, and went on to attend and take part in many of the national centres meetings and training courses, including those we hosted in Canberra. There are lots of similarities between the ways Sweden and Australia have developed their approach to medicines safety, and I've always found UMC and its people to be energetic, sensible and on the same track.

Reaching an agreement to share and use details of the data held in the WHO database without the need for individual consent to each request was vital, because the arrangements had previously been based on a veto system. There were reservations from some countries about the change, but this crucial principle was eventually established, and it has supported UMC's work ever since.

Energetic, sensible and on the same track

UMC's early statistical work to develop the use of neural networks to link patterns of health effects to specific medicines was another big advance. And this was greatly supported by the expert human analysis of reports by an array of great staff and volunteers.

Indispensable

Medicines are becoming more sophisticated and complex all the time. Many are now designed to target particular cell receptors to treat cancer and other diseases, but this means they create new risks of immune-system reactions, which can be rare but severe. Public and media pressure to release drugs onto the market without extensive human trials also put more emphasis on post-market safety. So UMC's monitoring will continue to be an indispensable part of protecting patients worldwide.'

Success in… *Malaysia*

Safeguarding young children from harm

Malaysia's National Pharmaceutical Regulatory Agency (NPRA) based in the city of Petaling Jaya has made a number of medicines safety breakthroughs related to adverse effects experienced by young children.

Pharmacovigilance success doesn't always come quickly

Between 2011 and 2014, the Agency took action to tighten the use of metoclopramide (a common treatment for nausea and vomiting that's also given to patients with gastroesophageal reflux disease and migraine headaches). More than 350 reports were received of people suffering neurologic adverse effects, including eye problems, spasms and muscle contractions.

More than half of the reports involved patients under the age of 18, so the NPRA issued a directive in January 2015 to restrict use and dosage of the drug. Since then, the proportion of reports involving children and young people has dropped to 35 per cent of the total.

The Agency has also been active in controlling the use of the anti-histamine sedative promethazine for children with coughs and colds. More than a quarter of the 54 reports received between 2000 and 2012 involved children aged below two years, and in one case a baby of just four weeks. Adverse effects included skin discolouration, breathing difficulties and jerky movements.

Since the Agency issued its last reminder to prescribers and case studies in 2013, there have been no further reports of similar problems involving children.

Another, long-running case affecting adults concerns allopurinol (a medication used to control high levels of uric acid in the blood, which is often caused by gout, kidney stones, and the effects of chemotherapy). Between 2002 and 2007, the NPRA noted an increasing number of adverse reaction reports involving serious skin reactions, especially when the drug was prescribed outside of the approved indication.

The Agency issued its first circular to remind prescribers about appropriate use of allopurinol in 2008, and has since published a series of reminders, plus recommendations to change the product labelling and tightening of the approved drug's category to make it a specialist treatment.

The numbers of adverse reaction reports initially fell sharply in response to these actions, but have increased again in recent years; leading the NPRA to do further research into prescribing practices and the impact of auxiliary warning labels. The allopurinol story shows that pharmacovigilance success doesn't always come quickly, and that determined persistence is sometimes required to safeguard patients ●

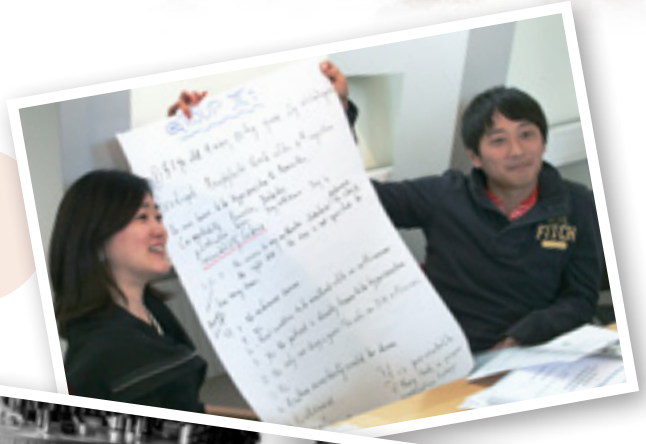
Training and capacity building

The most important role in nurturing any family is to pass on accumulated wisdom and knowledge to the next generation. This sits at the heart of UMC's approach and accounts for an ever-growing part of its work across the world. The Centre's training, learning, advocacy and support have helped to create pharmacovigilance systems from scratch in dozens of countries. UMC thinks global and acts local – building the particular skills and capabilities needed to succeed in each location.

Outreach and advocacy

As membership of the WHO Programme took off, it soon became obvious that it was easier and more efficient for a few UMC staff to travel to newly-joined countries than expect all their centre staff to visit Sweden. This approach also makes it possible to maximise use of all the local knowledge, expertise, contacts and understanding to help pharmacovigilance flourish.

New centres do face roadblocks – where competing interests don't always align, or there are parties who would prefer medicine safety systems not to succeed. In these situations, UMC's role as an expert, global advocate is invaluable in helping to explain the benefits of a systematic approach to safety. People tend to be most persuaded by others like them, so the outreach team's ability to showcase gains from neighbouring nations has helped to overcome many objections.



International training courses

Since 1993, UMC has invited new and developing pharmacovigilance talent from WHO Programme member countries to come to Uppsala for an intensive ten-day training programme. Originally biennial, the training courses proved so popular that from 2005 they became annual events.

As well as getting the chance to visit and sample the atmosphere and working environment of the Centre, learners complete a packed and carefully structured curriculum, delivered by some of the biggest and most respected names in pharmacovigilance. Updated each year, the course introduces the science's essential topics while keeping people up to date on the latest trends, concerns and breakthroughs.

UMC's role as an expert, global advocate is invaluable

Like all the best training, a great deal of learning occurs in the breaks between sessions from the synergy created by bringing together highly-motivated and like-minded people with their peers and predecessors. The training courses foster lifelong contacts and friendships, and many learners later return as tutors to pass on their experience. UMC also offers a growing prospectus of online learning, covering core aspects of pharmacovigilance practice

Patients and producers

The ultimate test of UMC's effectiveness in promoting greater safety of medicines lies with the end users – all of us as the world's patients, and the companies that create the medicines we use.

François Houÿez

'Patients are more precise than doctors'

François Houÿez has been the Director of Treatment Information and Access and Policy Advisor at EURORDIS in Paris, France since 2003. It is an alliance representing almost 800 rare disease patient organisations and the voice of 30 million people affected by rare diseases throughout Europe.

François is a pioneer of patient advocacy, and was part of the first patients' delegation to engage in dialogue with the European Medicines Agency (EMA) in 1996. He is part of the Agency's Patients' and Consumers' Working Party and represents EURORDIS at the Health Technology Assessment (HTA) Network and EUnetHTA – an initiative to promote European cooperation in sustainable health technology assessment.

Safety as a luxury

'In my early work around HIV and AIDS treatments, concern about adverse effects was seen as a luxury – a problem of the rich and those able to receive medication. But as drugs to prolong life became a reality in the mid-1990s, side effects became a wider issue. It was through the studies funded to look into problems with extreme weight-gain and changes in body shape that I became aware of UMC and WHODrug.

When you're dealing with rare diseases, the larger the population you're able to reach and study the better, so UMC's database and the guidelines, methods and tools it has initiated and developed have been a big benefit. The Centre's campaigns to promote pharmacovigilance – like 'Take & Tell' – have also been excellent.

A whole new level

I'd like to see UMC do more to work with and support patients' organisations, so we can develop more 'direct to patient' pharmacovigilance. People experiencing illness often want answers to difficult questions, and in many cases patients are more precise than doctors in the information they ask for. So we have to work even harder to see if that data exists and how to get at it.

People experiencing illness often want answers to difficult questions

There's a growing lack of trust in science and authorised products in some parts of the world, accompanied by greater reliance on natural, alternative, illicit or untested treatments. This is opening up the risk of a whole new level of potential interactions and adverse effects, which the whole pharmacovigilance community is going to have to address.'

Sally Okun

'A remarkable capacity to advance'

Sally Okun is the Vice President for Advocacy, Policy and Ethics at PatientsLikeMe – a patient network in Cambridge, Massachusetts, USA, which is pioneering the future of personalised health. It's based on the fundamental principle that patients know what it's like to live with disease better than clinicians, and so giving people the tools to track their progress and compare themselves to others can lead to better outcomes.

Sally's work represents 21st century healthcare, realised through sharing, support and research. PatientsLikeMe is the world's largest patient network, with more than 600,000 members tracking, learning and contributing data for research into 2,800 conditions. Its revolutionary 'science in your hands' approach has established the patient voice and real-world evidence as pillars of medical advancement.

Always innovating

'From my perspective as a clinician who's integrated the first drug safety platform into a patient research network, I think UMC has demonstrated a remarkable capacity to advance 20th century pharmacovigilance into the 21st century. Its work supports safer and better living.

The Centre has developed innovative tools, methods and collaborations like VigiBase, which provides data for international safety monitoring, and vigiGrade to assess the quality of individual case safety reports.

UMC has also played a big part in the WEB-RADR project in Europe, to develop a mobile app for patients and healthcare professionals to report suspected adverse drug reactions to national regulators. And it's doing breakthrough work on using social media data to identify drug safety issues.

The Centre enjoys the respect of a broad, international community of people committed to ensuring effective use of medicines. Its commitment to public health and safety deserves to be more more well known by the world's citizens so that members of the WHO Programme can secure even greater patient participation.

Balancing cost and quality

The high cost of medicines remains one of the biggest global challenges; making it increasingly difficult to ensure access to safe and effective treatments. Low-cost alternatives can result in people unknowingly receiving counterfeit products. So patient education and engagement are vital.

The high cost of medicines remains one of the biggest global challenges

My experiences of working with the UMC team have always been delightful learning opportunities. I took part in the Centre's Risk Conference in 2014, which was an extraordinary event. It gave a truly global perspective on safety, from inspiring leaders from across the world.'

Jayesh Pandit

'A work of passion'

Bayer's Middle Africa Head of Pharmacovigilance, Jayesh Pandit, sees the potential for ever-greater collaboration and synergy between WHO, UMC and the pharmaceutical industry. He believes that patient safety has to be properly built in to all medical programmes, and that the first question every physician should ask for differential diagnosis is: 'are you taking any medicine?'

Jayesh set up and led Kenya's pharmacovigilance system at the country's national drug regulatory authority, the Pharmacy and Poisons Board, for ten years, before moving to one of the world's biggest pharmaceutical and life science companies, Bayer, in 2013. Working to fulfil his employer's vision of 'Science for a better life', Jayesh thinks partnership will be even more important in the years ahead.

Continuously adapting

'In my career, I've gone from being a regulator, to being regulated. I believe many people used to see pharmacovigilance as boring, and weren't attracted to it because it involved lots of form filling, asking question after question and data analysis. It felt like a niche specialism, where you worked for little recognition or reward! But thanks to WHO's and UMC's greater collaboration with national centres, stakeholders and partners, that's now different.

To me, pharmacovigilance is a work of passion. A passion to save lives. We have to continuously adapt to the challenges of new diseases, treatments and patient circumstances across the globe. We've made tremendous progress in helping pharmacovigilance to penetrate into Africa.

Using clear language to make things simple

Pharmacovigilance has saved lives in Africa over the last decade because it's been prioritised within healthcare systems, and national centres have been established inside the relevant competent authorities. WHO's and UMC's role in using clear language to make things simple has made it possible to assimilate and reproduce systems across the whole continent. Greater partnership has helped increase support towards establishing resilient and robust systems at grass root level.

If WHO is the father of our programme, then UMC is our mother. And like all good parents, they've always been easy to approach and there to listen, advise and encourage. As a family and with the pharmaceutical industry, we need to join hands and stand up together for the sake of patient safety.

Playing to strengths

We can't totally eradicate risk or the potential for harm, but we can show up substandard and counterfeit medicines for the crimes and sins they are. We need to work together, with each part of the system playing to its strengths. So for example, a particular nation might excel at providing training for establishing systems, another at data entry of adverse event reports, and another at evaluating trends or taking regulatory action. UMC can squeeze the juice out of all these sources, to feed it back into more training and masters programmes for the next generation of pharmacovigilantes.'

Christina Ström Möller

'Scientific innovation and new methodologies'

Christina Ström Möller is the Head of Drug Safety Physicians at Sobi - an international company dedicated to providing access to innovative treatments that make a significant difference for people with rare diseases. From its headquarters in Stockholm, Sobi's integrated biotechnology encompasses the entire value chain, from research, through preclinical and clinical development, to manufacturing, supply and distribution.

Christina previously worked as an anaesthesiologist and in intensive care at Uppsala University Hospital before joining global biopharmaceutical companies Pharmacia & Upjohn, and later AstraZeneca. She sees UMC as a helpful presence throughout her varied career.

Worldwide impact

'My first contact with UMC was when Marie Lindquist and Andrew Bate came to my previous company to demonstrate the quantitative signal detection system they'd developed. To my amazement they offered us the chance to pilot it – to see how it would work for one of our newly-launched products.

Between 2007 and 2010, I travelled widely throughout Asia, helping to set up pharmacovigilance systems for AstraZeneca. This is when I really became aware of UMC's worldwide impact. In markets where self-medication and counterfeit drugs proliferate, the Centre's work to develop and offer direct, affordable support and tools has been invaluable.

Adapting and adjusting to local situations

UMC has made a big difference in lots of low- and middle-income countries, and it's been very flexible in adapting and adjusting to local situations and regulations that are constantly changing. The Centre has reached out in a really innovative and international way, to provide training and advice that's very well aligned to WHO's core objective to ensure safe, effective and high-quality drugs.

Speed and safety

Looking ahead, I'd like to see UMC take on an even broader role – making use of its global connections to support scientific innovation and new methodologies. In an era when new treatments are launched simultaneously worldwide and reach markets very quickly, it's not enough to have robust pharmacovigilance processes and risk management plans for drugs. We also need proper healthcare systems to manage their global effects. UMC could maybe play a bigger role in supporting healthcare systems to manage the implementation of existing and new therapies.

As my company says: "Because we care, we need to act".'

Across the continents – Africa

With 54 countries and some of the world's greatest disparities in health, wealth and education, Africa is the active frontline of global patient safety. Political and economic circumstances in some parts of the continent make populations especially vulnerable to substandard or counterfeit medicines. And the continent has been affected by the numbers of skilled and educated professionals leaving to work elsewhere. But technology is helping the most successful nations to leap ahead in modern, connected quality of life.

Rachida Soulyamani-Bencheikh

'Collaborators not competitors'

Rachida Soulaymani-Bencheikh is the Director of UMC's partner WHO Collaborating Centre Anti Poison et de Pharmacovigilance du Maroc (CAPM) in Rabat Morocco. Originally mandated to support pharmacovigilance in French- and Arabic-speaking countries, her Centre now serves all Arab and African nations within the WHO Programme. After qualifying as a physician, Prof Soulaymani-Bencheikh completed a Clinical Pharmacology degree in France before returning to her birth country, which became Africa's first WHO Programme member in 1992.

Introduced to UMC at a training course in Uppsala, Rachida went on to serve as a WHO-nominated member of the Centre's Board and member of the WHO Advisory Committee for Safety of Medicinal

Pharmacovigilance needs to be a clinical practice, not just a medicinal one

Products. She feels she has gained strong friendships and great scientific learning from her 25-year association with UMC.

Stability and continuity

'I was inspired by what I saw in Uppsala right from the beginning – it made me believe we could do the same in Morocco. UMC has provided the technical stability and continuity to help everyone involved in pharmacovigilance feel like we're working on the same platform, as part of a family. UMC sees and works with CAPM and the other centres as collaborators not competitors.

We all share a common vision, and deliver a far greater degree of patient safety together than we or WHO could possibly achieve alone. I see UMC staff several times a year, but we can communicate on a daily basis about technical and strategic issues. So it's much more than a virtual network based on data sharing, it's a real one – based on professional and human relations and understanding. I feel we belong to one big family, in which everyone – both visible and behind the scenes – plays their part to benefit patient safety.

Staying relevant

I think the WHO centres and Safety and Vigilance department at WHO in Geneva are doing a good job in promoting safer use of conventional medicines. But to stay relevant, we have to do the same for all vaccines, herbal and alternative treatments. Pharmacovigilance needs to be a clinical practice, not just a medicinal one. So we need to make it more accessible to regulators, physicians, pharmacists, patients and all healthcare professionals.'

Substandard and falsified medicines

It's estimated that between 30 and 50 per cent of the medicines on sale in some countries are either imitation products or substandard in some way. While not confined to Africa, the continent's vast scale, national boundaries, economic disadvantages and ethnic, cultural and language differences make regional markets especially vulnerable.

Ambrose Isah

'We're all in this boat together'

Ambrose Isah is a Professor of Clinical Pharmacology at the University of Benin in Nigeria, and a Consultant Physician at the University Teaching Hospital. He teaches and trains medical students, staff and pharmacists, while running general medical wards and providing specialist advice to ensure the use of safe and effective medicines. He has served as Chairman of the National Drug Safety Advisory Committee for several years and is a member of the WHO Expert Panel on Medicinal Products and Global Advisory Committee on Vaccine Safety (GACVS).

With support from UMC, WHO and the Federal Ministry of Health, Ambrose set up Nigeria's hospital-based adverse drug reporting scheme and a supporting drug and poisons information service to improve medicinal drug use locally and nationally. He first felt the motivating force of UMC's work at a training course in Uppsala in 1996, which helped him to establish Nigeria's pharmacovigilance system.

Proactive and systematic

'UMC's training was absolutely key in the early stages of our work to set up a system for pharmacovigilance. It was a totally new discipline, and we needed help to engage people in the potentially ugly side of medicines. The learning and support we got from the Centre and WHO in Geneva laid the whole foundation for our approach.

UMC has been the engine room for pharmacovigilance in Africa. It has deployed a commendable arsenal of methodologies, tools and experts across the continent, in a proactive and systematic way. Africa owes UMC for bringing it into the international medicines safety community.

A commendable arsenal of methodologies, tools and experts

The proportion of total reports coming from Africa may still be quite small, but the impact and pattern is clear to see. There's a swell of trained, African pharmacovigilantes who are now making their presence felt in all their countries.

Inspiring trust

When you visit UMC, the international style is striking – you can see and feel how this perspective informs everything it does. It inspires trust that no part of the world is going to be left behind.

We need to make sure that this vision and resource is maintained and sustained. We're all in this boat together, so we need to keep the UMC ship in sail and keep it moving forward. Pharmacovigilance in Africa is a long way from being done. We need to carry on training people who will stay in the community and harmonise data sources so that we can target our collective resources better and build a true culture of patient safety.'

Wiltshire Johnson

'I came back and put pharmacovigilance together'

Wiltshire Johnson is Registrar and Chief Executive of the Pharmacy Board of Sierra Leone. There are around 50,000 patients for each physician in his country, and the majority of the population doesn't have access to essential medicines. Sierra Leone was one of the nations hit hardest by the Ebola outbreak in West Africa during 2014-206, which led to more than 11,000 confirmed deaths.

The Pharmacy Board is Sierra Leone's medicines regulatory agency, which is a semi-autonomous agency within the Ministry of Health and Sanitation, with its headquarters in the capital, Freetown. The country joined the WHO Programme in 2008.

Good, available and used properly

'The big challenge facing developing countries is to ensure access to safe, efficacious, good quality medicines, and to ensure that they're used properly. These challenges are what led me to attend the international training course in Uppsala in 2005. It was a big eye opener – it helped me to realise how critical product safety is, and the balancing act that's involved in working closely with the pharmaceutical industry. So I came back and put pharmacovigilance together here!

To start with, there was just me plus one other member of staff and a secretary. The whole concept of drug safety was alien to most health professionals. Many asked what the point of safety was when so many people don't have proper access to medicines at all. So UMC's capacity building and the technological tools it provides have been hugely important in helping to build awareness and establish our systems.

The next level

The Ebola outbreak exposed lots of inadequacies in public health services, and showed that we need better protocols to handle emergencies. And with so many

potential vaccines being offered to prevent repeat epidemics, pharmacovigilance has been absolutely critical in deciding what gets approved for use.

What we do is not just about science; it's a way of life – a catalyst to improve people's quality of life. We now need to take things to the next level, with specialist training for data mining and signal detection that recognises the context for safety in a country like Sierra Leone is completely different to that in Europe or the USA.

It's like buying a Rolls Royce in a place where there are no roads

We've made great strides in rooting out counterfeit medicines in the formal sector, but there are still plenty of bad people who will bring fake products across our borders in order to make a quick buck. And now we have well-intentioned private donors spending millions of dollars on providing medicines to African countries, without realising the need for systems to oversee their use. It's like buying a Rolls Royce in a place where there are no roads!

To tackle these bigger problems, I'd like to see UMC advocating more at levels beyond WHO, so that we can make medicines safety a top priority for global security. And I'll continue to make sure that every member of pharmacovigilance staff in Sierra Leone attends the UMC training course. It's an essential pilgrimage.'

Success in… *Eritrea*

Homegrown pharmacovigilance yields results

Independent since 1993 and a member of the WHO Programme from 2012, Eritrea lies in the Horn of Africa, with borders to Sudan, Ethiopia and Djibouti, and a coastline along the Red Sea. It has a multi-ethnic population of around five million people.

Difficulties experienced by some mothers led to their babies suffering severe protein malnutrition

To support the country's early development of pharmacovigilance, UMC based two staff at the national centre in the capital, Asmara, to help tailor systems to meet local needs. In nations where there is a small national database and limited workforce dedicated to safety of medicines, detecting signals can be a challenge. It's impractical to search for statistical signals in the way that larger and higher-income countries do, so weekly case-by-case assessment and hands-on involvement by volunteer physicians are the main strategies in Eritrea.

In 2016, the combined team of local staff and seconded UMC colleagues detected a signal of adverse effects related to the women's contraceptive injection depot medroxyprogesterone acetate (DMPA). VigiFlow highlighted a cluster of seven, individual case safety reports, which showed that the injections led to failed or suppressed lactation in some new mothers. A search of VigiBase then revealed a total of 57 similar cases worldwide, with a strong level of probability that DMPA was the common, causal factor.

The breastfeeding difficulties experienced by some mothers led to their babies suffering severe protein malnutrition. In places where clean water supplies are limited or unreliable, it can be hard for mothers to access, use or afford formula alternatives to breast milk. So being unable to breastfeed or stopping it sooner than normal can create significant health risks for infants.

Warnings have now been added to the contraceptive patient information, and DMPA is undergoing a large-scale, randomised, epidemiological study to further research these adverse effects. It's a live example of how 'homegrown' pharmacovigilance can make a difference both domestically and in other countries.

Eritrea's national centre now ranks second in Africa (after Cabo-Verde) for the number of reports per million of population submitted to the WHO database each year ●

Communications

UMC's work involves high stakes and world-class science, but its success in promoting safer use of medicines largely rests on effective communications, awareness and relationships between people. No matter how good the reporting, analysis, detection and alerts about the adverse effects of medicines, if people don't get to hear about them, or fail to fully understand what they mean and how to respond, hazards will remain unchecked. So clear, accessible and timely communication is a crucial element of UMC's business.

Five core principles

In 1997, 69 participants from 30 nations met in Erice, Sicily to discuss effective communication in pharmacovigilance. Delegates included representatives from WHO, UMC, healthcare professionals, regulators, the pharmaceutical industry, consumer groups and the media.

The outcomes from the conference were distilled into the Erice Declaration on Communicating Drug Safety Information. And more than two decades on, its five core principles remain the foundation for all such work, worldwide.

1. *Drug safety information must serve the health of the public. Information should be ethically and effectively communicated, to distinguish facts, hypotheses and conclusions, acknowledge uncertainty and provide information in ways that meet both general and individual needs.*

2. *Education in the appropriate use of drugs, including interpretation of safety information, is essential for the public at large, as well as for patients and healthcare providers. Drug information directed to the public should be balanced with respect to risks and benefits.*

3. *All the evidence needed to assess and understand risks and benefits must be openly available, with barriers to communication recognised and overcome.*

4. *Every country needs a system with independent expertise to ensure that safety information on all available drugs is adequately collected, impartially evaluated, and made accessible to all. Countries must be encouraged and supported to share data and evaluations.*

5. *Innovation in drug safety monitoring needs to recognise and deal with new and emerging healthcare problems promptly, so that information and solutions are effectively communicated.*

While these principles continue to underpin all UMC's efforts to communicate the benefits of pharmacovigilance, a new generation of experts met again in Erice in 2016 to update and strengthen the declaration. Their call to action covered the impact of social media and the need to make information publicly available in ways that are transparent, accurate, accessible, relevant and timely.

SIGNAL

***SIGNAL* is UMC's regular research newsletter for WHO Programme national centres and regulatory authorities. As the title suggests, it covers signals of suspected medicine safety problems derived from the individual case safety reports in VigiBase.**

The Centre periodically screens the database to identify previously unknown or incompletely documented adverse reactions. A signal review panel of experienced scientists and clinicians then assesses the clinical evidence and decides whether or not it is strong enough to represent a signal.

SIGNAL communicates suspected causes of harm, with varying levels of likelihood, to alert the regulators who are responsible for deciding on any further action. This might include sharing the information with health professionals and the relevant market authorisation holders, updating information for patients, issuing a public warning, or in the most serious situations, withdrawing a drug from the market.

Since 2012, UMC signals have been publicly available online in the *WHO Pharmaceuticals Newsletter*

Uppsala Reports

UMC's quarterly news magazine covers the world of pharmacovigilance, to keep subscribers up to date with the latest news on safer use of medicines, safety practice and activities within the WHO Programme.

Uppsala Reports reflects the Centre's focus on people and the global family with individual stories about patient safety breakthroughs, successes and setbacks in all parts of the world. It also reports on the annual national centres meetings, training courses and other major events.

UMC prints and sends the magazine in hard copy to all WHO Programme members and other key stakeholders, or it's free to subscribe online. Past issues can be downloaded from the UMC website and 2018 sees the publication of the 80th edition of Uppsala Reports. Since its revamp in 2016, the magazine has seen a steep increase in subscriptions and the circle of contributors

Annie & Mac's Adventures

First published in 2016, this comic book brings vital learning about safety of medicines to children aged 9 to 13. The concept was developed by UMC's head of global communications Paula Alvarado, in collaboration with Swedish author Fredrik Brounéus and illustrators Paul Crumpacker and Tomas Paulsson. The stories follow the heroine Annie and her pet hummingbird Mac in their attempts to stop the evil Lord Fake from producing and selling counterfeit medicines.

The comic gives children in different parts of the world a chance to learn about medicines in a fun way, and – it is hoped – take this new knowledge back to their homes and families to boost everyone's understanding of benefits and risks. Storytelling is a central part of UMC's approach, and children are the most natural storytellers and story consumers of all.

The team considered many different options before deciding on the principal characters. Annie is inquisitive and brave, and Mac is an eagle in the body of a hummingbird. Together, they make the perfect team to tackle important issues about the safer use of medicines.

A chance to learn about medicines in a fun way

The comic book pilot ran in almost a dozen countries, from Armenia to Nigeria and India. It is now poised for distribution in a range of different languages


Safer use of medicines: the basics
Global Pharmacovigilance
The Bigger Picture
Half a century of Global Pharmacovigilance
Online Courses
Online Pharmacovigilance Training
Welcome to Uppsala Monitoring Centre!
A global culture of patient safety

Web and social media

Since the start of the new millennium, we've lived through the greatest shift in technology since the Industrial Revolution transformed world economies and markets in the 18th and 19th centuries. While the impact of digital communications has been dramatic, the benefits so far have been unevenly spread – simultaneously widening some types of disadvantage while offering developing countries the chance to jump straight to the information age.

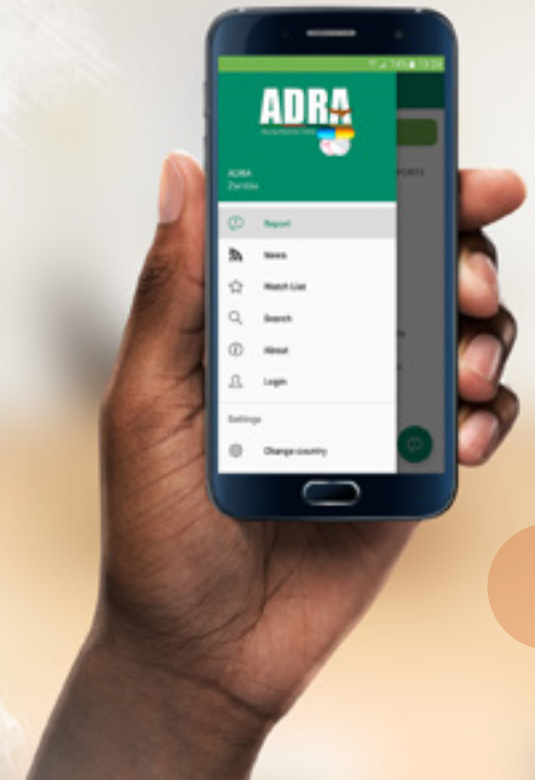
Online and digital tools have already reinvented many aspects of healthcare – from electronic patient records to apps for personal diagnosis or monitoring, and many people's first stop for medical advice: the open-all-hours, worldwide surgery of Dr Web.

Social media can give a different insight into problems with medicines

The growth in social media has also opened up a valuable new platform for pharmacovigilance – giving patients and professionals the chance to report, share and evaluate examples of adverse effects in almost real time. Social media can give a different insight into problems with medicines as patients perceive them. So in recent years, UMC has developed systems to capture and study these sources, using free-text analytic software that searches for key words and phrase patterns.

UMC's website and social accounts are the main ways in which it now disseminates its work and builds the global community – the Centre's shop window onto the world of patient and medicines safety. Followers and friends on Facebook, Twitter and LinkedIn have grown rapidly, along with traffic to UMC's YouTube channel.

Open and unfiltered access to data is an important feature of modern life, where people rightly expect to be included in decisions about their health. So the next generation of information technology will see more of UMC's work happening live online – open for all to see and interrogate using an expanded line-up of cloud-based data and tools. Like medical science, digital and data practice will continue to become more complex, powerful and important as it adapts to exponential growth in the numbers of patients, medicines and reports. UMC will be there



Take & Tell

Launched in 2015, UMC's Take & Tell campaign encourages patients to be active in their health and wellbeing by monitoring their experience of using medicines and reporting problems to their doctors. It uses different versions of a catchy song, a dedicated website and a mobile app to explain side effects and what action to take.

The original campaign included a soul song, which has been translated into Chinese and adapted for reggae and Latin funk versions. The songs are all available on UMC's Sound Cloud channel.

Under the strapline 'together for safer medicines', the campaign's simple message is that patients should tell their doctor or pharmacist about possible side effects, rather than ignore them or suffer in silence. Take & Tell offers a practical toolkit to help people report and discuss adverse effects, and so contribute to safer medicines and better health for all.

See www.takeandtell.org

Up on the wall

Posters are among the many ways that UMC promotes its research and thinking. Alongside published scientific papers, these are a powerful means of reaching the many thousands of healthcare professionals and scientists who attend conferences around the world. They challenge UMC's team to express complex ideas in engaging visual formats and to make the science and its purposes more attractive and accessible. The Centre has won several international prizes for best posters, like those shown here

Bruce Hugman

'The startling complexity of human life'

After a varied and successful career in education, criminal justice and marketing, British communications consultant, Bruce Hugman has applied his talents to promoting UMC and its work since 1995. He's an inspirational teacher of core communication and engagement skills at the Centre's annual pharmacovigilance training courses and around the world.

Bruce is the author of several of UMC's significant publications, including the essential handbook on all aspects of anticipating and managing medicinal product crises, Expecting the Worst. He has played a vital part in defining and growing UMC's voice in pioneering safer use of medicines, and its reputation for clear, useful communication.

Representing the world

'My role with UMC was to help it make the critical transition from a largely technical organisation into an outward-facing enterprise seen to be doing complex, useful work. When I first came to UMC in the mid-1990s, it did not have a strong, coherent public identity or much in the way of public communications. Ralph Edwards' vision to promote the humanitarian vision of pharmacovigilance changed this. By asserting the critical importance of communication, we've been able to focus on its benefits to patients and everyone concerned about the safer use of medicines, and to see it on the agenda of nearly every country in the world.

UMC represents the whole world, in all its diversity, in a pursuit that's relevant to everyone. At a time when post-truth misinformation and fake news are so abundant, the Centre's role in sharing timely, accurate information to prevent harm and to resist pseudo-science is more important than ever.'

No simple answers

Working for UMC and travelling widely has shown me the startling complexity of human life, and highlighted the fact there are no simple answers to difficult problems. But solutions can be found in the extraordinary degree of community and goodwill that is possible when you bring like-minded people together with a dynamic common purpose. The WHO Programme is such a community.

Sharing timely, accurate data to detect harm and expose falsehood is more important than ever

As a teacher and consultant, I've seen the huge obstacles people face in promoting safer use of medicines. But I feel optimistic when I witness motivated and talented professionals in action – often against great odds. Effective communications lie at the heart of good pharmacovigilance; empathy, clarity, attention, engagement. These are the qualities that will translate the science into compassionate, useful materials for patients and health professionals. The world of pharmacovigilance is full of good people who can make a real difference if they master the multiple skills that the discipline requires. Great communication is among the most critical, and UMC has pioneered its importance.'

Paula Alvarado

'Pharmacovigilance is a journey'

Paula Alvarado joined UMC as Head of Global Communications in 2014. She has previously worked for the International Federation of the Red Cross Red Crescent Societies (IFRC), WHO, Conservation International and the Government's Human Rights Office in her home country of Peru.

Paula and her team are responsible for producing all UMC's communications materials, including Uppsala Reports and the Annie & Mac comic book and global campaigns like Take & Tell. Working with international journalist Dan MacDougall she has travelled to remote settings and urban areas in Cabo Verde, Croatia, Morocco, Peru and Singapore to produce a documentary about the challenges faced by those implementing medicines safety strategies in their countries.

Detecting harm and saving lives

'I find inspiration in the dedication of so many professionals whose passion and perseverance make an enormous contribution to people's lives. Their journeys are unique, yet they are all part of the same family.

Working in multi-cultural environments and seeking to achieve sustainable change

My own journey has taken me to work across all continents and meet incredible individuals from very different backgrounds who've sparked my curiosity, creativity and empathy. I enjoy working in multi-cultural environments and seeking to achieve sustainable change.

Sharing stories

I'm a storyteller at heart – I believe that each person has their own unique story to tell. We need these stories in pharmacovigilance, and we're not shy about using songs, articles, comic books or whatever approach will deliver our content best.

The global communications team also delivers services to the whole organisation, including in-house training and helping colleagues to find the right ways to get their message across. We lead tailored workshops and produce materials for conferences, scientific events, product marketing and educational podcasts and videos.'

Watch UMC's documentary about global pharmacovigilance at www.youtube.com/c/UppsalaMonitoringCentre

Sharing the science

UMC continues to produce research that's published in top medical and other scientific journals and provide the raw material for class-leading theses. This maintains the Centre's profile and reputation for scientific excellence, and supports the mission of WHO Programme member countries to monitor the ever-expanding range of medicines, interactions and adverse effects.

A body of research – key UMC scientific publications

Global journals

Depression associated with diltiazem

Cecilia Biriell, John McEwen and Emilio Sanz
British Medical Journal, 1989
The first time a signal from the work of UMC staff and a national centre was followed up and supported by an observational study

Quality criteria for early signals of possible adverse drug reactions

Ralph Edwards, Marie Lindquist, Bengt-Erik Wiholm, Ed Napke
The Lancet, 1990
The first practical attempt to define what a 'signal' should be, which still remains relevant

Tachycardia during cisapride treatment

Sten Olsson and Ralph Edwards
British Medical Journal, 1992
The first signal of a potentially lethal adverse effect – at first refuted by observational studies, despite positive re-challenge in some cases. Very controversial, but now acknowledged as showing the limitations of too-small studies

A Bayesian neural network method for adverse drug reaction signal generation

Andrew Bate, Marie Lindquist, Ralph Edwards, Sten Olsson, Roland Orre, Anders Lansner and others *European Journal of Clinical Pharmacology*, 1998
The first paper to describe automated disproportionality analysis of 'big data' in pharmacovigilance by data mining

Safety monitoring of new anti-malarials in immediate post-marketing phase

Ralph Edwards
Médecine tropicale: revue du Corps de santé, 1998
The first paper describing cohort event monitoring for use in public health programmes, derived from work done in the Intensive Medicines Monitoring Programme in New Zealand

A retrospective evaluation of a data mining approach to aid finding new adverse drug reaction signals in the WHO international database

Marie Lindquist, Malin Ståhl, Andrew Bate, Ralph Edwards, Ronald Meyboom
Drug Safety, 2000
Evidence that data mining can predict early signals of adverse effects of medicines

Statins, neuromuscular degenerative disease and an amyotrophic lateral sclerosis-like syndrome

Ralph Edwards, Kristina Star and Anne Kiuru
Drug Safety, 2007
Signal of a possible association between statins and progressive damage to nerve cells causing involuntary movements

Temporal pattern discovery in electronic patient records

Niklas Norén, Johan Hopstadius, Andrew Bate, Kristina Star and Ralph Edwards
Data Mining and Knowledge Discovery, 2010
The first major publication on methods to screen electronic medical records for possible adverse drug reactions, based on UMC's pioneering research in this area since 2004

Social media and networks in pharmacovigilance: boon or bane?

Ralph Edwards and Marie Lindquist
Drug Safety, 2011
A paper on the advantages and challenges of using social media information as a source for early new signals about the problems patients have from drugs

Improved statistical signal detection in pharmacovigilance by combining multiple strength-of-evidence aspects in vigiRank

Ola Caster, Kristina Juhlin, Sarah Watson and Niklas Norén
Drug Safety, 2014
A new approach to screening collections of individual case reports for possible adverse drug reactions accounting for multiple aspects of strength of evidence, including quality and content of reports and geographic spread

Quantitative benefit-risk assessment of methylprednisolone in multiple sclerosis relapses

Ola Caster and Ralph Edwards
BMC Neurology, 2015
UMC's first benefit-risk investigation performed on a new signal, using an approach that combines different types of data

Pharmacovigilance – critiques and ways forward

Ralph Edwards and Marie Lindquist (editors)
Adis/Springer International Publishing, 2017
Papers on the strategic future of pharmacovigilance, inspired by ISoP discussions

Current safety concerns with Human Papillomavirus Vaccine

Rebecca Chandler, Kristina Juhlin, Jonas Fransson, Ola Caster, Ralph Edwards and Niklas Norén
Drug Safety, 2017
Analysis of adverse events following HPV vaccination revealing cases with signs and symptoms overlapping those of earlier safety signals

PhD theses by UMC staff

The use of a Bayesian confidence propagation neural network in pharmacovigilance

Andrew Bate
PhD thesis, Umeå University, 2003

Seeing and observing in international pharmacovigilance – achievements and prospects in worldwide drug safety

Marie Lindquist
PhD thesis, University of Nijmegen, 2003

Statistical methods for knowledge discovery in adverse drug reaction surveillance

Niklas Norén
PhD thesis, Stockholm University, 2007

Drug interaction surveillance using individual case safety reports

Johanna Strandell
PhD thesis, Linköping University, 2011

Detecting drug risks and weighing them against benefit – statistical and decision-analytical approaches

Ola Caster
PhD thesis, Stockholm University, 2011

Safety of medication in paediatrics

Kristina Star
PhD thesis, Uppsala University, 2013

For a full list of UMC's research and scientific publications, see www.who-umc.org

UMC today

UMC delivers its work through an integrated suite of advanced data methods and products and services to support safer use of medicines, backed up by ever-expanding world networks and expertise through its learning, outreach and advocacy. WHO and the Centre now work in a highly globalised world – where diseases, drugs and dangers can instantaneously leap national and cultural borders. This joined-up world needs the joined-up approach to pharmacovigilance embodied in UMC's scientific leadership, methodologies and data products.

Vision and mission

UMC's vision is a world where all patients and health professionals make wise therapeutic decisions in their use of medicines.

The Centre achieves its mission to support and promote patient safety through effective and global pharmacovigilance practice by:

- Providing independent and high-quality medical references
- Exploring the benefits and harms of medicines
- Transforming medicines safety data into best practice
- Developing global capacity for patient safety
- Encouraging local and regional initiatives by opening access to adequate resources and providing tailor-made guidance
- Building partnerships that bring together resources, expertise and a shared vision
- Turning knowledge into action by enabling stakeholders to identify issues, find answers and drive change
- Pursuing technological change, developing communications and maintaining financial sustainability.

UMC's Board

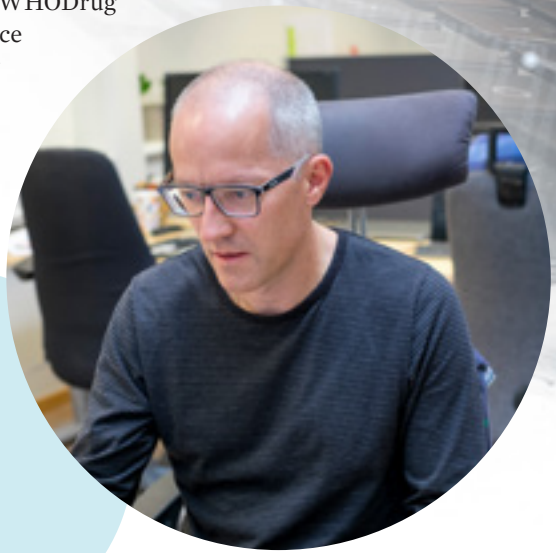
Originally an all-Swedish group, since 2000 UMC has had an international Board, to which WHO and the Swedish Government each appoints three members. The Board has overall responsibility for the Centre's governance and support for the WHO Programme. It also oversees the organisation's scientific development, financial strategy and use of surpluses

Products, tools and methods

The data systems developed by UMC for its own use and by national centres and the pharmaceutical industry, form a powerful, integrated suite that's constantly evolving to cater for ever-growing numbers of medicines, conditions and suspected adverse effects. The Centre has given the world fresh and effective ways to think about the safer use of medicines, plus the tools to identify and address problems.

WHODrug

WHODrug Global (the WHO Drug Dictionary) is the international dictionary of choice for medicinal product information, covering both conventional medicines and herbal remedies. Its unique, hierarchical coding system allows users to identify medicines (including active ingredients and anatomical or therapeutic classifications) from more than 140 countries. WHODrug Global is an indispensable source for interpreting and evaluating suspected adverse reactions to medicines to ensure accurate signal analysis



Data systems and analytical tools

VigiBase is a relational database management system, which includes the WHO global database of individual case safety reports. It's continuously updated with information provided by Programme member nations.

VigiLyze is an online, analytical resource that gives a quick and clear overview of VigiBase. It helps users to explore the database and drill down to study reports by country, age, type of reaction and other variables.

VigiAccess makes high-level, aggregated statistical data available to the public. To maintain patients' confidentiality, no individual case information is visible.

VigiFlow is a web-based management system for individual case safety reports. It helps member countries to collect, process and share data.

Methods

vigiGrade measures the quality of each case safety report. It gives a completeness score for the amount of clinically relevant information in each database entry.

vigiMatch is an algorithm that uses pattern matching to automatically detect duplicate safety reports.

vigiRank uses a predictive model to rank potential safety signals in VigiBase. It analyses reporting patterns and the quality and content of individual reports.

VigiBase – from data to wisdom

VigiBase is the driving force at the heart of UMC and the WHO Programme. Its purpose is to ensure that early signs of previously unknown medicines-related safety problems are identified as rapidly as possible. It is the largest database of individual case safety reports of its kind in the world.

Alongside its data management and quality assurance tools, VigiBase is linked to medical and medicines classifications such as MeDRA, WHO ICD and WHODrug. These classifications enable the structured data entry, retrieval and analysis, which are vital in order to enable effective and accurate analysis.

VigiBase depends on national centres for the timeliness, completeness and quality of reports, and relies to a large extent on the goodwill of the participating pharmacovigilance centres. Each incoming report is checked according to predefined quality criteria. Syntactic accuracy is obtained using controlled vocabularies, with entries checked against reference classifications and 'look-up tables' of permissible data values.

VigiBase collects post-marketing medicines data from a majority of the world's countries in one place. This increases the probability of detecting rare adverse drug reactions from international data, which might not be apparent from the data of a single country. It also offers opportunities to make comparisons between countries and to identify and analyse regional differences

VigiFlow – at the heart of safety data management

VigiFlow (UMC's individual case safety report management system for national pharmacovigilance centres) has played a major part in expanding the WHO Programme and the contributions to VigiBase from low- and middle-income countries. The web-based system enables users to collect, process and share reports data in one, unified tool.

VigiFlow complies with the international ICH E2B standard, allowing countries with limited resources to input and submit their reports coded to international norms. It has also integrated the latest versions of international terminologies such as WHODrug and MedDRA.

Data from VigiFlow can be shared and exchanged in a common format with pharmaceutical companies, public health programmes and other partners, and there's an optional eReporting module, which offers seamless reporting from patients and healthcare professionals.

VigiFlow has been a vital support for many national centres' work and their ability to collaborate with others around the world. And the continuing growth of quality reporting from newer members of the WHO Programme owes much to this important innovation

Leaders – the Chair

Anders Milton

'We are prepared'

Independent healthcare consultant Anders Milton has chaired UMC's Board since 2010. He was formerly Chair of the Swedish Medical Association, President of the Swedish Red Cross, President of the European Regional Network on HIV/AIDS and President of the Swedish Confederation of Professional Associations (SACO).

Dr Milton originally studied economics before turning to medicine. After graduating as a medical doctor he served as a clinician at the Department of Nephrology at the University Hospital at Uppsala. He has been closely involved in a number of Parliamentary Select Committees on topics including better psychiatric treatment and reducing the numbers of unwanted pregnancies.

Making patients' lives safer

'UMC's Board is a very specialised group – and quite different to those I've worked with elsewhere. This is mainly because so many of the members are pharmacovigilance experts – people who really know what they're talking about! With half of the members being appointed by WHO, we've got practising scientists and clinicians from Japan, Kenya, Canada, India and the UK, as well as staff from the headquarters in Geneva.

Having all this expertise around the table doesn't mean you always agree of course. As chair, my job is to make sure that everyone has the right to speak; make sure we listen to each other and reach conclusions that everyone is willing to accept and support. Our role

is partly about control – making sure UMC works within its rules and governing agreement, but also about pushing the boundaries, by encouraging the organisation to try new and different things.

Important and *recognised* as important

Our commitment to making life better for patients worldwide helps pharmaceutical companies develop more effective drugs and builds a stronger understanding of how they can be used in real life. I believe that UMC has helped pharmacovigilance to become much more important and recognised as important. Everyone in our network of global relationships who has helped to achieve this should be very proud of what they do.

Working well

The algorithms and data tools we've developed mean that it's possible to recognise when something adverse is happening, and trigger action before it becomes a crisis. It's possible to detect problems even on just a few reports – you don't need evidence from hundreds of thousands of cases.

Medicine and patient safety is not a stationary thing – it's always developing, and is likely to throw up serious issues in the future, to which UMC will need to adapt. There's going to be much more direct reporting from patients, which needs translating into a form that can be used for analysis. So we'll need to be right on top of big data and artificial intelligence so that we're able to give the value of this information back to the world.

We're going to fulfil our purpose in different ways that will require even more scientific development and greater efficiency and productivity. But I'm confident that we've identified these challenges and are well placed to meet them. We are prepared.'

Leaders – the Chief Medical Officer

Pia Caduff-Janosa

'Science built on trust'

Chief Medical Officer and Deputy Director Pia Caduff-Janosa sees the Centre's work as the glue that binds global medicines safety together. She safeguards the medical integrity of everything UMC does, so that it stays focused on patients across the world and is useful to them.

Former clinical anaesthesiologist Pia joined UMC in 2013, after 14 years responsible for pharmacovigilance at Switzerland's Agency for Therapeutic Products, Swissmedic.

A beacon

'Our science is built on trust - between colleagues, national centres, the pharmaceutical industry, donors, and of course patients. The individuals we exist to protect are not physically in the room with me when I'm at work, but their stories are – and I feel them very much as people every day.

UMC is a beacon of best practice, where there's a genuine belief in what we do, and a commitment to action, not just words. Our international staff team helps us maintain a truly global view. And being financially and politically independent means we can go down paths that others won't or can't.

Freedom

I love working here - there's a freedom to work and get things done at pace. I'm surrounded by broad-thinking people with sharp minds, who are constantly generating ideas and who strive for excellence. Being a WHO Collaborating Centre opens doors and helps us develop our standing in member countries. As an independent Swedish foundation, we can stay focused on the truth and facts, rather than political expedience.

Freedom to work and get things done at pace

We have to meet and work with people where they stand, not where we or anyone else thinks they should be. Our role is to walk with developing countries, and hopefully help them jump straight to digital systems, based on better-informed patients and a wider range of data sources.'

Leaders – the Chief Information Officer

Johanna Eriksson

'People make it special'

Chief Information Officer Johanna Eriksson is responsible for UMC's portfolio of products and services to meet the unique needs of WHO Programme members and WHODrug customers. Amid all this technology, she's clear that it's the collaboration between people that really makes UMC tick - by sharing the Centre's work with all parts of the world through the global pharmacovigilance family.

Johanna worked in the IT industry with product development pioneer Per Manell (see page 30) during the late 1990s, before joining the WHO Drug Dictionary project in 2004 and playing a key role in expanding its coverage from around 60,000 entries to more than a million different records.

People who see issues as challenges not problems

WHODrug is now used by more than 1200 regulatory authorities, clinical research organisations and pharmaceutical companies worldwide. Johanna's 55-strong Products and Services team are the multi-talented experts behind VigiLyze – the powerful search and analysis tool that provides access to the data in VigiBase.

Staying ahead

'Our ability to understand end users' needs, to stay abreast of technological trends and draw on the knowledge from other parts of the organisation and member and customer networks is what makes UMC's products and services successful.

The agile working approach we've applied since 2008 is a big part of this. It enables close interaction with end users throughout the development and testing phases – so they can share their insight, knowledge and feedback to make the result even better. And we can only do this because of our long-term presence at the heart of the WHO Programme and ability to reinvest income back into our work with member countries.

All this is down to UMC's competent and engaged staff over four decades – people who see issues as challenges not problems, with a passion for building capacity for pharmacovigilance. No matter how good our systems are, it's people who make everything happen and make it special.'

Leaders – the Chief Science Officer

Niklas Norén

'Courage to take the lead'

Chief Science Officer Niklas Norén keeps UMC's research at the cutting edge of pharmacovigilance theory and practice. He personifies the intelligence, pace and productivity of how the Centre works – constantly seeking new and better ways to harness the power of both numbers and detailed testimonies to protect patients in all parts of the world.

Niklas entered the world of pharmacovigilance after studying for a master's degree in Engineering Physics at Chalmers University of Technology. He completed his thesis with a small data mining technology firm working on behalf of UMC, from which the Centre hired him in 2004. As part of his work, he then completed his PhD at Stockholm University and has led the UMC's research since 2009.

Pioneering methods

'We believe in free thinking, focused effort and having the courage to take the lead. The WHO Programme provides not only the data necessary to understand real-world effects of medicines, but also the opportunity to interact with bright, stimulating people in every continent. Real value for patients and health professionals can only be achieved through joint efforts with the national centre teams who understand the clinical realities of each country.

Our own specialty is to pioneer new and better ways of gaining insights from health data. We work with reports of adverse events, of course, but also with electronic medical records and patient-generated data on the internet.

To bring research more rapidly to real-world use and to stay focused on the most important topics, we've adapted the principles of agile software development. This encourages us to work in short cycles of development, evaluation and deployment, so new ideas can be stress-tested early on and refined or abandoned as appropriate.

I see people growing here

Everyone, from medical doctors to data scientists, is involved in both methods research and signal detection, which means we can unleash huge amounts of expert resource from different domains. I see people growing here from working this way.

It's rewarding, dynamic work in an organisation that keeps on changing.'

Leaders – the Chief Financial Officer

Birgitta Lindner

'Everything we do is international'

Chief Financial Officer Birgitta Lindner looks after UMC's strategic and day-to-day financial health so that everyone else can stay focused on the serious business of patient safety. She believes that the Centre is on the brink of a new era in pharmacovigilance, and is laying the foundations for that to happen.

Birgitta joined UMC in 2006 after working with a Swedish pharmaceutical company. She enforces a simple fiscal philosophy that allows the Centre to devote a third of its accumulated capital each year to developing the WHO Programme and new systems to support this growth. The Centre's reserves are then maintained from the annual surplus (80 million SEK in 2017/18).

Good for the world

'My job is to create an easy working environment – by avoiding waste, spending wisely, keeping control and staying ahead on our finance and infrastructure. Doing this properly allows more time for our research and science, and gives us the freedom to explore new things. I cherish the diversity of intellectual thought and agility we have here – UMC is a unique mix of competencies from mathematicians to medical experts with good business brains.

Around 98 per cent of our operating income flows from sales of WHODrug, so that's a critical part of our business. Thankfully, subscriptions are still growing, and we've been able to keep it affordable by fixing the price since 2005. The WHO brand is important – it signals that we stand for something good in the world.

We've got staff from dozens of different countries working here, and with so much of our income coming from abroad; it means that everything we do is international.

The WHO brand is important

My biggest challenge now is deciding how best to invest in programmes and research that will have the biggest impact. This means going beyond our current blend of science and business to maintain the legacy of UMC's first 40 years through a fresh practical and philosophical level of support for global safety of medicines.'


B3/C3
Drug name: 1500
ATC text: 110
Uppsala
Monitoring
Centre

The future

The 40th (UMC), 50th (WHO Programme), and 70th (WHO) anniversaries marked in 2018 present an ideal point to pause, reflect and redirect effort to the most pressing priorities in patient safety. It's also an opportunity to refresh and harness global science and goodwill, at a time when the world seems more unequal and divided than at almost any time in living memory. What UMC does next matters to us all.

An array of game-changing trends and developments are on the horizon or already affecting worldwide patient safety practice. Many of these advances flow from breakthroughs following the international Human Genome Project to map the human DNA sequence, new materials and processes created at the atomic scale and advances in information technology.

A new and growing generation of professionals

Greater effort is now going into strengthening overall regulatory systems and harmonising safety practices and processes across the world. There is also a new and growing generation of professionals who are applying agile working methods and the latest mobile technology to accelerate development.

New disciplines

Pharmacogenetics studies how inherited differences can affect the metabolic pathways that govern people's individual responses to medicines, both therapeutic and adverse effects. Pharmacogenomics then uses information about a person's genetic makeup to choose the treatments and doses that are likely to work best for that particular person. Together, these new disciplines equip modern physicians with a much greater ability to target the drugs they prescribe.

Personalised medicine

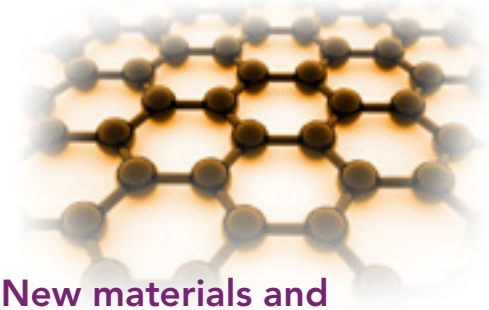
Pharmaceutical research and development is increasingly focused on medicines that are designed and administered to match patients' needs as individuals. Tailoring treatments to take account of each person's genetic disposition, personal characteristics and circumstances has the potential to massively increase clinical effectiveness and reduce the risk of harm. Real-time information

from implanted and wearable devices is already beginning to provide vast amounts of data about people's behaviour and responses to medication.

Artificial intelligence

Information technology has moved far beyond programming and software that delivers what humans instruct it to do. There is now clear evidence that – in some areas at least – machines can take over human tasks. And affordable systems to bring that intelligence into everyday use are rapidly coming onto the market.

In healthcare, the application of artificial intelligence (AI) may help doctors to diagnose some conditions, find the right treatments and perform surgery with much greater degrees of accuracy. While continued development and pressures on countries' health budgets mean that its use looks set to accelerate, this will present new ethical dilemmas for healthcare professionals and societies.



New materials and nanotechnology

Graphene and other, manufactured super-substances and tiny technologies are making the microscopic treatments imagined in the 1960s film The Fantastic Voyage a reality. Miniature, robotic devices can now be inserted into patients and guided to the source or location of diseases to deliver topical treatments exactly where and when they're needed. The pharmacovigilance community will need to develop and share the know-how to carry out safety monitoring for these very different sorts of medicines and devices.

The changing face of pharmacovigilance

Proactive and real-time safety surveillance

In resource-limited countries with previously restricted access to medicines, large populations burdened by communicable diseases can now be treated thanks to medicine donations. Monitoring their use for both safety and efficacy is a high priority, since some are novel drugs, and others are now being used in settings and populations very different to those for which they were originally approved.

More proactive safety management involves new methods of structuring and analysing safety information, plus advanced data collection, analytical tools and processing power to deliver real-time monitoring and reporting.

As more sources of information become available from healthcare databases, patient records, active monitoring and digital media, the collaborative use of these data sources to find and evaluate new information will be critical for effective pharmacovigilance.

Big data

Current methods designed to screen and analyse case reports and electronic health care records are not sufficient to analyse patient safety information from online sources, smartphone applications and wearable devices. The catchphrase 'big data' refers both to data itself – huge amounts of loosely structured data; and the tools and processes required to handle the data.

To unlock the intelligence that's latent in very large patient databases and other sources of real-world data, links will need to be forged on a global scale with organisations that build, use and analyse large data sets. A big challenge will be to make appropriate judgements on when and how to use this data to improve healthcare, while respecting individual privacy.

Patient engagement

Greater openness, more stakeholder dialogue and better feedback mechanisms are essential to engage new audiences in pharmacovigilance and patient safety. Today's patients rightly demand a more active role in their own treatment, and already provide large amounts of information on the benefit and harm of their medications. So patient defined outcomes (how people assess the effects of medical interventions on their quality of life) are an important part of the move towards more patient-centred healthcare systems.

Predicting harm and benefit

Risk management planning, risk communication and crisis management are vital elements of many countries' regulatory requirements for the pharmaceutical industry. These approaches determine what safety measures will be needed for each product, depending on the knowledge available at the time of registration and on the drug's proposed use.

Current regulatory processes are not enough to predict and prevent adverse effects, Knowledge needs to be made available to patients and health professionals, when and where they need it, together with decision-making tools that enable an open, structured approach to making judgements on the strength of disparate information.

Impact assessment

Since health problems caused by adverse events related to medication continue to be a widespread and serious problem, it's essential that the impact of pharmacovigilance is audited for effectiveness. The global community engaged in safer use of medicines needs to know how effective it is, and how resources can be best deployed. So outcomes research to identify shortfalls in practice and to promote strategies for improved healthcare is an increasingly important tool for organisations, governments and the pharmaceutical industry

The new generation – the Product Strategy Manager

Malin Jakobsson

'There's little bureaucracy'

Product Strategy Manager Malin Jakobsson is the driving force behind the continuing development of UMC's core WHODrug product. She joined the Centre on a part-time, short-term contract while studying Molecular Engineering at Uppsala University in 2005, and discovered her fascination with pharmacy.

Malin was drawn to the world of medicine side effects, signals and data by the chance to play a part in a small organisation where it's possible to work right alongside the decision makers, while being part of a bigger, global cause.

Making improvements

'My job is to listen to and understand what WHODrug users want, so we can translate their needs into extensions and improvements to the Dictionary. We've made some important changes – particularly in switching to an active approach that means we go out and search for new medicines to include, rather than waiting for reports of adverse effects.

Digitisation and being able to visualise data with the WHODrug browser has been another big step forward, and the new WHODrug Global dictionary brings all traditional, herbal, Chinese and other medicines together in one place. I love it when we get positive feedback from users – that's what I live off.

The Dictionary means we're involved in commercial business, but our work also definitely has an emotional edge – because we're dealing with people whose health and lives are affected by medical treatments. This feeds into our working relationships – we get hugs when we meet our customers!

There's always room for good ideas

UMC is a place where there's always room for good ideas. There's little bureaucracy, so it's possible to do things quickly. Maybe though sometimes we don't focus enough on the things that will have the most impact. It's human nature that we all tend to fall in love with our own ideas, so we have started to validate our choices by checking what really matters and works with end-users. I think we have high integrity as a first-rate scientific centre. We're firm about doing what's right; and that's a real test of our values.

Big trends

My next big task is to help develop a coding robot, which will help to increase efficiency greatly. The major trends we must also tackle include falsified medicines, utilising the possibilities of electronic health records and focusing on the known misuse of drugs. It's all about seeing and making use of the patient's perspective.'

The new generation – the Research Pharmacists

Afifa Trad

'A double-edged sword'

Born in Sweden to Tunisian parents and educated at an international school, Research Pharmacist Afifa Trad grew up with a global view and interest in different world cultures. Before graduating from Uppsala University, she did a WHO Internship that placed her with UNITAID (a major global health initiative working to end Tuberculosis, HIV/AIDS, Malaria and Hepatitis C epidemics).

Afifa started her career managing a pharmacy in rural central Sweden then worked in the pharmaceutical industry before joining UMC. Fluent in Swedish, English, French and Arabic, her current role gives her the chance to use her language skills and apply her passion for understanding processes, seeing the big picture and tackling problems.

Opening doors

'When I saw the advertisement for a job at UMC, it was exactly what I was looking for. Being a WHO Collaborating Centre enables us to work with diverse colleagues all around the globe. The Centre has been able to build up really strong networks, even in smaller countries where things have had to start from scratch.

Measuring the precise impact of what we do is one of the most difficult challenges. We're constantly evaluating ways of tracing causality between our inputs and health outcomes. But the feedback from national centres, and the way they're able to take forward local initiatives, is good evidence that we're making a positive difference.

Intelligent assumptions

I'm reminded daily though that very often we're working with assumptions. So a big part of the job has been to build up and maintain intelligence about each member country, so that we can really grasp what's happening there. It's like being a stock trader constantly studying the market. It's not enough to observe, we have to truly understand, so we can make the best strategic decisions and make sure we remain relevant.

It's important to work for an organisation that can really make a difference

My priority is to make sure we get better data and are able to interpret that data, by establishing and using strong networks across the world. This is very demanding, but it's also one of the most attractive and stimulating things about working here. So it's a double-edged sword.

Calibre of talent

I feel it's important to work for an organisation that can really make a difference and to be part of a positive global cause. The calibre of talented people here is amazing.'

Daniele Sartori

'Stronger, empowered patients'

Italian Daniele Sartori followed his parents' profession by graduating in Pharmacy at the University of Pavia, and then choosing a postgraduate course at Verona University specifically because it offered the chance to do an internship at UMC. He describes this six-month exposure to global pharmacovigilance as like 'being thrown into a whirlwind' – but he survived and thrived to return as a fully-qualified Research Pharmacist in 2014.

Daniele's interest in the safer use of medicines was sparked by hearing about the WHO Programme and framework for international cooperation from a professor at his first university.

A crash course

'My internship at UMC gave me a crash course in pharmacovigilance. I got straight into detecting signals, and was introduced to the reality of the science. I enjoyed the first three months so much that I begged to be allowed to stay on for three more. And when a permanent job came up here, I didn't hesitate to move to Sweden.

We've developed very good analytical methods here, and collaborate well with national centres to help and encourage them to use our systems. Methods like vigiRank, which allow us to assess the strength of a signal set the world standard and are a great example of our brand to deliver inspiration, innovation and integrity. The next step is to support centres in analysing their own reports – some are sitting on gold mines of data, and it makes sense to use that as quickly and as close to the source as possible.

Space to innovate

We've recently combined UMC's Global Services and Research teams, which is a good start in tearing down the walls that can otherwise build up between different disciplines. Collaboration is so important and we need to make sure that everyone's purpose and talents are free to interact. Big projects can also squeeze out or stifle creativity, so we must also make space for innovation.

Sitting on gold mines of data

I enjoy coming up with weird ideas and being able to pitch them and break new ground. There's no fear of failure here, although if something doesn't work, it's good to discover that quickly. As scientists, we make progress by learning from and documenting our setbacks. I'm motivated by knowing that I can make a positive difference to many more people's lives by working with this bird's eye view of safety than if I was a hands-on pharmacist in a community.

Everyone has a voice

In the future, I want to see UMC do even more to help patients make decisions and be in charge of their own health. We need to give stronger, empowered patients the best possible evidence to make wise decisions with their clinicians. With social media and smartphones everybody has a voice today. But ideally, very few people should say 'If I had known about the adverse effects, I wouldn't have taken the medicine.'

We need to be constantly on the look out for new data sources, and try to catch them early so we can shape the way they develop to offer the most benefits. UMC's 40th anniversary is an important milestone, so we need to be thinking about the next 40 years and what that might bring.'

The new generation – the Head of Customer Engagement

Anders Gräns

'Everyone's effort is important'

After completing a master's degree in Business at the Swedish University of Agricultural Sciences, Head of Customer Engagement, Anders Gräns, worked as a forestry industrial economist at a sawmill in Sweden. He soon realised that the world of wood was not for him, and got the chance to review UMC's commercial relationships as a consultant. This led to a permanent role in 2016.

A more transparent and higher level of service

Anders sees his role as a facilitator – helping other parts of the Centre to perform their functions better, and injecting the customer view into any project or decision. His customer engagement team complements UMC's agile working approach.

Fair and professional

'The opportunity to look into the commercial links here was super interesting, and I was keen to work in an English-speaking environment. The consultancy project showed that UMC's business model and pricing structure could be simplified to offer a more transparent and higher level of service. Given the nature of our organisation and mission, it's vital that we work with customers in a fair and professional way, with minimal waste.

We created a new team to focus on customer relationships and gather views from users of UMC's service to feed into new products and initiatives. We've got some great partnerships in place with international companies and universities, to help develop greater use of all the data we possess.

UMC has been incredibly successful in building up global awareness of pharmacovigilance, and a network to support it. Over the years, there's been a steady shift from simply collecting data to analyzing it, using it and spreading the knowledge and capacity to do this.

Growth and development

I really enjoy the collaborative atmosphere at UMC – seeing the organisation develop and people grow. If you have ideas and motivation, you can do things here – and it's a place where you're allowed to make mistakes and learn from them. There are lots of unsung people making a big contribution, and everyone's effort is important.

We need to keep on upping the service and make sure that we spend time on the things that matter most to our customers. I think we can do more to make data more available and useable for industry and the public as well as drug safety centres and regulators.'

The new generation – the Legal Counsel

Dina Stolt

'A good place to be'

Legal Counsel Dina Stolt comes from the Swedish-speaking population of Finland, and worked in commercial dispute resolution for a Finnish law firm in Helsinki before joining UMC in 2016. Her role involves negotiating and updating the Centre's contracts and licences with customers, and providing an internal legal service on every aspect of the business.

Dina enjoys the sense of purpose that comes from working for a non-profit organisation, but one that has a keen commercial edge.

Putting out fires

'I strive to be a fixer – someone who takes a pragmatic approach to sorting out the legal aspects of any process that needs to be improved or streamlined. Because of UMC's rapid growth starting in the 1990s, some of our agreements need to be modernised and extended to take account of the wider range of products we offer now.

I aim to lower the threshold at which people come and talk to me as a lawyer – it's much better to ask what might seem a silly question early on, than leave something until it becomes a problem. Organisations that grow fast like ours inevitably experience growing pains and problems, so I'm here to put out the necessary fires and help us move on. We also handle a large amount of sensitive, personal information, so integrity and confidentiality are also very important.

One of a kind

The Centre has done amazingly well to become financially self-sufficient and be so successful, while still charging reasonable prices. It really is one of a kind. UMC is a positive place to work, with a strong mix of people and abilities. Younger people like me benefit a lot from the experience of our older colleagues, while we bring the skills of being the technology generation. We now use special legal software and offer customers online contract handling, which saves everyone time and means we can free up time for other tasks.

We deal with some of the world's mega players every day

It's exciting that, as a relatively small organisation from a modest-sized city in Sweden, we deal with some of the world's mega players every day – holding our own among huge companies and government departments. I'd like to see UMC have a much higher profile among health professionals, students and the public, but otherwise it feels like we're at a strong, mature stage in our development – it's a good place to be.'

The new generation – the Software Developer

Ziring Tawfique

'The future is unwritten'

With a master's degree in Computer Science from Uppsala University, Ziring Tawfique is part of a team that's constantly developing WHODrug and UMC's other products. Born in Iraqi Kurdistan, and educated in the United Arab Emirates and UK, he typifies the diverse, international talent behind the delivery of WHO's drug safety Programme.

Ziring found out about UMC and its need for software developers from a chance conversation his wife had with a friend. He is now involved in applying artificial intelligence to coding for WHODrug and is also responsible for development of the Centre's main public website.

Healing and saving lives

'I'm inspired by working for a non-profit organisation, where the information I help to provide makes a real difference to improving healthcare right across the world. I may work in the back office, but genuinely feel that my role is about healing people and saving lives. It all comes down to the fact that we structure and know our data really well – and how we constantly listen to feedback from our customers.

UMC is good at engaging – through the training we offer for national centres, which gives us the chance to pass on new ideas and methods. It works like a circle: we try – we learn – we share – they learn. Keeping people up to date through this knowledge transfer is really important.

Close to customers

My job here allows me to do what I love. UMC is a super nice place where if you're interested and have got good ideas you can pitch them straight to managers and help put them into practice. It's not like working for a big company where you can be invisible.

We know our data really well

I've been working on an auto-encoder for WHODrug, which will use machine learning and other techniques to help medical coders in the pharmaceutical industry with their daily job. It will automate the tedious part of their work so that they have extra time to focus on the more interesting cases.

The future is unwritten of course, so we don't know exactly how the Centre's work will develop in the decades ahead. All we can do is be prepared by staying close to our customers and being financially stable. I'm sure UMC will continue to be a huge player at the front of the field.'

The new generation – the Agile Coach

Matilda Ahnfelt

'I enjoy experimenting'

While others travel the world to spread the science of pharmacovigilance and build up national centres' capacities and capabilities, Agile Coach Matilda Ahnfelt focuses hard on what happens in Uppsala. She's convinced that Swedish personality traits are a crucial part of UMC's style and success, but excited by the rapid development of local centres across the globe.

Matilda helps UMC's teams to apply agile working techniques to every part of the business – identifying the goals they want to achieve, then moving towards them in steady, iterative steps, with feedback at every stage.

Constant progress

'I see my role as one of the signs of UMC becoming more and more professional. There's a great focus on getting things done here, and we have the satisfaction of knowing that all the money we earn gets reinvested back into our work.

Creating a new system or software product is intense. And moving in a fast world requires agile ways of working, doing things in small parts to get quick feedback. I enjoy experimenting empirically – trying new things to constantly improve our ways of working. There are lots of challenges, but lots of laughter too. Being at the cutting edge of IT is fun, even though it means I rarely go outside the building!

In Sweden we tend to speak our minds

In Sweden we tend to speak our minds, and we're great collaborators. This means that once we reach consensus on something, we've got everyone's brain involved and we all work together. Combined with a diverse, multi-national workforce, this can be very powerful.

The way that national centres are now able to do more local analysis of case reports feels like the perfect shift in our work. It means that we're not too pre-occupied with the tools, and we're really empowering people to do what works best in their countries.'

The new generation – the Medical Doctor

Rebecca Chandler

'A language people understand'

Medical Doctor Rebecca Chandler is passionately committed to the Centre's role in highlighting rare and individual reactions to medicines – and sharing this intelligence in ways everyone can understand and use. She is a pioneer researcher into the effects of the HPV (human papilloma-virus) vaccine on children and young people.

The daughter of two pharmacists from Tennessee in the United States, Rebecca trained in infectious diseases investigation and control, before coming to work at the Swedish Medical Products Agency in 2008. Since then she's 'fallen in love' with the developing science of pharmacovigilance, and sees UMC as filling a unique niche in global healthcare.

Focusing on patients

'Having worked as one, I realise that the questions medicine regulators ask are not always the most scientifically important or clinically relevant. But that's inevitable when you're often far away from patients and driven by administrative priorities.

There's no such thing as an 'average' patient

At UMC we have the space to really think, observe and put the clinical pieces together in ways that support wise therapeutic decisions. We have to keep patients in focus all of the time – to hear, interpret and tell their stories of how they've reacted to different medicines. It's vital to use a language people understand, so they can act on our signals and reports.

There's no such thing as an 'average' patient – and we deal with the rare and outlier cases here, that can often be overlooked or ignored. I hope that UMC is ahead of the curve in showing how individuals in different places react differently to medicines.

Our science has arrived, but we can't afford to settle for things as they are. The challenge now is to use real world data to demonstrate how heterogeneous populations are, and help public health agencies to embrace this. Countries like Togo and the Democratic Republic of Congo have shown what they're capable of with their work on malaria and anti-parasitic drugs.

Other member states are primed and ready for the next generation of pharmacovigilance – and UMC is here to help them.'


We have to stay focused on
achieving tangible results that
improve the lives of patients

Endword – from the Director

'My heartfelt thanks to everyone who has contributed to this publication, and who has played a part in the Centre's 40-year history.

I believe that science is not about finding the truth; it's about the quest for truth. Our job is to develop and apply the latest technology to generate new knowledge, and make sure this reaches the people who use medicines, at the right time and in the right way.

This is a continually evolving process, and we have to accept that many decisions on how medicines are used are based on uncertain evidence, which has to be revised as new evidence comes to light. So we do our utmost to provide the best available evidence and understanding at any given time.

It's good that there's now legislative support for rigorous risk management practices in more and more parts of the world. But there's a risk that regulatory requirements, and plans to meet them, become so detailed and extensive that we get distracted by the processes and methodologies themselves, instead of generating the knowledge that health professionals and patients need to improve medicines safety and prevent harm.

We have to stay focused on achieving tangible results that improve the lives of patients. The challenge is not only to look at what happens at the population level, but to identify the critical factors that determine when and how a medicine can be used safely by a particular individual. Each of us has a unique set of characteristics and dispositions, which affect the way we react to medicines.

The most important thing for the future is to make sure that pharmacovigilance becomes an ever more integrated part of all healthcare delivery. UMC's reach goes beyond WHO Programme members and the pharmaceutical industry. So we will carry on promoting our vision – a world where all patients and health professionals make wise therapeutic decisions – to governments, academics, professional organisations and a growing number of patient and consumer groups. All of these rely on the reliable tools, thinking and teaching, which we're here to provide.

I believe that, while not always so visible as other aspects of our work, UMC's determination to push intellectual and scientific boundaries is key to our success. But most of all, pharmacovigilance has to be by people and for people.

Through our role in delivering the WHO Programme, developing the science and fostering the global family that's dedicated to safer use of medicines, we have a rich, shared heritage. And together, our work continues into an exciting future.'

Dr Marie Lindquist
Director

Thanks

This celebration of UMC's 40-year history was made possible by the generous contributions from dozens of friends and colleagues across the world. Thank you to everyone who shared their views so willingly about the Centre and its work, and who helped to assemble these important memories.

Special thanks

Special thanks from UMC to:

Acknowledgements

Researched and written by Ian Hembrow
Edited by Bruce Hugman and Geoffrey Bowring
Designed by Leif Eriksson, Vajer [wire]

To get this publication in large print, audio, Braille or another language, please contact globalcommunications@who-umc.org

INSPIRE – ENGAGE – TRANSFORM

UppsalaMonitoringCentre
uppsala-monitoring-centre
UMCGlobalSafety
UppsalaMonitoringCentre
uppsalamonitoringcentre

Contact us

To find out more about Uppsala Monitoring Centre's work to make the world safer and healthier, please contact:

Postal address:
Uppsala Monitoring Centre
Box 1051 · SE-751 40 UPPSALA · Sweden

Visiting address:
Bredgränd 7 · SE-753 20 Uppsala · Sweden

Phone: +46 1865 6060
E-mail: info@who-umc.org
Web: www.who-umc.org

ISBN 978-91-639-7587-5

Uppsala Monitoring Centre

WHO Collaborating Centre for International Drug Monitoring