Medical Writing



ALSO IN THIS ISSUE...

- Update on CHEERS 2022
- Results of our predatory publishing survey

Volume 31 Number 1 | March 2022



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Medical Writing is the official journal of the European Medical Writers Association (EMWA). It is a quarterly journal that publishes articles on topics relevant to professional medical writers. Members of EMWA receive Medical Writing as part of their membership. For more information, contact mew@emwa.org. A. EMAA. EMAA. EMAA. EMAA. EMAA. EMAA. EMAA. EMAA. FM

Medical Writing

2



Editorial: Stepping up:

THIS ISSUE March 2022 | Volume 31 Number 1

Sustainable communications

"Scientific communicators and medical writers are wellpositioned to contribute to current debates on environmental problems and their impact on human and planetary health." Elisa Sala, Surayya Taranum, p. 2

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Stepping up: Sustainability and medical writing

elcome to this special issue on sustainable communications. Sustainability is a key focus area across all economic sectors, including the pharmaceutical, medical technology, and healthcare industries. Scientific communicators and medical writers are well-positioned to contribute to current debates on environmental problems and their impact on human and planetary health.

The 17 sustainability development goals (SDGs) listed in the 2030 Agenda for Sustainable Development of United Nations (https://sdgs.un.org/goals) are relevant for us personally and professionally. In particular, the SDG 3 to promote "health and well-being for all at all ages"; the SDG 4 to "ensure

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inclusive quality education and promote lifelong learning opportunity for all" and the SDG 12 on "sustainable production and consumption patterns" strongly resonate with the daily activities of medical writers and communicators. In this issue, we are pleased to present a collection of articles that focus on some of these SDGs.

Sustainable production and consumption

Biomedical research is resource-consuming and has an impact on the environment. In the first article of this issue, **Raquel Billiones** reviews the literature on the carbon footprint of clinical trials. **Kimi Uegaki** and **Raquel Billiones** explain ways to prevent biomedical research waste and opportunities for medical writers in contributing toward making our industry sustainable.

Environmental risk assessments (ERA) evaluate the effects of drugs for human use on the environment and are part of the new requirements for marketing authorisation of drugs in Europe. **Archana Nagarajan** and **Kimi Uegaki** discuss the current ERA



guidelines and highlight challenges in writing this document. Louisa Marcombes provides an overview of sustainability in the veterinary world and the role of medical communications professionals in engaging all stakeholders. Also check out the roadmap towards sustainability

created by the EMWA infographics team.

Equity, education, and inclusion

In the area of ensuring equality and inclusive quality education, and promoting lifelong learning opportunities, Jennifer Bell delves into strategies to ensure quality education for all. Erika Ornago, Elisa Sala, and Massimo Zaninelli discuss the role of health literacy in the healthcare decision-making process. Fake news cannot be combatted without sufficient investment in resources to promote public health literacy. M. Ayelén Milillo, Soledad Gori, M. Victoria Ennis, and Pablo M. Méndez describe the initiatives taken up by the Science Anti-Fake News team in Argentina to fight the infodemic. Rossella Ferrari tackles diversity and equity by giving an overview of race and ethnicity in biomedical literature.

The financial sustainability of the healthcare industry needs to be seriously considered. This is one of the aims of the updated "Consolidated Health Economic Evaluation Reporting Standards: CHEERS 2022". Michael Drummond, Chris Carswell, and Don Husereau describe the role of medical writers in using the CHEERS guidance and its accompanying checklist. Next, Alex Schuman shares her inspiring career journey in corporate sustainability.

Don't miss the article on a medical writing primer for oncology dossier by Julia Forjanic Klapproth and Maurice Lowens. And in the Medical Communications and Writing for Patients section, see Simon Linacre's report on a survey on predatory journals.

We would like to thank all the authors for their valuable contributions. We hope that you find this issue interesting and thought-provoking, with insights into how you can contribute to the exciting and critical field of sustainable communications.



About the Guest Editors

Elisa Sala is an Italy-based, freelance medical writer with a scientific background in pre-

clinical and clinical oncology research. She is a supporting

member of the EMWA Sustainability Special Interest Group.

Surayya Taranum is a scientific writer at 4Clinics. She is the Regional Director, Corporate Relations Operations & Insights in the Healthcare Businesswomen's Association Europe region and a committee member of the EMWA Sustainability Special Interest Group.





EUROPEAN MEDICAL WRITERS ASSOCIATION

Submissions:

For instructions to authors, go to the journal section of EMWA's website (www.journal.emwa.org). All manuscripts should be submitted to mew@emwa.org.

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From the Editor A call to action

n September 2021, more than 200 biomedical and scientific journals simultaneously published an editorial that called for "Emergency Action to Limit Global Temperature Increases, Restore Biodiversity, and Protect Health." *MEW*, with the endorsement of the EMWA Executive Committee and the support of the Sustainability

SIG (SUS SIG), has declared full support for this collective and concerted call for action. See the full list of authors and supporters at https://www.bmj.com/content/full-list-authors-and-signatories-climate-emergency-editorial-september-2021.

For this issue dedicated to sustainability, it is my privilege to reprint the same editorial

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> Raquel Billiones Editor-in-Chief editor@emwa.org

Call for emergency action to limit global temperature increases, restore biodiversity, and protect health

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Wealthy nations must do much more, much faster

he UN General Assembly in September 2021 [brought] countries together at a critical time for marshalling collective action to tackle the global environmental crisis. They [met] again at the biodiversity summit in Kunming, China, and the climate conference (COP26) in Glasgow, UK. Ahead of these pivotal meetings, we – the editors of health journals worldwide – call for urgent action to keep average global temperature increases below 1.5°C, halt the destruction of nature, and protect health.

Health is already being harmed by global temperature increases and the destruction of the natural world, a state of affairs health professionals have been bringing attention to for decades.¹ The science is unequivocal; a global increase of 1.5°C above the pre-industrial average and the continued loss of biodiversity risk catastrophic harm to health that will be impossible to reverse.^{2,3} Despite the world's necessary preoccupation with COVID-19, we cannot wait for the pandemic to pass to rapidly reduce emissions.

Reflecting the severity of the moment, this editorial appears in health journals across the world. We are united in recognising that only fundamental and equitable changes to societies will reverse our current trajectory.

The risks to health of increases above 1.5°C are now well established.² Indeed, no temperature rise is "safe." In the past 20 years, heat related mortality among people aged over 65 has increased by more than 50%.⁴ Higher temperatures have brought increased dehydration and renal function loss, dermatological malignancies, tropical infections, adverse mental health outcomes, pregnancy complications, allergies, and cardiovascular and pulmonary morbidity and mortality.^{5,6} Harms disproportionately affect the most vulnerable, including children, older populations, ethnic minorities, poorer communities, and those with underlying health problems.^{2,4}

Global heating is also contributing to the decline in global yield potential for major crops, falling by 1.8-5.6% since 1981; this, together with the effects of extreme weather and soil depletion, is hampering efforts to reduce undernutrition.⁴ Thriving ecosystems are essential to human health, and the widespread destruction of nature, including habitats and species, is eroding water and food security and increasing the chance of pandemics.^{3,7,8}

The consequences of the environmental crisis fall disproportionately on those countries and communities that have contributed least to the problem and are least able to mitigate the harms. Yet no country, no matter how wealthy, can shield itself from these impacts. Allowing the consequences to fall disproportionately on the most vulnerable will breed more conflict, food insecurity, forced displacement, and zoonotic disease—with severe implications for all countries and communities. As with the COVID-19 pandemic, we are globally as strong as our weakest member.

Rises above 1.5°C increase the chance of reaching tipping points in natural systems that could lock the world into an acutely unstable state. This would critically impair our ability to mitigate harms and to prevent catastrophic, runaway environmental change.^{9,10}

Global targets are not enough

Encouragingly, many governments, financial institutions, and businesses are setting targets to reach net-zero emissions, including targets for 2030. The cost of renewable energy is dropping rapidly. Many countries are aiming to protect at least 30% of the world's land and oceans by 2030.¹¹

These promises are not enough. Targets are easy to set and hard to achieve. They are yet to be matched with credible short and longer term plans to accelerate cleaner technologies and transform societies. Emissions reduction plans do not adequately incorporate health considerations.¹² Concern is growing that temperature rises above 1.5°C are beginning to be seen as inevitable, or even acceptable, to powerful members of the global community.¹³ Relatedly, current strategies for reducing emissions to net zero by the middle of the century implausibly assume that the world will acquire great capabilities to remove greenhouse gases from the atmosphere.^{14,15} This insufficient action means that temperature increases are likely to be well in excess of 2° C,¹⁶ a catastrophic outcome for health and environmental stability. Critically, the destruction of nature does not have parity of esteem with the climate element of the crisis, and every single global target to restore biodiversity loss by 2020 was missed.¹⁷ This is an overall environmental crisis.¹⁸

Health professionals are united with environmental scientists, businesses, and many others in rejecting that this outcome is inevitable. More can and must be done now – in Glasgow and Kunming – and in the immediate years that follow. We join health professionals worldwide who have already supported calls for rapid action.^{1,19}

Equity must be at the centre of the global response. Contributing a fair share to the global effort means that reduction commitments must account for the cumulative, historical contribution each country has made to emissions, as well as its current emissions and capacity to respond. Wealthier countries will have to cut emissions more quickly, making reductions by 2030 beyond those currently proposed^{20,21} and reaching net-zero emissions before 2050. Similar targets and emergency action are needed for biodiversity loss and the wider destruction of the natural world.

To achieve these targets, governments must make fundamental changes to how our societies and economies are organised and how we live. The current strategy of encouraging markets to swap dirty for cleaner technologies is not enough. Governments must intervene to support the redesign of transport systems, cities, production and distribution of food, markets for financial investments, health systems, and much more. Global coordination is needed to ensure that the rush for cleaner technologies does not come at the cost of more environmental destruction and human exploitation.

Many governments met the threat of the COVID-19 pandemic with unprecedented funding. The environmental crisis demands a similar emergency response. Huge investment will be needed, beyond what is being considered or delivered anywhere in the world. But such investments will produce huge positive health and economic outcomes. These include high quality jobs, reduced air pollution, increased physical activity, and improved housing and diet. Better air quality alone would realise health benefits that easily offset the global costs of emissions reductions.²²

These measures will also improve the social and economic determinants of health, the poor state of which may have made populations more vulnerable to the covid-19 pandemic.²³ But the changes cannot be achieved through a return to damaging austerity policies or the continuation of the large inequalities of wealth and power within and between countries.

Cooperation hinges on wealthy nations doing more

In particular, countries that have disproportionately created the environmental crisis must do more to support low and middle income countries to build cleaner, healthier, and more resilient societies. High income countries must meet and go beyond their outstanding commitment to provide \$100bn a year, making up for any shortfall in 2020 and increasing contributions to and beyond 2025. Funding must be equally split between mitigation and adaptation, including improving the resilience of health systems.

Financing should be through grants rather than loans, building local capabilities and truly empowering communities, and should come alongside forgiving large debts, which constrain the agency of so many low income countries. Additional funding must be marshalled to compensate for inevitable loss and damage caused by the consequences of the environmental crisis.

As health professionals, we must do all we can to aid the transition to a sustainable, fairer, resilient, and healthier world. Alongside acting to reduce the harm from the environmental crisis, we should proactively contribute to global prevention of further damage and action on the root causes of the crisis. We must hold global leaders to account and continue to educate others about the health risks of the crisis. We must join in the work to achieve environmentally sustainable health systems before 2040, recognising that this will mean changing clinical practice. Health institutions have already divested more than \$42bn of assets from fossil fuels; others should join them.⁴

The greatest threat to global public health is the continued failure of world leaders to keep the global temperature rise below 1.5°C and to restore nature. Urgent, society-wide changes must be made and will lead to a fairer and healthier world. We, as editors of health journals, call for governments and other leaders to act, marking 2021 as the year that the world finally changes course.

Acknowledgments

This editorial is being published simultaneously in many international journals. Please see the full list here: https://www.bmj.com/content/fulllist-authors-and-signatories-climate-emergencyeditorial-september-2021

Footnotes

Competing interests: We have read and understood BMJ policy on declaration of interests and declare the following: FG serves on the executive committee for the UK Health Alliance on Climate Change and is a trustee of the Eden Project. RS is the chair of Patients Know Best, has stock in UnitedHealth Group, has done consultancy work for Oxford Pharmagenesis, and is chair of the Lancet commission on the value of death.

Provenance and peer review

Commissioned; not externally peer reviewed.

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Erratum

ecause of a production error, there were two mistakes as published in the printed version of Volume 30, Issue 4, in the article "EMA guidance meets reality: An evolving story", which appeared in the Regulatory Matters section, pages 56–58. Module VII of the Good Pharmacovigilance Practices guidelines was incorrectly referred to as Module XVII. Module VIII was incorrectly referred to as XVIII. The online edition has been corrected.

President's Message The past – The present – The future

D ear colleagues, friends, and EMWA members,

Happy 30th EMWA anniversary!

We have an exciting new year ahead of us. To celebrate EMWA's 30th anniversary, we will take a deep dive into EMWA's history, celebrate our present accomplishments, and aim to set the outlines for EMWA's Five-Year Strategic Plan.

On p.9, please see a reprint from our website of the story of EMWA's history by Geoff Hall, a founding father of our organisation and one of our first presidents.

According to Geoff's article, EMWA's first meeting took place in Brussels in February 1992. Fun fact for all conspiracy theorists: Besides Mike Matthews, Stephen de Looze, and Brenda Moore, the SmithKline vaccine crew were the key drivers of the formation of a European-based Medical Writers Association. Did the SmithKline vaccine crew foresee back then that 30 years later, the medical writing profession would be preoccupied with vaccine-related communications?

Throughout this year, we will share such

anecdotal stories on our social media channels (#EMWA30) and within each issue of this year's MEW, you will find information on the history of EMWA.

To commemorate this milestone, we even created a special EMWA logo (see it below) You can download it from our website and even use it in your email signature.

With this MEW issue on *Sustainable communications: Emerging health topics and debates,* we aim to make our profession aware of this important topic that surely was not on the agenda 30 years ago. As a UN Sustainable Development Partner Organisation, EMWA is committed to the UN Sustainability Development Goals (SDGs; see our issue cover and the infographic opposite). For this purpose, EMWA set up its own Sustainability Special Interest Group (SUS SIG) in 2019. As the chair of the SUS SIG, I am very proud that a group of people – who have never met in person – have the dedication to promote sustainability within our profession and beyond. The SUS SIG interacts with many other SIGs (see infographic opposite) and this year we hope to be organising Meet & Share sessions where we can facilitate the interconnectivity of SIG topics.

In the near future, EMWA aims to collaborate with the Committee on Publication Ethics (COPE).

We are hopeful that we can organise a Face-2-Face EC meeting this spring where we will discuss our vision for EMWA's future to be embodied in the Five-year Strategic Plan. If you wish to engage in that process, please write an email to president@emwa.org.

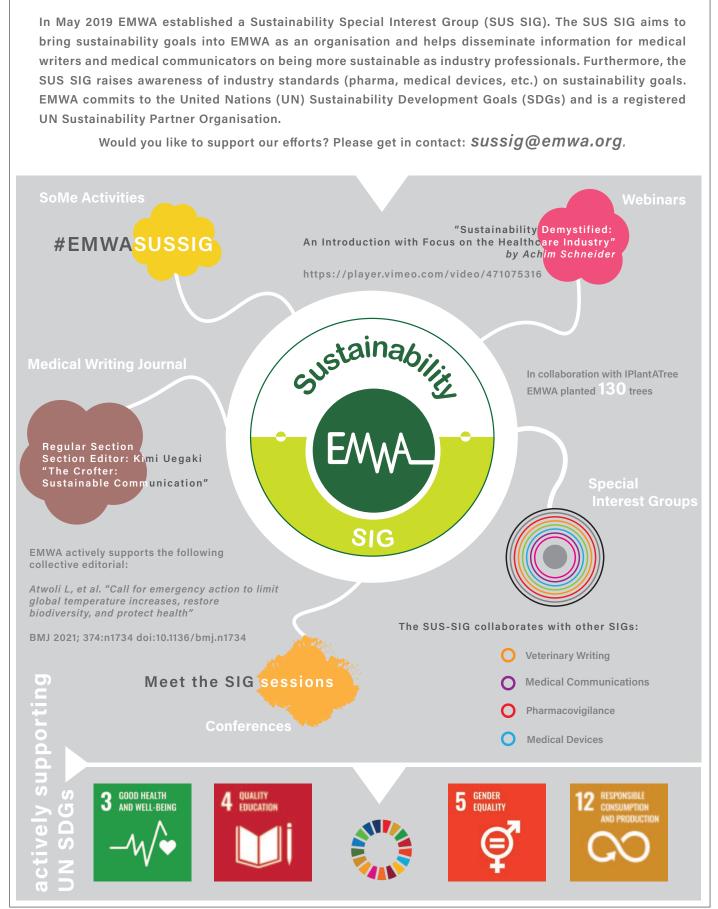
Greetings from Germany!



Carola Krause president@emwa.org



EMWA's commitment to sustainability



The history of EMWA (1992–2008) Personal and possibly unreliable recollections

In this issue we look back fondly, and sadly, with this reprint from our website, written in 2008, about the history of EMWA. We look back fondly because this year we celebrate our 30th anniversary as an organisation. We look back sadly because this article was written by one of our founders, Geoff Hall, who passed away in 2010 and whom we miss greatly.

By Geoff Hall

S itting down to write the history of EMWA reminds me of Tolstoy's comment on historians that they are like deaf people who go on answering questions that no-one has asked. My feeling is that EMWA's members are likely to be more concerned with the future of the association than its past. Nevertheless, in case there are a few people who are inwardly curious about the how, why, and in particular the when of EMWA, here goes. I tell a tale of flirtation, marriage, divorce, remarriage, betrayal and separation – and that's just the relationship between EMWA and its American cousin, the American Medical Writers Association (AMWA).

But let's start at the beginning, or before the beginning. My researches uncover a succession of meetings that took place before the generally recognised first meeting of EMWA in Brussels in February 1992. The initial idea grew out of an informal lunch enjoyed by Mike Matthews and Stephen de Looze in London after they had bumped into each other at the San Francisco AMWA meeting in 1986. There followed a meeting at the Alderley Park HQ of Zeneca between Stephen, Mike, Brenda Moore and others on 11 October 1990. Next, 14 individuals from 9 European-based pharma companies met at the Quorn Grange Hotel in Loughborough in the English East Midlands. Mike Matthews recalls, "There was a subsequent 'pre-Brussels' informal meeting somewhere in Belgium (Rixensart?) with the SmithKline vaccines crew, who were then key in carrying the whole thing forward."

Two individuals at SK Biologicals deserve the credit for taking the whole thing forward: Jane



Wynen – like so many important characters in the history of EMWA, an American based in Europe – and Ceara Roche. Ceara's daughter Moya was born in April 1993 and she returned to her native Ireland. When EMWA came to Dublin in 2000 we were delighted to honour Ceara's contribution.

The SK Biologicals connection is how I came to be involved. The advertising/PR group that I worked for was involved in the pre-launch creative stuff for the world's first hepatitis A vaccine. In addition to the marketing people, I met and worked with SK Biologicals' remarkable medical director Francis André and his team.

A key member of this group, whom I had met at various meetings, Anne Hepburn, phoned from Rixensart to tell me about a meeting in Brussels for medical writers. Do you know, I don't think I had ever previously heard the term medical writer? I was a writer who wrote about medicine – as well as other technical and nontechnical topics. Still, I was intrigued by the idea of meeting people whose daily life posed many of the same problems that faced me. Writing is the most solitary of professions. Anne had said she wanted me to attend because I was a writer first and a scientist second (or even third) and so would offer a different perspective from most of the others attending.

Aaron Bernstein, the second EMWA president (1993) reported in AMWA Journal Europe (subtitled The Newsletter from the European Medical Writers Association Chapter of the American Medical Writers Association), "The European Medical Writers Association met formally for the first time in Brussels, Belgium, on 21 February 1992. A total of 32 persons from seven countries attended this meeting with a view to form a permanent writers' group in Europe." There were no workshops – you could have squeezed the whole lot of us into one – but, although the main point of the meeting was planning for the future, there was a programme that included a presentation from Helen Frampton on the role of a medical writer in Hoechst and Art Gertel (whatever became of him?) who described keys to

improved reviewability of regulatory documents.

The rest of the day was given over to discussing the creation and structure of EMWA. Should we be affiliated with AMWA? Should we model our meetings and constitution on AMWA? We resolved that we would be a chapter of AMWA, the idea being that we could make use of AMWA's established structure and administration to help us get established. The vote was 24 to 5. The AMWA Board of Directors approved the formation of the chapter in March 1993.

Eindhoven in the Netherlands hosted the second meeting. The single day was filled with 3 one-and-a-half hour seminars and EMWA's first 3-hour workshop, entitled 'Writing Abstracts' and delivered by an AMWA past-president Howard Smith. The seminars were 'Globalising Clinical Research Reports' (Chris Preston, Hoffmann-La Roche, Basel), 'Illustrations for Scientific Publications' (Anthony Bowley ABCommunications, Switzerland - a helpful guide to the perennial poser of when to use graph, table or text) and 'An Overview of Statistical Errors in the Medical Literature' (James DeMuth, University of Wisconsin, Madison). This last remains one of the best talks on statistics I have ever heard.

The Bruges conference in March 1995 was an important milestone. It was the first conference with a programme of workshops – OK so there were only 4, but it was a start – and it was the scene of one of EMWA's few rows (over our relationship with AMWA, of course).

The EC presented the agenda for the business meeting in a bulky folder. First up was an overview of membership and finances by Philip Cooper. (No longer involved in EMWA, Philip played a vital role in EMWA's early years as our long serving and long-suffering treasurer. A genuine unsung EMWA hero.) Philip reported that we had 149 members, 51 more than the previous year, and SFr 18,000 in the bank – about USD 8,600/GBP 5,440/EUR 6,620 at that time.

Item 3 was the tricky one - the future of AMWA and EMWA. Members were to vote on whether or not to continue as a chapter of AMWA. The case in favour consisted of continuing to benefit from AMWA's greater infrastructure and experience. The case against was primarily the exorbitant costs of affiliation (85% of the membership dues were paid to AMWA) and the reluctance of AMWA to allow workshops run in Europe to count for AMWA accreditation. EMWA could not offer accredited workshops with local workshop leaders without a lengthy, (some might say tortuous), approval process for both the workshop leader and the workshop content, including attending the AMWA yearly conference to deliver the workshops. There were other issues, of course, as having members on another continent required a flexibility that AMWA simply was not prepared to accommodate. For example, the conference registration forms took longer by post to reach Europe and many workshops were already full before European members had even received their forms (this was pre-Internet, folks). One objection raised during my term as President was that the Americans were unsure if European degrees could be considered as equal in value to US degrees! Over the years, reasonable people on both sides attempted to reach sensible compromises only for them to be scuppered by a few intransigent individuals. No change was

agreed to in the relationship, but tempers flared and the fault lines were deepening.

The venue for the 1996 conference was Berlin and it was generously supported by Schering AG who contributed to speakers' and workshop leaders' expenses as well as providing free use of the company's first class conference facilities. The plans for the conference were thrown into some confusion when Colm Benson, the designated organiser of the event, left Schering to return to Ireland - to become a farmer, I recall. The baton was taken up by Jerry Wilson - at that time a fairly new face in EMWA - and the organisation's

first 3-day event was a huge success. EMWA was still a chapter of AMWA at this stage and Barry Drees re-designed AMWA's existing workshop of 'Tables and Graphs' and amazingly actually got it approved by AMWA. Together with Valerie Moore, they were the first Europeans to provide workshops for AMWA accreditation. There were

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just 6 workshops including Art Gertel's workshop on project management, extended to 6 hours, and a guest speaker.

And so to EMWA's first conference in the UK, in Edinburgh. Vice President Barry Drees and Julia Spivack took on the task of organising the event and it was memorable for a number of reasons. The conference banquet was a splendid traditional Scottish banquet featuring haggis, neeps and tatties and a piper in full regalia, addressing the haggis in the words of Rabbie Burns:

"Fair fa' your honest, sonsie face, Great chieftain o the puddin'-race! Aboon them a' ye tak your place, Painch, tripe, or thairm: Weel are ye wordy of a grace, As lang's my arm."

Barry Drees became President (wearing a kilt) and it was in Edinburgh that Art Gertel's massive contribution to and support for the fledgling EMWA was recognised with life membership. The scale of the task undertaken particularly by Julia Spivack in organising the conference was immense. In those days EMWA

EMWA Main Annual Conferences

Year	Venue	President elected
1992	Brussels, Belgium	Jane Wynen
1993	Eindhoven, Netherlands	Aaron Bernstein
1994	Basle, Switzerland	Leen Ashton-Vanherle
1995	Bruges, Belgium	John Aitken
1996	Berlin, Germany	Ben Young
1997	Edinburgh, Scotland	Barry Drees
1998	Madrid, Spain	Gerold Wilson
1999	Copenhagen, Denmark	Geoff Hall
2000	Dublin, Ireland	Keith Veitch
2001	Montpelier, France	Julia Forjanic Klapproth
2002	Prague, Czech Republic	Julia Cooper
2003	Lisbon, Portugal	Isabelle Thirolle
2004	Budapest, Hungary	Adam Jacobs
2005	Malta	Michelle Derbyshire
2006	Lyon, France	Michelle Derbyshire
2007	Vienna, Austria	Julia Forjanic Klapproth

was run entirely by volunteers, i.e. there was no paid Head Office. Workshops, speakers and the social programme all had to be arranged and I recall Julia, Marian Hodges and a few earlier arrivals frantically collating the conference packs before the scheduled registration time. Barry tells me that he was up until the wee hours of the

> morning cutting out delegate badges and putting them into their plastic holders. I especially enjoyed the visit to the Scotch Malt Whisky Society for a tasting and an amazing 4-hour tale of the history of Scotland and whisky, told seemingly in one breath. Organised by Nick Thompson this was a night to try and remember.

> The do-it-yourself approach to conferences was, however, getting more and more impractical with upward of 100 people expected for the next conference and Barry's key innovation as President was to appoint professionals and establish

Head Office. Enter Phillipa Clow and her small team. Another milestone was that EMWA became independent of AMWA and changed to affiliate rather than chapter status which meant that EMWA was essentially on its own. Importantly, this allowed us to keep our money and approve our own workshop leaders.

Madrid was the venue for our 1998 conference. In previous years we had aimed to invite an eminent keynote speaker. The choice for this year

> was David Sharp, deputy editor of The Lancet which led to EMWA's first bit of real fame – an editorial in The Lancet (Sharp D. A ghostly crew, Lancet 1998; 351:1076). This article set off a chain of events, articles (e.g. Jacobs A. Time for the ghosts to take on physical form, Lancet 2004; 364:487-488) and correspondence that culminated in the creation of European Medical Writers Association (EMWA) guidelines on the role of medical writers in developing peer-reviewed publications (Jacobs A and Wager E. Current Med Res & Opinion 2005; 21, 2: 317-321).

Gerold Wilson took over as President in Madrid and I was his Vice President. Our first priority was organisation. At that time we didn't really have a satisfactory constitution and, more importantly, we didn't have a bank account. All EMWA's cash was held in a bank account in

the name of the treasurer. If Philip Cooper had been struck down by a Basle bus the whole of EMWA's wealth would have been lost or at least subject to Swiss inheritance taxes. EMWA became EMWA limited, a 'company limited by guarantee'. Also, during an eventful 2 years, we established our own educational committee and educational programme to provide certification. The 10-year relationship with AMWA finally ended officially as EMWA was big enough to stand on its own feet.

At the Copenhagen conference, education officer Julia Cooper and

I set out to have more workshops than ever before. OK so it was only 15, but it was a step forward. Another innovation was the first autumn one-day conference in Henley in the UK. On the financial side, I had set a target of building up a reserve equivalent to one year's turn-over. The idea behind this was to cover for any disaster or emergency up to and including the cancellation of a spring conference.

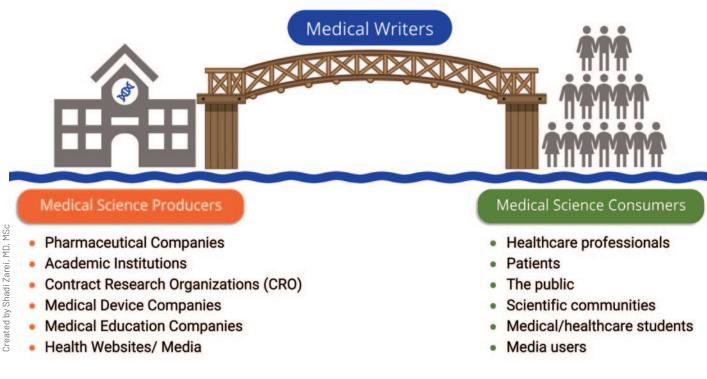
It seems somehow bizarre that several of the people I consider among my closest friends are people who I only see for a few days each year.

Dublin 2000 was a wonderful conference. Membership, which had been 240 in April 1999 rising to 260 in May, had swelled to 350 by April 2000. We now offered 19 workshops. The keynote presentation was from Patrick Salmon of the Irish Medicines Board and there were entertaining presentations from Art Gertel, Stuart Woods and Michael Paling - a pharmaceutical advertising guru who shared the inside information on Viagra. The social calendar featured a banquet with 'Riverdance' style traditional Irish dancing and included an attempt by the dancers to teach

several past-presidents a few steps on stage. Qualified medical help was present just in case.

And so on to Montpelier. At the banquet, President Keith Veitch noted sadly the loss of one of our most beloved members and, with the agreement of the Executive Committee, announced the creation of the Nick Thompson Fellowship in his memory. Art Gertel, already a life member, was naturally the first recipient. I will never forget the mixture of shock, pride and any number of other emotions that hit me when Keith announced that I too was to be given this award. From Montpelier, we headed east and a conference in beautiful Prague and then to Lisbon. Details of these and more recent conferences can be found on the EMWA website and this article is getting a bit too long.

For various reasons, I was unable to get to Budapest in 2004, but I have attended every other EMWA main conference since the start. I believe that what we have built over these past 16 years is remarkable. Obviously the educational programme stands out as the key achievement. However, for me the main benefit of EMWA membership has been the friendships made. It seems somehow bizarre that several of the people I consider among my closest friends are people who I only see for a few days each year. But it's the truth. I look forward to making more new friends at this year's conference in Barcelona.



EMWA News

SECTION EDITOR



Somsuvro Basu basu.somsuvro@gmail.com



Ambassadors Programme News

The EMWA Ambassadors Programme is continuing its efforts to reach out to new audiences to promote medical writing and EMWA.

 Maria Kołtowska-Häggström gave a talk (in Polish) on medical writing as a profession at the Translation and Localisation Conference in Warsaw, Poland, on September 30. The 40 attendees asked questions about topics such as the educational background needed to be a medical writer, what courses are offered at conferences, the general profile of a medical writer, the source of potential clients, and the possibility of combining translation services with medical writing. The presentation was well received with very positive feedback.

- Anne McDonough gave a presentation on current trends and challenges in MedComms at a webinar for Life Science students at the University of Essex on October 14 to over 60 students. There was a lot of interest and some very good questions from the participants.
- Abe Shevack gave a presentation on careers in medical writing and the benefits of

joining EMWA, on November 5 at the Annual Virtual Careers Fair at Birkbeck College, University of London. The event was attended by over 20 active participants who asked several interesting questions during and after the presentation.

If you are an experienced medical writer and EMWA volunteer and are interested in becoming an EMWA Ambassador, or know of any upcoming career events in your locality, please contact Abe Shevack (aspscientist@gmail.com).



We have been made aware of a scam e-mail purporting to come from someone connected to EMWA.

Please report anything suspicious you receive to Head Office (info@emwa.org). Do not respond with any personal or payment information. Thank you for your vigilance on this issue.



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A report on the live hubs across Europe that were part of the 52nd EMWA Conference

A beautiful montage by Satyen Shenoy brings together the memories of the EMWA hybrid conference day:

https://www.emwa.org/news/a-report-on-the-live-hubs-across-europe-that-are-part-of-the-current-emwa-conference/

10% discount for referring new members to EMWA

Existing EMWA members can receive a 10% discount off their next year's EMWA subscription for referring a new member. A new member may be completely new to EMWA or they may be a lapsed EMWA member who has not belonged for a minimum of 36 months. This discount is only valid for a maximum of one new member per year, and a new member must pay a full year's subscription before the discount can be given to the referrer. The new member also must include the name of their referrer on the membership application form. Please note that discounts are not cumulative, nor can they be rolled over into subsequent years – i.e., the maximum discount possible in any given year is 10%.

For more information, please contact Head Office at info@emwa.org.

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We have been working behind the scenes on an improved Member Directory. However, EMWA members need to actively opt-in to be listed on the new Member Directory. Please login to your account to opt-in. There you can also set your specific preferences for which information to show.

We will be providing more information and guides soon, but you can already assist us in populating the directory by updating your preferences.



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In memoriam

It is with great sadness and shock that we share the news that EMWA member and volunteer Amanda Hunn died suddenly on February 8, 2022. Amanda had



been an EMWA member for 3 years and was an active member of the Regulatory Public Disclosure SIG committee. Amanda was passionate about patient communication and drafted the EU guidance on writing lay summaries of clinical trial results published in 2018. She was Joint Head of Policy and Public Affairs at the UK Health Research Authority from 2012 to 2019, after which Amanda was a freelance medical writer and expert consultant. Amanda was very well respected and always willing to share her extensive knowledge and expertise. We will miss collaborating with her. Our thoughts and prayers are with her family at this most difficult time.

Carbon footprint of clinical trials: A high-level literature review

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Abstract

Thousands of clinical trials are conducted globally each year. Yet, little is known about their environmental impact. This paper presents the results of a high-level literature review of the carbon footprint of clinical trials. Five papers were identified and their contents summarised qualitatively. All papers were authored by UK researchers. Carbon footprint metrics from 14 trials were presented in carbon dioxide equivalents (CO₂e). Emissions were broken down by three broadly defined clinical trial activities: operations, travel, and supplies. Recommendations for carbon reduction are discussed. The review showed a dearth of publications on greenhouse gas emissions generated by clinical trials. More work in this area is needed to achieve sustainable, low carbon clinical research.

Introduction

he pharmaceutical industry is among the highest producers of greenhouse gas emissions.¹ One of its key carbon intensive activities is clinical research. Thousands of clinical trials are conducted globally each year. As of January 13, 2022, a total of 400,873 studies are listed in ClinicalTrials.gov. Yet, the current regulatory landscape of healthcare products does not take into account the environmental impact of clinical trials.

Search protocol and selection

To learn more about the carbon footprint of clinical trials, a high-level review of literature was conducted. A PubMed search conducted on December 30, 2021 using the terms "clinical trials AND carbon footprint" with no filters yielded a disappointing 12 publications. The retrieved publications were screened for eligibility based on relevance to the topic. Of the 12 publications identified, only four were deemed eligible and further scrutinised. A manual search of the identified publications revealed one relevant paper which was also included. The 5 papers included are summarised below (see Table 1).

Methodology to estimate emissions

Three papers reported relevant data on greenhouse gas emissions of select clinical trials and followed similar methodology. Data from 14 trials were collected retrospectively on all trial elements that would generate carbon emissions according to the greenhouse gas (GHG) reporting protocol² developed by the World Business Council for Sustainable Development. Using the GHG calculation tools, emissions of the clinical trials were expressed in carbon dioxide equivalents (CO2e) using generally accepted conversion factors. Sources of emissions were broken down by different trial activities, roughly categorised as operation of coordination centre or study site (i.e., fuel for electricity, waste disposal, water), travel (i.e., trial staff commute, trial-related travels), and trial supplies (i.e., manufacture and distribution of drugs, documents, and other equipment).

Publications retrieved

1. Sustainable Trials Study Group (2007). Towards sustainable clinical trials.

The oldest publication identified by PubMed, this paper³ is probably the first published report quantifying greenhouse gas emissions of a clinical trial. The CRASH trial was a multicentre, international study conducted between April 1999 and May 2004 to evaluate the effect of corticosteroids on death and disability in adults with head injury. The analysis was performed by the Sustainable Trials Study Group, a group convened by the London School of Hygiene and Tropical Medicine. The group's mandate was to find ways of reducing greenhouse gas emissions from clinical trials.

There is a dearth of publications on greenhouse gas emissions generated by clinical trials. It is clear that more work needs to be done in this field of research.

Based on a one-year carbon audit, the estimated emission of the whole trial was 630 tonnes CO₂e. There were 10,008 participants and 1945 primary endpoint events, amounting to greenhouse gas emissions of 63 kgCO₂e per participant or 324 kgCO₂e per primary endpoint event. Operation of the coordination centre accounted for the majority of the emissions (39%). Key carbon reduction recommendations include simplifying study design and processes, and minimising travel. This paper mentions the contribution of clinical trial documentation to a study's carbon footprint, thus directly linking medical writing to carbon emissions.

Lyle et al. (2009). Carbon cost of pragmatic randomised controlled trials: retrospective analysis of sample of trials.

To the best of current knowledge, this is the first and only meta-analysis⁴ published to date on the CO₂ emissions of clinical trials. Though not identified during the PubMed search, this paper was cited by three papers retrieved by the initial search. This retrospective study analysed 12 pragmatic (see Merali & Wilson⁵ on the definition of pragmatic vs. explanatory trials), randomised, controlled trials (RCTs) funded by the Health Technology Assessment programme of UK's National Institute for Health Research (NIHR) from 2002 to 2003. The CRASH trial previously presented was not eligible for inclusion in the analysis. The 12 trials involved more than 4800 participants and a wide range of

> healthcare interventions, including pharmaceuticals, devices, and psychological therapies.

> In addition to metrics related to site operation, travel, and supplies, this paper also calculated emissions related to information technology equipment used in the trials. Interestingly, freight distribution of trial documentation was not considered in the metrics, probably due to use of electronic rather than paper-based documents.

> The mean emission estimates were 306 kg CO_2e per participant and 78 tonnes CO_2e per trial. The largest proportion of emissions



came from staff commute (26%) and operations (23%) whereas information technology footprint was lowest (2%; see Table 1).

Data from this analysis were used in developing the NIHR Carbon Reduction Guidelines $(p.19).^6$

Subaiya et al (2011). Reducing the environmental impact of trials: a comparison of the carbon footprint of the CRASH-1 and CRASH-2 clinical trials.

This paper⁷ follows up on the 2007 paper³ and compared the original CRASH trial with a similar study (designated as CRASH-1 and CRASH-2, respectively). CRASH-2 was conducted between May 2005 and February 2010, starting one year after CRASH-1 ended. The two trials were of similar design but CRASH-2 made a greater effort to reduce the carbon footprint using several of the strategies outlined in the NIHR carbon reduction recommendations. CRASH-2 recruited approximately twice the number of participants (N=20,211) but emitted 73% less carbon per randomised patient than CRASH-1 (25 kg vs 92 kg CO₂e per participant; Table 1). The main drivers for lower CO2 emissions in CRASH-2 were increased efficiency in study design, recruitment and conduct, and more compact trial supplies.

The emission data presented for CRASH-1 in this paper slightly differed from CO₂e reported in the 2007 CRASH paper.¹ As carbon calculation tools are regularly updated, the different values were most likely due to different metrics (e.g., updated tools and conversion factors).

4. Pencheon (2011). Managing the environmental impact of research.

This was a commentary⁸ on the environmental impact of healthrelated research, particularly clinical trials. It heavily cited and reported data from the 2011 CRASH-2 vs CRASH-1 paper by Subaiya et al.⁷ Recommendations were broader and went beyond just clinical trials and covered the whole life cycle analysis of health interventions. Examples are finding ways to "incorporate the

environmental cost as well as the financial cost into the process of commissioning research" and the proposal to calculate "potential health gain per tonne of carbon expended".

5. Adshead et al (2021). A strategy to reduce the carbon footprint of clinical trials.

Approximately 10 years passed before another paper $\!\!^9$ on this topic was published. This

commentary builds on the four previous publications and extrapolated the CO₂e estimates in these papers to the roughly 350,000 clinical trials registered in ClinicalTrials.gov to arrive at an estimated 27.5 million tonnes of emission gases attributable to clinical trials globally.

The paper also cites new developments in this field over the last decade. Results from the previous carbon footprint studies^{3,4,7} were used to

The need for reliable clinical trial data has to be weighed against the urgency of the climate crisis. develop the UK NIHR Carbon Reduction Guidelines.⁶ A carbon footprint measuring tool is being tested by the Sustainable Healthcare Coalition. These tools will assist in building CO₂ reduction strategies into study planning and design.

The paper calls for more transparency of the environmental impact of trials and proposes a

thorough environmental cost-benefit assessment to justify the need for conducting a trial based on systematic review of literature and clinical trial registries.

An interesting proposal by this paper is the potential policing of clinical trial CO_2 emissions by regulatory agencies, ethics committees, and biomedical journals. While this suggestion has some merits, the authors concede it comes with

Table 1. Publications on the carbon footprint of clinical trials

Publication / Type	Source of trial data / Trial information	Greenhouse gas kg per participant	emission estimates (tonnes per trial per year	in CO₂e) ^b tonnes for whole trial	other metrics reported
Sustainable Trials Study Group, 2007 / original research	CRASH Trial ^a / Multicentre international trial of 10,008 participants over 5.1 years	63	126	630	324 kg per primary endpoint event
Lyle et al., 2009 / meta-analysis	12 pragmatic RCTs funded by the HTA programme of >4800 participants during 2002 and 2003 Mean number of centres: 16, in the UK only Mean number of participants: 402	Mean: 306.2 Range: 80.0 to 883.7	Total: 222.3 Mean: 18.1 Range: 8.9 to 30.1	Total: 941.2 Mean: 78.4 Range: 42.1 to 112.7	Mean: 0.1 kg per £ spent Mean: 5.6 tonnes per 1 full time staff
Subaiya et al., 2011 / original research	CRASH-1 Trial ^a Multicentre international trial of 10,008 participants over 5.1 years	92	181.3	924.6	NI
	CRASH-2 Trial Multicentre international trial of 20,211 participants over 4.7 years	25	108.2	508.5	NI
Pencheon, 2011 / commentary	Refers to data provided by Subaiya et al.				
Adshead et al., 2021 / commentary	350,000 trials registered in ClinicalTrials.gov as of June 16, 2021	NI	NI	NI	27.5 million tonnes (cumulative)
^a CRASH trial and CRASH-1 trial are the same but the values reported in the 2 papers differ, possibly due to different metrics.					

^b Calculations were according to the greenhouse gas reporting protocol² http://www.ghgprotocol.org/ but scoping and conversion factors could potentially differ.

Abbreviations: CO₂e = carbon dioxide equivalents; NI = no information provided; NIHR = National Institute for Health Research; RCT = randomised controlled trials

additional bureaucratic burden. Clearly, the need for reliable clinical data has to be weighed against the urgency of the climate crisis.

Discussion and synthesis

This review identified important information on

the carbon footprint of clinical trials and opportunities for carbon reduction. This information is a good starting point towards sustainable and low carbon clinical research.

A total of five papers on the carbon footprint of clinical trials were reviewed and summarised

(Table 1). Two papers were commentaries, two were original research that provided data on the CRASH trials whereas one reported a metaanalysis of 12 pragmatic RCTs. Data from a total of 14 trials were summarised.

The main clinical trial activities that drive

Clinical trial activities as CO _{2e} contributor (% of total trial emission)	Recommendations to reduce emissions
 Coordination centre operations (39%) Distribution of drugs and documents to sites (28%) Trial-related travel (23%) Trial team commuting (5%) Deliveries related to production of trial drugs (5%) 	 Reduce bureaucracy (regulatory agencies and ethics committees) Simplify study designs Choose better research questions Reduce travel Avoid unnecessary data collection Save electricity by using renewable-energy resources Use systematic reviews to answer research questions first before proposing new trials
 Trial team work commute (26%) Study centres operations (23%) Staff trial-related travel (19%) Trial participants' travel (16%) Manufacture and distribution of trial supplies (14%) Information technology equipment (2%) 	 Minimise trial-related travel Reduce number of face-to face study visits Develop tools and methods to allow the carbon cost of a trial to be considered at the planning stage (e.g., use NIHR carbon reduction guidelines)
 Distribution of trial drugs (48%) Coordination centre operation (30%) Trial-related travel (21%) Trial team commuting (1%) Coordination centre operation (37%) Distribution of trial drugs (32%) Trial-related travel (29%) 	 Improve trial efficiency (e.g., recruitment, data entry, validation, monitoring) Reduce travel (e.g., web-based training, teleconferences) Improve logistics (e.g., more compact materials, lighter packaging)
	 Embed sustainability as a core part of research governance Have a more holistic and enlightened view to the process of conducting research Incorporate the environmental cost well as the financial cost into the process of commissioning research Make valid comparisons and use consistent metrics
NI	 Confirm through systematic reviews the necessity of a trial (i.e., cost-benefit analysis) Make carbon footprint measures a part of study design Provide funding incentives for carbon reduction Use NIHR carbon reduction guidelines Involve regulatory bodies, ethics committees, and biomedical journals in policing carbon footprint Develop a tool to measure reliably the carbon footprint of trials and identify which elements are carbon-heavy

emissions are the study site operation, trialrelated travel, and trial supplies. Key recommendations to reduce carbon footprint include more efficient study designs and conduct, and minimising trial-related travel. Most of the recommendations (Table 1) by these papers have been incorporated in the UK NIHR Carbon Reduction Guidelines.⁶

There are a number of caveats that may limit the generalisability of the review results. Only one database (PubMed) was used for the literature search. All five papers identified were from the UK. The meta-analysis included only UK pragmatic RCTs funded by the NIHR Health Technology Assessment programme. No data from explanatory clinical trials sponsored by the industry are available. Also, all these studies were performed before 2020. Clinical trial conduct has

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changed drastically during the pandemic, restricting travel, and relying on remote monitoring and virtual meetings.

Literature on the greenhouse gas emissions of clinical trials was surprisingly sparse. This dearth of publications on the carbon cost of clinical research indicates a domain that is underserved. Some of the gaps identified that warrant more research are:

- Development of harmonised and validated carbon footprint quantification metrics.
- Incorporation of carbon metrics and reduction strategies in trial planning and design.
- Involvement of funders, regulatory agencies, ethics committees, biomedical journals, and other governance bodies in the disclosure and management of the carbon profile of clinical trials.
- Data from other countries, especially the US, China, and the European Union.
- Data on carbon emissions generated by other research types and study designs.

Though not explicitly mentioned in these papers, in one way or another, medical writers and communicators are involved in clinical trials, and thus, contribute to the emissions. We can also play an active role in the decarbonisation process of clinical research (see also p. 22, Table 1, Uegaki paper).

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Disclaimers

The opinions expressed in this article are the author's own and not necessarily shared by her employer or EMWA.

Disclosures and conflicts of interest

The author is employed in the pharmaceutical industry.

Data availability statement

Search results in PubMed are available for sharing. All five papers summarised are open access. Please contact the author for more information.

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On the Carbon Reduction Guidelines of UK's National Institute for Health Research (NIHR)

What are the NIHR Carbon Reduction Guidelines?

nder the Climate Change Act of 2008, the UK government has committed to significantly reduce UK greenhouse gas emissions by 2050. Healthcare is one of the key drivers of these emissions.

The National Institute for Health Research (NIHR) guidelines are part of the National Health Services (NHS)'s commitment to meet the targets set by the Climate Change Act.

"The NHS has a carbon footprint of about 21 million tonnes of CO2 per year, representing around 25% of public sector greenhouse gas emissions... As the leading funder of health research in the NHS, the NIHR must play a role in reducing carbon emissions from health research."

The guidelines were published on July 30, 2019. There are plans to update these guidelines soon.

Who should use the guidelines and how should they be used?

The guidelines are "aimed at researchers conducting research funded by the NIHR and

outlines some approaches for reducing the greenhouse gas emissions from health research." However, the principles of the guidelines are applicable to all research, regardless of the type of research, source of funding, or geography.

The guidelines are not mandatory; they provide a framework to reduce the carbon footprint of clinical research without adversely impacting the quality, validity, and reliability of research.

Who developed the guidelines?

The guidelines were developed by UK researchers based on data published in two research papers:

- Sustainable Trials Study Group. Towards sustainable clinical trials. BMJ. 2007 Mar 31; 334(7595):671–3. doi:10.2471/BLT.19.249508.
- Lyle K, Dent L, Bailey S, et al. Carbon cost of pragmatic randomised controlled trials: retrospective analysis of sample of trials. BMJ. 2009 Oct 30;339:b4187. doi: 10.1136/bmj.b4187.

What are some of the key recommendations of the guidelines?

The recommendations of the guidelines fall under two main categories: sensible study design and reducing the environmental impact of the NHS through research.

The high-level headings are as follows:

- Setting the research question and making full use of existing evidence
- Efficient study design
- Study set up and conduct
- Avoiding unnecessary data collection
- Sensible clinical trial monitoring
- Good practice in reporting research
- Reducing the environmental impact of the NHS through research

The NIHR Carbon Reduction Guidelines are available at

https://www.nihr.ac.uk/documents/the-nihrcarbon-reduction-guidelines/21685

New Special Interest Groups

Welcome to our new special interest groups!



Preventing biomedical research waste



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Abstract

An estimated 85% of efforts in biomedical research are wasted due to inefficiencies. This wastage represents a global financial loss of greater than US\$200 billion per year, a barrier to practicing evidence-based medicine, and a considerable amount of carbon emission. Inefficiencies exist throughout the research life cycle, from strategic planning, design, execution, reporting, and publication. Medical writers and communicators are well-positioned to help prevent research waste and mitigate adverse effects on planetary health through actions related to good research practice, data stewardship, responsible reporting, and open science.

Introduction

A n estimated 85% of biomedical research efforts are wasted due to inefficiencies, many of which are preventable. These inefficiencies span the life cycle of biomedical research from strategic planning, design, execution, reporting, and publication. Research waste represents a financial loss greater than US\$200 billion globally per year and it interferes with the aim and practice of evidence-based medicine.^{1,2} Considering the significant carbon footprint of the healthcare industry.^{3,4} this wastage also has a considerable impact on planetary health.⁵

At the strategic planning stage, for example, research waste can occur when researchers ask questions or collect data on outcomes that are not relevant or necessary to clinicians and patients. This is compounded at the design stage when new studies are not informed by systematic reviews of the existing evidence, a shortcoming that has been noted in more than 50% of studies.⁶ Research waste can also occur when study designs do not take adequate steps to reduce sources of bias. Other examples of research waste include the failure to fully publish study results, poor reporting, and the inability to re-use data. Given that relevant and essential research is the foundation of evidence-based medicine and healthcare, biomedical research waste translates into foregone benefits such as preventing illness or death, curing disease, promoting wellness, and fostering innovation. Furthermore, redundant studies translate into people and animals being unnecessarily exposed to risk and experimental procedures.²

In recent years, the issue of biomedical research waste has been gaining attention. The purpose of this article to provide an overview of various strategies to prevent research waste and how medical writers and communicators (MWCs) may contribute to these efforts.

How can we prevent research waste?

Four interlinked strategies that can help prevent research waste and contribute to a sustainable future are good research practices, data stewardship, responsible reporting (including transparency and disclosure), and open science (Figure 1). In this section, we discuss each of these strategies.

Good research practices

Good research practices help prevent research waste by ensuring that relevant and necessary questions are addressed by research efforts, and that appropriate methodological standards (e.g. Good Clinical Practice⁷) are followed. Good research practices also encompass timely and accurate registration of study protocols, and

such registration is linked to responsible reporting, transparency, and public disclosure.

Informing new research based on a synthesis of earlier research is a cornerstone of the scientific process; however, in practice, this is unfortunately not always the case. For example, an analysis of phase III randomised controlled trials published in 3 high-impact journals, (*The New England Journal of Medicine, Lancet,* and *JAMA*) between 2016 and 2018 indicated that less than half of the randomised control trials justified their undertaking with

a systematic review.⁸ Low rates of justifying research based on systemic review findings have also been reported in high-impact journals for orthopaedic trauma (between 2015 and 2018; 33%),9 urology (between 2014 and 2019; 54%),10 and ophthalmology and optometry (until 2018; 22%).11

To address this source of research waste, along

Research waste represents a financial loss greater than US\$200 billion globally per year, interferes with evidence-based medicine, and has a considerable impact on planetary health. with the continued failure of published studies (48.6%) to assess new research findings in the context of existing evidence,¹² an international network to promote evidencebased research (EBR) was established in 2014. EBR is defined as "the use of prior research in a systematic and transparent way to inform a new study so that the research is answering questions that matter in a valid, efficient and accessible manner." The EBR approach also includes consulting clinicians and patients to determine what are

relevant and necessary research questions and clinical outcomes. 13

While research funders and regulators have key roles in ensuring the EBR approach is

implemented in practice,¹⁴ MWCs who are involved in grant applications can also contribute. For instance, while funders currently differ with regards to explicitly justifying the need for new studies based on systematic reviews,¹⁵ MWCs can act as early-adopters and educate their colleagues or clients on EBR and advocate for this approach. Furthermore, MWCs have a critical role in writing clear study protocols that adhere to good research practices, ensuring timely and accurate registration of study protocols, and implementing good documentation practices (Table 1).

Data stewardship

Stewardship refers to caring for and managing a resource. Data stewardship is an essential component of sustainable research practices and in recent years, it has become embedded in the requirements of research funders and scientific journals.¹⁶

In practice, data stewardship involves establishing procedures for managing data before, during, and at the end of a research study, and ensuring that data are FAIR (findable,

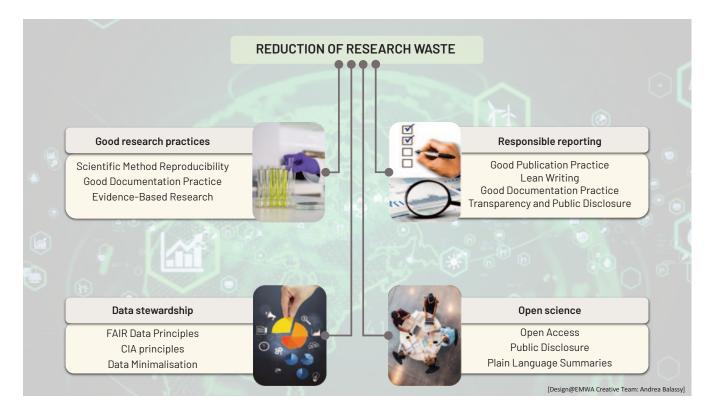


Figure 1. A schematic representation of how the reduction of research waste is based on actions/policies/standards related to good research practices, data stewardship, responsible reporting, and open science Abbreviations: CIA = confidentiality, integrity, accessibility; FAIR = findable, accessible, interoperable, reusable.

Finally, data

stewardship also

means data

minimisation, that

is, only data that

are necessary for

the research

purpose should be

collected.

accessible, interoperable, and reusable) for humans and machines. It also involves meeting legal and ethical requirements for upholding confidentiality and privacy of participants as well as ensuring that the wish of patients to have access to their own data and have their data reused are fulfilled.^{17,18}

Benefits of good data stewardship include increased research transparency and ease of replication, and accelerated discovery and innovation as data sharing is possible and feasible. Good data stewardship goes beyond individual researchers and involves organisations. An illustration of this is the recent collaboration to improve the interoperability between two key clinical terminology vocabulary

systems: the Systematised Nomenclature of Medicine – Clinical Terms (SNOMED CT), which is used by physicians and other healthcare providers; and Medical Dictionary for Regulatory Activities (MedDRA), which is used by regulatory authorities such as EMA. Thanks to this commitment, SNOMED-based data in electronic health records/databases and MedDRA-based data in regulatory databases can be exchanged seamlessly from one to the other. As such, for example, adverse event data in electronic health records can now be converted into MedDRA and used by EMA for pharma-

> covigilance tasks; conversely, adverse event data in MedDRA can be converted into SNOMED CT and used to inform clinical decision-making.¹⁹

The European Health Data Space (EHDS) is another example of data stewardship. It "aims to make full use of digital health to provide high-quality healthcare and reduce inequalities. It will promote access to health data for prevention, diagnosis and treatment, research

and innovation, as well as for policymaking and legislation.^{"20} Finally, data stewardship also means data minimisation, that is, only data that are necessary for the research purpose should be collected. Less data means less computing power is needed for storage and analyses.

While MWCs may not be directly involved in

data collection and management per se, they can ensure that data stewardship is considered in the study design and that requirements regarding FAIR data management practices are adequately addressed in grant applications. MWCs can also provide the public with accurate information about data sharing and address concerns about confidentiality and privacy. Furthermore, when writing laboratory manuals and study protocols, MWCs can advocate for data minimalisation to ensure that only absolutely necessary data and samples are collected (Table 1).

Responsible reporting

Responsible reporting, transparency, and public disclosure are closely intertwined when it comes to dissemination. Dissemination of research results regardless of the outcomes is one of the ethical principles written in the Declaration of Helsinki.

Researchers, authors, sponsors, editors and publishers all have ethical obligations with regard to the publication and dissemination of the results of research. Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and

Strategy	Recommended Actions	
Good research practices	 Advocate for scientifically sound, efficient clinical trials Advocate for following the EBR approach Adhere to the GCP principles 	 Advocate for clear and easily implementable protocols Ensure timely and accurate registration of study protocols Follow good documentation practices
Data stewardship	 Advocate for data minimisation Educate clients on adherence to FAIR data management as part of funding requirements 	• Educate public/patients about FAIR data management through medical communications
Responsible reporting	 Ensure timely posting of results publicly Write clear, accurate, fit-for-purpose documents Protect personal data through proactive anonymisation, thereby producing "redaction-friendly" documents 	 Practice "lean writing" Follow good documentation practice Extend reach to patients and public via plain language summaries
Open science	 Report scientific information accurately and responsibly Advocate for publishing negative results Develop a publication plan Advocate for publication in open access journals 	 Adhere to reporting guidelines (EQUATOR) Avoid predatory journals Adhere to good publication practice, including transparency of involvement of MWCs in a publication

Table 1. Recommended actions for medical writers and communicators to help prevent research waste

Abbreviations: EBR = evidence-based research; EQUATOR = Enhancing the QUAlity and Transparency Of health Research; FAIR = findability, accessibility, interoperability, and reusability; GCP = Good clinical practice; MWC = medical writers and communicators.

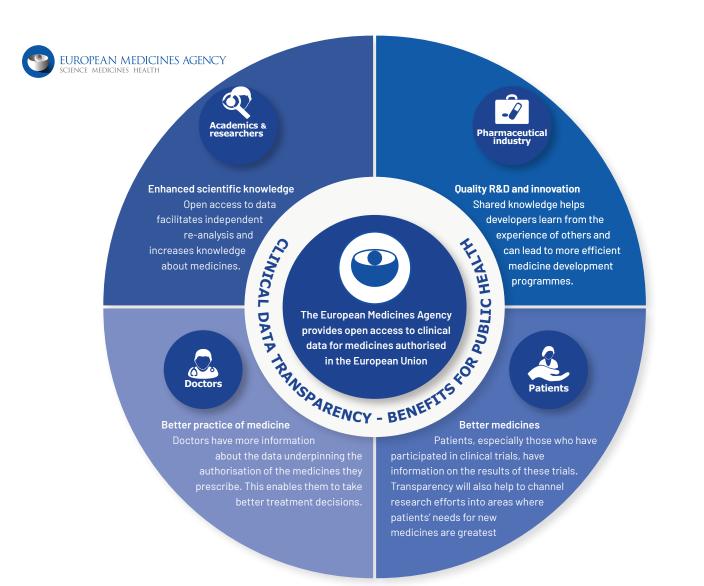


Figure 2. Benefits of clinical data transparency in clinical research

Used with permission from the European Medicines Agency and adapted for readability²⁴

accuracy of their reports. All parties should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results must be published or otherwise made publicly available.²¹

Dissemination comprises a range of research documentation. For example, the study protocol and related material such as trial registration, statistical analysis plans, and clinician training resources; various summaries for different stakeholders; data manuals; and primary and secondary publications.

Traditionally, however, reporting of research results has consisted of submitting documents

and datasets to regulatory authorities and disseminating results through biomedical publications. The former was cloaked in confidentiality whereas the latter was done voluntarily, usually when results were favourable. Indeed, a "negative" study is a strong predictor of nonpublication.²² Also, although reporting guidelines exist, adherence has been an issue and a contributing factor to research waste.²³ Data transparency is about making research information, regardless of outcome, available to the public, hence public disclosure. This transparency promotes public trust. Research results are wasted if they do not translate into societal benefits, which is impossible without

trust. The benefits of data transparency to promote innovation and enhance scientific knowledge that would translate into better practice of medicine and benefits for public health are detailed in Figure 2.²⁴

Funders have a role in encouraging dissemination; for example, the UK National Institute for Health Research Health Technology Assessment programme policies include withholding the final 10% payment of a study grant until the full report has been made available.¹⁴

The onus to publicly disclose lies not only on the researchers but also on regulatory agencies and health authorities. EMA spearheaded data transparency and public disclosure in 2016 with the launch of a clinical data website under EMA Policy 0070.²⁵ With this move, the agency went beyond disclosing their decisions through European public assessment reports; they also published the submitted documents on which they based their decisions. Since the launch of EMA clinical data website, 152 applications have been shared, including 10 on COVID-19

treatments and vaccines (as of end of December 2021).²⁶ Following EMA's example, Health Canada also started its own public disclosure portal in 2019.²⁷ In addition, two new electronic systems have been launched in Europe to centralise public disclosure of clinical trials, the Clinical Trial Information System (CTIS) for medicinal products and the European detchese for medical devices (Fu

database for medical devices (Eudamed). Both are expected to be fully operational in 2022.

MWCs have a pivotal role preventing research waste through responsible reporting, transparency, and public disclosure. By ensuring accurate, complete, and easy to review documents, MWCs facilitate efficient and speedy reviews of manuscript submissions and regulatory applications. MWCs can protect personal data through proactive anonymisation, which facilitates the production of "redaction-friendly" documents. Through timely dissemination of both favourable and unfavourable results, MWCs help minimise duplicating efforts and repeating mistakes. Furthermore, public dissemination through biomedical publications support healthcare professionals in their efforts to practice evidencebased medicine. Lastly, in developing plain language summaries of research results, MWCs extend their reach beyond regulators and healthcare professionals to the patients and the public (Table 1).

Open science

Good research practice, data stewardship, and responsible reporting culminate in open science. According to UNESCO, open science is about making scientific knowledge openly available, accessible, and reusable for everyone. The term has its roots in the open access initiative of providing free access to scientific literature to everyone. Open science goes beyond biomedical journals; it extends to lab books, regulatory documents, datasets, open-source software, and open hardware. The aim is for scientific information to be effectively and reliably harnessed for universal benefit.²⁸

Adopted by the Council in 2016, the EU's open science policy is among the strongest in the world. Under Horizon Europe, all publicly funded research should adhere to FAIR and open data sharing of results, using for example the European Open Science Cloud. Once fully

> implemented, the cloud will provide European researchers, innovators, companies, and citizens with a federated and open multi-disciplinary environment where they can share, find, and re-use data, tools, and services for research, innovation, and educational purposes.²⁹

MWCs have a big role to play in the open science environment. They enable timely and accurate

reporting of research results in biomedical journals by following reporting guidelines and adhering to ethical principles and good publication practice. In doing so, they promote public trust in science (Table 1).

Conclusions

Good research

practice, data

stewardship, and

responsible

reporting

culminate in open

science.

Research not shared is research wasted. And like all human activities, biomedical research has an ecological impact. We have identified four interlinked strategies that can help minimise wastage in terms of money, time, and resources during the life cycle of a biomedical research project. MWCs play an important role in all these strategies, as summarised in Table 1. In doing our part, we help minimise research waste, reduce the carbon footprint of research projects, and contribute towards a sustainable future for biomedical research and the planet.

Disclaimers

The opinions expressed in this article are the authors' own and not necessarily shared by their employers, clients, or EMWA.

Disclosures and conflicts of interest

Kimi Uegaki provides freelance medical writing and editing services to clients in academia and the biomedical/healthcare industry. Raquel Billiones is employed in the pharmaceutical industry.

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Ins and outs of environmental risk assessments (ERAs) of medicinal products for human use

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Abstract

An environmental risk sssessment (ERA) is the process of evaluating the effects of drugs for human use on the environment. ERAs must accompany all new drug market authorisations in Europe. In this article, we discuss the current guidelines on ERAs for drugs without genetically modified organisms for human use. We also discuss the role of medical writers/communicators and aspects of the guideline that may be improved upon.

harmaceuticals are a vital component of the medical profession's arsenal to prevent and cure illness and maintain health. Availability of and access to effective pharmaceuticals benefit society in terms of improved quality of life, productivity and longevity.¹ However, simultaneously, pharmaceuticals are a threat to the planet's health and since the 1990s, awareness of the environmental risks of pharmaceuticals to water (ground, surface, sewage), soil, air, and biota has grown.²

Indiscriminate use of antibiotics in humans, pharmaceutical manufacturing facilities, and agriculture has resulted in antibiotic run-off into the environment that, together with the natural bacterial communities and the discharged resistant bacteria, create "superbugs".^{3,4} Such events can see the emergence of pathogens with

This article has been updated to correct several errors. An erratum is published in the June 2022 issue of the journal. antibiotic resistance genes (ARGs), which are a bigger challenge to treat.⁴ Another concern is the emergence of endocrine disrupting chemicals (EDCs). They are non-natural chemicals that can disrupt hormonal action when ingested by mimicking the hormones, affecting the hormonal pathway, altering the receptors, or acting as hormone antagonists. Some of the modern drug delivery systems (intravenous, oral, and transcutaneous routes) contain nanoparticles and microplastics that are probable EDCs and thus, can disrupt hormonal functions in the human body. Moreover, EDCs can also be passed from the mother to the foetus,⁵ are ubiquitous, and can make their way to water bodies.

Minimising the impact of pharmaceuticals on the environment is part of Good Clinical Practice (GCP) and is stated in the 11th principle of the Declaration of Helsinki.⁶ Furthermore, conducting environment risk assessments (ERAs) for the risks associated with the use of

medicinal products is part of EMA's regulatory submission for market authorisation application (MAA). It should be noted that the risks associated with the synthesis or manufacture of medical products is outside the scope of ERAs. The legal basis of ERAs for human medical products (HMPs) can be found in Article 8(3) of Directive 2001/83/EC and Directive 2001/18/EC.7 ERAs are submitted as part of Module 1.6 of the electronic common technical document (eCTD).7 The two main guidelines for ERAs of medical products for human use are:

- the EMEA/CHMP/SWP/4447/00 Rev. 1 (2018) for medicinal products for human use in general; ⁷ and
- the EMEA/CHMP/BWP/473191/2006 Corr (2006) for medicinal products containing, or consisting of, genetically modified organisms (GMOs).⁸

In this article, we provide an overview of the guidelines on ERA for drugs for human use without genetically modified organisms (GMOs). We also discuss the role of medical writers and communicators in the preparation of ERAs and aspects of the guidelines that may be improved upon.

MEA/CHMP/SWP/4447/00/Corr2 (2006) for human medicinal products

ERAs for HMPs follow a two-phase, stepwise assessment procedure (Figure 1), similar to that for veterinary medicinal products.⁹ The results at the end of Phase I determine whether the Phase II Assessment is required. However, certain substances such as EDCs and antiparasitics undergo Phase II Assessment regardless of their Phase I outcome. It is also possible that an ERA consists solely of a justification for not submitting ERA studies.⁷

The active pharmaceutical ingredient (API)

Minimising the

impact of

pharmaceuticals

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Clinical Practice

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11th principle of

the Declaration

of Helsinki.

is usually the parent compound. ERAs are based on a "total residue approach", which has two assumptions: the body does not metabolise the API and excretes it as the parent compound, and metabolites have similar or lower toxicity than that of the parent compound.⁷

Phase I: Environmental exposure screening

The exposure estimated at this phase is based only on the API and not on the route of administration, pharmaceutical form, metabolism, and excretion.

In Phase I, the following types of studies may be conducted:

- Risk assessments to determine the possibility of an organism in the environment becoming exposed to the API and ecotoxicity occurring;
- Persistent, bioaccumulative, and toxic (PBT) assessments, which evaluate the degree to which APIs degrade in the environment (persistent), accumulate in organisms (bioaccumulative),

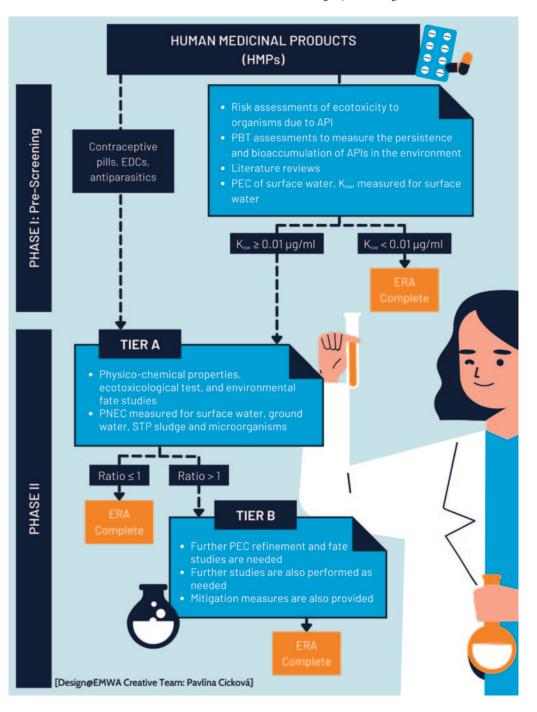


Figure 1. The environmental risk assessment (ERA) process outlined by EMA.

Abbreviations: API, active pharmaceutical ingredients; PBT, persistent, bioaccumulative, and toxic; PEC, predicted environmental concentration; PNEC, predicted no effect concentration; STP, sewage treatment plant; EDCs, endocrine disrupting chemicals.

and are toxic. PBT assessments address the intrinsic properties of APIs, which make long-term environmental risks unpredictable

• Complete literature reviews.

The next step is the calculation of the predicted environmental concentration (PEC) of surface water, measured as K_{ow} . If the value is less than 0.01µg/l, then further tests are not conducted and the drug substance is considered to not pose any danger to the environment and the ERA is complete.⁷ However, as mentioned earlier, this does not apply to any APIs such as EDCs that disrupt reproduction in vertebrates.⁴ When the

value of $K^{}_{\rm OW}$ is equal to or above 0.01 $\mu g/l$, then the drug substance enters Phase II.7

Phase II: Environmental fate and effects analysis

Phase II consists of two tiers, A and B. In Phase II, the following studies of the APIs may be conducted:

- Physico-chemical properties
- Environmental fate
- Ecotoxicological effects
- Mechanism of action

The studies address environmental risk for soil, water (ground, surface), functioning of sewage treatment plants, sediment, and secondary poisoning of predators. In Tier A of Phase II studies, predicted no effect concentration (PNEC) is calculated for surface water, ground water, and microorganisms. If the ratio is less than one, the API is considered safe, and no more testing is required. If the ratio is above one (above 0.1 for microorganisms), then Tier B tests for fate and effects assessment are required (see Figure 1). ERA guidelines state that if animal studies are conducted, such studies should implement the 3R principles of animal welfare (replacement, reduction, refinement) in accordance with Directive 2010/63/EU for studies to be Good Laboratory Practices (GLP)-compliant and follow test guidelines issued by the Organization for Economic Cooperation and Development (OECD), European Commission, or comparable guideines.⁷

How are findings from ERAs used?

If findings of an ERA indicate that the possibility of environmental risks cannot be excluded, then the applicant proposes appropriate risk mitigation strategies to minimise release of the medical product into the environment. Currently, the key mitigating strategy is to provide clear instructions for proper disposal of the medicinal product, e.g. returning used patches, medicine delivery devices, and unused medicines to the pharmacy or recycling centres with designated collection boxes. Other strategies include presenting information about potential environmental risks and proper storage, and use of the medicinal product on package labelling and inserts (information for use). With regard to aquatic toxicology studies and fate studies, sharing information on analytical verification of APIs on a given applicant's website or in a general database is "encouraged". This is so that those in water management are able to monitor substances of concern.¹⁵ However, the quantity and quality of data sharing are currently debatable.10,11

ERA structure and the role of medical writers in writing ERAs

ERAs are part of MAA of HMPs and they have a well-defined structure. The introductory section requires a clear identification of the active ingredient, including company name/code, International Union of Pure and Applied Chemistry (IUPAC) name, Chemical Abstract Service (CAS) number, empirical formula, structural formula, Simplified Molecular Input Line Entry System (SMILES) code, and molecular weight.⁷

If relevant, a rationale for the absence of environmental studies is provided. Otherwise, the studies from Phase I and/or Phase II are summarised as texts and tables, as required. The full study reports and references are listed in the annex of the ERA. Finally, the document must carry a dated signature of the author, information



on the author's education, training, and professional experience, and a statement of the author's relationship with the applicant⁻⁷

A medical/scientific writer working for pharmaceutical companies can write ERAs in collaboration with the scientists/toxicologists involved, who can oversee and review the documents. This is because medical writers have a strong understanding of the science involved and experience in translating documents into a structured, well-written study report. Such teamwork can produce a well-rounded document for submission to the EMA. Furthermore, medical communicators may communicate the findings from ERAs to the public in plain language, which exemplifies their vital role in society.

Some shortcomings in the current ERA regulation

There are a few shortcomings in the current ERAs for HMPs.

The first is related to harmonisation. Currently, module 1.6 of the CTD is a nationspecific chapter. As such, ERA requirements are not necessarily harmonised across the EU as are other components of a regulatory submission.¹² In addition, while improvements have been made, discrepancies with other environmental assessment guidelines still exist. For example, the current ERA guidelines are not harmonised with the Classification, Labelling and Packaging (CLP) Regulation, and there are differences between the PNEC and Environment Quality Standard (EQS) approaches.¹³

Second, the ERAs bring the onus of the usercreated risks to the environment and ecosystem on the manufacturers to ensure that manufacturers evaluate the benefit-risks of HMPs and offer mitigation measures. However, these assessments do not look at the manufacturing processes and the subsequent release of API and other chemicals into the environment. Changes in ERA requirements such as including an assessment of risk during the manufacturing process would increase this document's relevance.²

Third, Wess et al. identified that current ERA guidelines do not include antibiotic testing requirements to evaluate their impact on critical microscopic, planktonic algae called diatoms.¹² As diatoms generate about 20% of the earth's oxygen annually,¹⁴ they should be part of environmental assessments as well.

Last, the public cannot access the complete ERAs created by manufacturers of HMPs and other official assessment reports based on them. Currently, the law only requires the publication of public assessment reports (PARs), which do not necessarily contain information from the ERAs.¹⁰ Also, manufacturers who are the authorisation holders of HMPs may exercise the right to refuse disclosing contents of ERA by citing that the ERA is commercially/industrial confidential information (CCI).¹⁰

However, Oelkers¹⁰ recently published arguments that under environmental information law, the release of pharmaceuticals into the environment constitutes an "emission into the environment". As such, there is a legal basis for full public disclosure of ERAs and their official assessment reports. Sharing data on APIs through publicly accessible databases is proposed as a resource-saving solution.¹⁰ This is a precondition for being able to detect emerging environmental trends and risks early and to prevent resource waste from unnecessary repetition of (animal) studies and loss of knowledge. The Swedish Pharmaceuticals and Environment database is an example of such an effort.11

Conclusions

While pharmaceuticals provide society with health benefits, they are also a threat to the planet's health. ERAs aim to identify the environmental risks and ways to mitigate them at the user level. Medical writers and communicators are well-suited to collaborate with toxicologists and communicate the findings of ERAs to the public. Coordinated efforts by governments, regulators, and pharmaceutical companies to promote and facilitate data sharing from ERAs are critical for planetary health.

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The opinions expressed in this article are the authors' own and not necessarily shared by their employers, clients, or EMWA.

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Kimi Uegaki provides freelance medical writing and editing services to clients in academia and the biomedical/health care industry. Archana Nagarajan declares no conflict of interest.

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Veterinary sustainability

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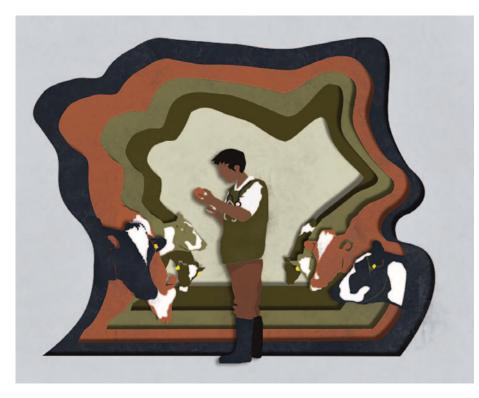
Abstract

Respected for their knowledge of animal health and disease, veterinarians safeguard animal health and welfare and, where applicable, the productivity of animals under their care. With the threats posed by climate change, the veterinary profession must use this privilege to support the whole spectrum of the human-animal-environmental interface to shift towards the objectives outlined in the United Nations 17 Sustainable Development Goals. This article provides medical writers with an overview of the challenges specific to veterinary sustainability, both in supporting others to make sustainable choices and improving sustainable veterinary practice. A veterinary-led initiative that produces sustainability guidelines for the veterinary profession is also showcased as a model of information-sharing and engagement. This is discussed against a food security and sustainability background, likely unfamiliar territory for the medical communications professional

Introduction

he vast majority of the discourse surrounding the impact of climate change is anthropocentric: it is a crisis for humanity.¹ This narrative minimises, or omits completely, the effects on the non-human species that share the planet with us, whether domesticated, feral, or wild. Apart from the ethical and philosophical questions it raises about the imposition of climate change by human activity on non-human species, the narrow focus on humankind is a reductive approach that threatens to undermine efforts to become a genuinely sustainable global society.²

Humanity's interaction with domesticated species has environmental (gaseous emissions,



water and soil pollution, ecosystem damage, and depleted species diversity); animal welfare (intensive production systems and breeding); and human and animal health (threat of zoonoses and antimicrobial resistance) consequences. As health care providers of all non-human species, the veterinary profession could be considered a part of the problem, particularly in prescribing practices and the support of intensive farming industries. However, acknowledging the substantial environmental impact of food animal production on the environment, veterinary expertise to improve animal health and welfare, increase productivity, and reduce waste will be essential for the development of sustainable animal agriculture. A new academic field has even been introduced, the Veterinary Humanities, out of a need to properly define the relationship between animal protection and sustainability.²

All sectors of the global society are redefining their roles in society for a sustainable future using the UN Sustainable Development Goals (SDG) framework. Many domains, including the veterinary profession and animal welfare, have found that the SDG framework does not directly address their domain (yet).³ However, the scope of the SDGs is broad enough to ensure that high animal welfare standards are not incompatible with the SDGs and vice versa.⁴

This article describes the veterinary profession's role and responsibility in sustainable development, here defined as a "negotiated path toward some notion of sustainability."²

The focus is on humankind's interaction with domesticated species. However, mention must be given to wildlife trade, a major driver of environmental change.²

The central role of the veterinary profession in supporting sustainable development is illustrated using three examples: food production animals, aquaculture, and pets. The obstacles and solutions to mitigating the environmental impact of veterinary practice itself are then discussed. Finally, the challenge of disseminating the sustainability message to the broader profession is discussed. This article aims to provide the medical communications professional with an overview of veterinary sustainability.

Veterinary sustainability in the global political arena

Three prominent global bodies, the World Health Organization (WHO), the Food and Agriculture Organization (FAO), and the World Organisa-

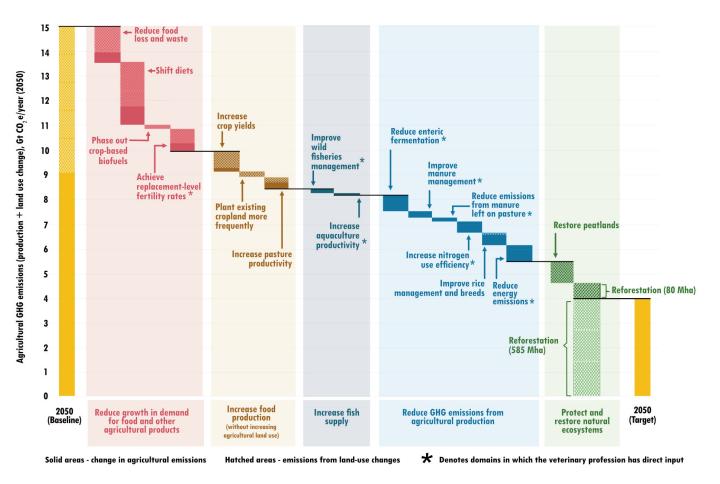


Figure 1. Closing the greenhouse mitigation gap

Qualitative representation of the per-sector contribution of mitigation measures to the reduction of total annual agricultural GHG emissions in 2050 to a target of 4 Gt CO₂ e/year. Areas where the veterinary profession has direct input are also depicted.

Abbreviation: GHG, greenhouse gas

Source: World Resources Report, World Resources Institute, July 2019

tion for Animal Health (OIE), came together in 2010 to produce the Tripartite Concept Note.5 This unprecedented collaboration was formed to facilitate a globally integrated network to manage the increased risk of a zoonotic disease that had arisen due to climate change impacts at the human-animal-ecosystem interface. The OIE has 182 member countries, and national delegates include veterinary surgeons, chief veterinary officers, and veterinary leaders. It provides a crucial platform for the veterinary profession to communicate with international policymakers. Food sustainability and the importance of animal health and welfare is also detailed in the European Union's "Farm to Fork" strategy, part of the European Green Deal.⁶

Furthermore, in June 2021, the Federation of Veterinarians of Europe (FVE) published a position statement that committed members to the active contribution to sustainable food systems through "the promotion of animal health, welfare, and public health", which represents "the backbone for improved sustainability, global health, and security."⁷ In the UK, the British Veterinary Association has produced a position statement supporting the sustainable development of animal agriculture, with a strong emphasis on animal welfare.⁸

In summary, veterinary policymakers at the national, international, and global levels are universally committed to finding sustainable solutions to the role of animals in agriculture.

Some environmental impacts of domesticated species (and their sustainability solutions)

Veterinarians are not just healthcare professionals. Those who work in farm practice have a central role in food production and security, a subject with which medical writers may be unfamiliar. Veterinarians are also ideally positioned to advise and educate animal owners to make more sustainable choices.

As is commonly reported in the mainstream media, the global agriculture sector is one of the industries with the highest environmental impact due to land use, consumption of natural resources, and greenhouse gas (GHG) emissions.⁹ The global livestock population is estimated to contribute about 8% of the total anthropogenic GHGs, of which beef cattle production contributes a disproportionate amount of this impact. Figure 1 provides a quantitative overview of how veterinary input can help reduce GHG emissions associated with food production.

Methane from the bovine gastrointestinal

tract is, perhaps for obvious reasons, the GHG pollutant that has caught the imagination of the public. However, nitrous oxide (N2O) and ammonia (NH₄) emissions from the vast quantities of slurry produced, contribute to a substantial cumulative effect.¹⁰ GHG emissions are the metrics most commonly used to compare the environmental impacts of human activity. However, there is an inherent bias in reporting agricultural emissions solely in the context of GHGs, which has arisen because they are relatively easy to measure. Other relevant factors, such as soil organic carbon (SOC), have the potential to be a carbon sink (or "negative emission technology")¹¹ and counterbalance GHGs. However, measuring SOC is difficult and expensive, and it is often left out of the discussion altogether. Apart from the possibility of SOC being the means to sequester atmospheric carbon, this also highlights a need for the discourse around climate change and emissions to be more balanced.

Veterinarians have played a central role in efforts to reduce the impacts of livestock production generally, and beef cattle specifically. A "less and better" policy has been proposed as part of the sustainable development, where citizens reduce their consumption of food animal products, but health and welfare are protected by maintaining costs.⁸ There are three main areas to mitigate the impact of cattle farming:

- 1. resource efficiency and environmental management,
- 2. modification of enteric fermentation to reduce GHG emissions, and
- 3. selective breeding of animals that produce fewer GHGs and are resilient to climate change.¹⁰

Central to these is the improvement of cattle health to reduce waste caused by disease and reproductive inefficiency. National health schemes, such as those tackling mastitis, lameness, and bovine viral diarrhoea virus in the UK can help to improve efficiency. Improving the submission rate (a measurement of fertility) from 50% to 70% is estimated to reduce methane emissions by 24%.¹⁰

Aquaculture, the farming of aquatic species, is a rapidly growing industry that now provides over 50% of fish for human consumption,¹² overtaking wild-caught fish about 4–5 years ago. The exponential growth of this industry brings with it similar demands for veterinary services and resources of other animal production systems (Figure 1), such as feed, welfare

(particularly at slaughter), waste management, and preventative health plans (against sea lice and amoebic gill disease). However, the rapid growth of aquaculture has raised questions about its sustainability and effects on the fragile aquatic ecosystem, particularly the administration of veterinary medicinal products, which can flow freely into bodies of water.¹³

The sea louse, *Lepeophtheirus salmonis*, is a parasite that causes 3.62%-16.5% biomass loss per production cycle in farmed salmon,¹⁴ due to spoilage or even mass mortality. This inefficiency represents a significant sustainability challenge. The efficacy of "natural" treatments, such as cleaner fish, is supported by weak evidence and dogged by environmental, economic, and welfare concerns.¹⁵ CleanTreat[®] is an innovative

treatment system that removes farmed salmon from open water to treat the parasite.¹⁶ Treatment residues and parasite debris, including eggs, are then washed off the fish before they are returned to their open water pens. CleanTreat®, the active ingredient of which is a neonicatinoid, obtained regulatory approval in Norway in July 2021¹⁷ and a vessel equipped with the CleanTreat filtration

system is currently deployed there. It is an example of how technology can be used to protect the environment whilst still optimising production animal health and welfare.

Although, by far the most significant environmental impact is from food production animals, the sustainability challenges presented by companion animals need to be taken into consideration. The ecological burden associated with the feeding of a combined total of almost 200 million cats and dogs in Europe¹⁸ has prompted life cycle analysis (LCA) ("cradle to grave") of commercial pet food.19 Dog food production has a higher environmental impact than that for cats, simply due to the volume produced. Furthermore, wet food requires a greater consumption of natural resources (for example, tin plating for packaging). Some have suggested that the high protein content (> 30% crude protein on a dry matter basis) in many commercial diets is more due to client demand than an evidence-based nutritional requirement.¹⁹ And given protein is the most ecologically demanding macronutrient, reducing protein content could be a means to improving sustainability. Some producers now offer commercial pet food ranges derived from insect protein.²⁰ Veterinarians are best positioned to counsel owners on sustainable diets for their pets, with precision advice based on the individual animal's healthcare needs.

Putting one's own house in order

Any profession claiming a leadership role in sustainable development must first practice what they preach. Additionally, as a healthcare system, the veterinary practice must "develop strategies to mitigate (avoid the unmanageable) and adapt (manage the unavoidable)" in response to environmental issues.²¹ There is relatively little published literature on sustainability in the veterinary workplace compared to the human

> healthcare sector. One recent systematic literature search found only three opinion papers (one on the environmental impact of veterinary anaesthesia and the other two on farm animal impacts).²² This is compared to a systematic search of the human literature seven years earlier, which returned 49 articles on sustainable hospital design, energy and water efficiency, travel, procurement of medical materials, waste, and staff

behaviour.

Any profession

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leadership role in

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development

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Gaseous anaesthetics were identified as environmentally damaging in 1975,²¹ and the majority of waste anaesthetic gases are scavenged and vented into the atmosphere. At the human healthcare scale, it is estimated that 5% of the National Health Service's carbon emissions in the UK are due to anaesthetic gas emissions. Although this is a relatively small proportion of total GHG emissions, nitrous oxide (N2O) and desflurane are particularly potent pollutants, having 310 and 2540 times the global warming potential of CO2 over 100 years, respectively.21 Furthermore, N₂O persists for 110 years in the atmosphere. Reducing anaesthetic emissions is possible, either by capturing and recycling waste gases, or rendering them chemically inert.²¹ Other measures, such as swapping to a less potent gaseous anaesthetic, utilising total intravenous anaesthesia (TIVA), or local anaesthetic blocking techniques, are effective mitigating strategies.

Waste and the inefficient use of resources are significant problems in clinical practice. Two studies have estimated a 32%-51% wastage of the injectable anaesthetics in human hospitals,²¹



which, if not addressed, negates the sustainability gains of switching to TIVA. Single-use surgical gowns, drapes, and gloves, which are expensive to dispose of, make up a large proportion of clinical waste. But is the environmental cost really offset when considering the water and electricity consumption required to clean reusable gowns and drapes? In the veterinary clinical practice setting, changes are being made to conserve high priority resources, such as electricity, gas, oil, water, and paper,²¹ through efficient waste sorting and incorporating sustainability practices into the procurement of materials and equipment. Changing the tap that surgeons use to scrub into a sterile operation, from an elbowoperated faucet to a foot-operated pedal, saves 5.7 L of water per scrub. Switching to ecofriendly autoclaves (or retrofitting older models) can save 60,000 gallons of water per year.²²

Disseminating the veterinary sustainability message to the profession: a case study of communication and engagement

In 2019, a group of veterinarians in the UK founded Vet Sustain (www.vetsustain.org), the first sustainability support organisation for veterinary professionals.²³ This Community Interest Company aims to provide members of the veterinary profession with the tools to cultivate sustainable practice, in whichever sector of the profession they may work. This has been

achieved through building a network of veterinary professionals, working with veterinary schools to integrate sustainability topics into the curriculum, and equipping veterinary professionals with the tools to support the uptake of sustainable development policies. To this end, Vet Sustain's 5-year strategic plan is to ensure that 50% of UK veterinary practices and all key UK veterinary associations have a sustainability policy in place by 2025.

Vet Sustain has defined six sustainability outcomes, which have been aligned with the SDGs (Figure 2):

- 1. Diverse and abundant wildlife
- 2. A good life for animals
- 3. Net zero warming
- 4. Health and happiness
- 5. A no-waste society
- 6. Clean water for all

In the two short years since its launch, Vet Sustain has forged partnerships with the prominent veterinary membership organisations in the UK. They also foster a global vision and, to this end, have been reaching out to veterinary organisations in Australia, North America, the Caribbean, and Europe to support them in the establishment of local veterinary sustainability initiatives. Vet Sustain is also developing strategies to engage the animal-owning public by introducing a sustainable practice accreditation system, which will enable clients to select practices according to sustainability credentials. Many pet owners would seek out a clinic that operates sustainably,²⁴ indicating that adopting sustainable practice need not result in an economic penalty.

Conclusion

Veterinary sustainability is not just a cut and paste of sustainability measures adopted in human healthcare, although many translate directly from the human to the veterinary clinical setting. Veterinary sustainability is also not just about using expertise to tackle the vast issues of food security and sustainable food production. Veterinary sustainability also brings the role of non-human species into the sustainability development discussion, where previously, animals were either considered inert bystanders or vessels through which to achieve SDGs. Active engagement of the profession by dedicated organisations such as Vet Sustain is essential for the sustainable development of the profession, and the demand for their resources is likely to grow.

The COVID-19 pandemic has taught us how inextricably interlinked animal and human health is, and that one cannot focus on one without considering the other. The key to the medical communicator's role in veterinary sustainability is education. Through increased understanding of the unique issues that affect veterinary sustainability, the services of the medical communications professional will be essential for the engagement of all stakeholders. These stakeholders range from policymakers deciding on key veterinary sustainability issues, to the practising veterinarian who needs support keeping up to date with sustainability science, and needs to be provided with the language and methods to discuss climate change with a diverse client base.²⁴ And finally, the use of appropriate plain language is key in educating the animalowning public to make sustainable choices for the benefit of their animals, the environment, and themselves.

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Figure 2. This figure created by and used with permission of Vet Sustain

Protecting waterways from pollution
Supporting soil health and management

· Supporting the conservation and recycling of water in agriculture

Disclosures and conflicts of interest

The author declares no conflicts of interest.

Disclaimers

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Content from SUS-SIC (Kate Silverthorne) | Designed by EMWA creative team (Louisa Marcombes

The June 2022 edition



Medical devices

The implementation date of the EU Medical Device Regulation has arrived, marking a new era of heightened attention to medical device safety and performance.

This issue will explore the experiences, challenges, and lessons learned over the last years preparing for the MDR requirements as well as potential opportunities these changes bring. Moreover, we touch base on the implementation of the EU In-Vitro Diagnostic Regulation and on other aspects of writing for medical devices.

Guest Editors: Kelly Goodwin Burri and Beatrix Doerr

Lifelong learning opportunities are available for all

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Abstract

The United Nations Sustainable Development Goals (SDG) call all UN member states - low-, high- and middle-income - to promote prosperity while protecting the environment. The 17 goals are part "of a shared blueprint for peace and prosperity for people and the planet." The objective of SDG 4 Quality Education is "to ensure inclusive and equitable quality education and promote lifelong learning opportunities for all." Many people are thinking about solutions to overcome SDG 4 challenges. Some are European Medical Writers Association (EMWA) members. Global news has taught us about vaccine innovations, collaborations, complications, and delays. Ideas and innovations have flowed due to pandemic challenges faced by the world. A Trends in Biotechnology opinion piece called "Build a Sustainable Vaccines Industry with Synthetic Biology", in part, prompted this article. One proponent in West Africa responded that the model outlined in the article "would build an entirely new system of education." This article aims to raise awareness of SDG 4 Quality Education for all; One Health; EMWA involvement in supporting SDG 4; and distributed manufacturing as a case to help communities engage in education.

he European Medical Writers Association (EMWA) is in the process of registering as a UN Sustainability Partner Organisation. The EMWA Sustainability Special Interest Group¹ identified that EMWA fits well with three of the 17 sustainable development goals (SDGs),² and one of those goals is Goal 4 Quality Education. This article gives some information concerning SDG 4 Quality Education. Unfortunately, some of the SDG 4 UN statistics recorded throughout the pandemic do not favour the ability of some communities to support SDG 4.^{3,4} But it is important to remember that quality education is not "one size fits all". What works in one geographical region might not work in another. Moreover, every region has different cultures and infrastructures to consider.

"Quality" is a useful and subjective term

SDG 4 concerns quality education. The word "quality" is often associated with positive attributes. However, depending on how you look at it, the quality of something can be good or bad. Different industries use tools to remove subjectivity and formally measure the quality of what they are doing to meet industry standards and regulations to ensure good quality.

Statistical process control is one of those useful tools.⁵ [Enter "the use of statistical process control to monitor quality education" in an internet search engine to learn more.] Statistical process control can help during ongoing education needs analysis to ensure good quality.

For example, codes of conduct, such as the "Code of Professional Conduct of Teachers" by the Teaching Council of Ireland⁶ and frameworks to support education quality systems, such as the "Three Pillars of Quality Education",⁷ are useful tools. The "three pillars" to support quality education include:

- **Quality teaching,** which needs development and recruitment of high calibre teachers. Teachers need continuous professional development. This ensures they stay current in how and what they teach. To keep good teachers, they need respect as people and professionals. They must receive good salaries, and their living and working conditions must allow them to do their best.
- Quality tools for inclusive teaching and learning where all students are entitled to learning experiences that respect diversity, enable participation, remove barriers, and consider a spectrum of learning needs. Other tools are appropriate, including

curricula and learning materials and resources. A curriculum outlines the subjects taught to students.

• Quality environments for teaching and learning that should be supportive, comfortable, safe, and secure. The teaching environment should have appropriate facilities to encourage learning and effective teaching. Quality environments allow everyone to get involved. Quality environments can be found at home and in the community. They must be stable with freedom from hunger to enable students to focus on their studies.

Involving people is very important where everyone can work together to educate the



community, including parents, students, teachers, school authorities, and support staff.

mRNA vaccine production might help communities engage in education

The World Health Assembly convened from May 24 to June 1, 2021.⁸ They made decisions on global responses to COVID-19. An open letter says, "as we learned through the Ebola pandemic, poverty and geography should not be the determinants of access to life-saving vaccines." One of the signatories on this letter is Mosoka Fallah, who continues to work to get access to Covid-19 vaccines for the people of Africa.

Mosoka Fallah is the CEO of Refuge Place International. He was educated in the USA and has a PhD in immunology. He returned home to Liberia during the 2014 Ebola outbreak to help his community. He read "Build a Sustainable Vaccines Industry with Synthetic Biology".⁹ After reading it, he wrote a personal communication to one of the authors.

"Thanks for writing this masterpiece solution

to our current and future dilemmas with rising infectious disease and the demand for vaccination of the world. It would build an entirely new system of education to support this decentralisation of vaccine and generate market while affording vaccine to people

at their point of need."

"Build a Sustainable Vaccines Industry with Synthetic Biology" mentions the mRNA vaccine manufacturer Moderna. In October 2021, Moderna announced that it would build a state-of-theart mRNA facility in Africa to manufacture up to 500 million vaccine doses per year.¹⁰ This venture will probably result in local technology transfer, which will help build capacity and

improve access to medicines.¹¹ For example, since May 1, 2019, Nigeria has given 10 years for new pharmaceuticals to transfer to local production – product registration cancels if production does not transfer locally.¹² Other countries could adopt a similar approach to Nigeria.

In June 2021, the World Health Organization (WHO) announced it was supporting a South

[Distributed manufacturing] would build an entirely new system of education to support this decentralisation of vaccine and generate market while affording vaccine to people at their point of need.

African consortium to establish a COVID transfer hub for mRNA vaccine technology. In February 2022, South African biotech company researchers said they are on the verge of producing a COVID-19 mRNA vaccine.

The central aim of this consortium is to build a training facility for mRNA technology development for vaccine mass production and then transfer that entire package of technology to multiple recipients in low- and

middle-income countries. The WHO also announced it is increasing biopharmaceutical manufacturing capacity in at least 11 countries.

Business ecosystems will develop, and they



need skilled and educated workers.¹³ Distributed manufacturing needs university graduates. Graduates need to understand biology, computing, artificial intelligence, machine learning, and robotics. More education in a variety of fields improves communication. For example, biologists who understand computer information technology and *vice versa*.¹⁴ More engineers, mathematicians, and computer scientists are needed.

Distributed manufacturing offers an opportunity for innovation in how education systems work. It is essential to think about how appropriate a way of learning is to a particular situation. Different ways to learn aside from university are important. Paths of learning include:

- Primary, secondary, and third-level education systems
- Apprenticeships
- Online learning/massive open online courses
- Continuous professional development
- On the job training/learning while doing

Regulatory strengthening and education opportunities are increasing

Currently, Africa is actively strengthening its regulatory system. The Africa Centres for Disease Control and Prevention, and the Coalition for Epidemic Preparedness Innovations (CEPI), signed a memorandum of understanding in April 2021 to increase African vaccine R&D and manufacturing.^{15,16} The Africa Export-Import Bank (Afreximbank) and Africa Finance Corporation signed a collaboration agreement at the same time. Countries in Africa are working towards greater regional regulatory harmonisation. The rest of the world, including the EU and USA, is doing the same. Continuous regulatory system development offers more opportunities that need investments in education.

New vaccine production and new manufacturing site operations are risky. National regulatory authorities ensure medical treatments are safe and effective. Yet, in 2017, only 30% of WHO member country national regulatory authorities could regulate their medical products.¹⁷

The WHO Global Benchmarking Tool objectively evaluates and lists the maturity of country national regulatory systems.^{18,19} The tool shows that regulatory authorities of Ghana and Tanzania can regulate manufacturing activity. They are the only two out of 54 African countries with robust enough regulatory systems to do this. This means there are lots of educational opportunities. Building strong regulatory systems in the remaining 52 African countries is a challenge, a challenge we must meet. Establishing an information sharing and cooperation platform is important. Doing this will help transfer knowledge to ensure consistent activity in many regions.

Information sharing and cooperation will build world-class education systems

Developing countries can reach world-class education standards.

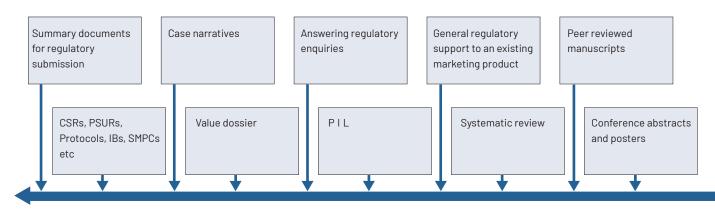
SDG 4 relates to primary, secondary and third-level education.²⁰ Education provides a bridge between these levels. In developed countries, primary and secondary level education are prerequisites for tertiary education. If you are successful in third-level education, you graduate. Is this model necessary for all regions? This is a discussion for each region to have.

The Global Biofoundries Alliance (GBA) London DNA Foundry is at Imperial College London.²¹ Imperial College London was ranked 7 for biology in 2017 by the Center for World University Rankings²² and often ranked in the top ten for other subjects, for example, computer science. For 2021–2022 its overall rank is 30 out of 2000 listed universities; it is in the top 1.5% of this list.²³

A biofoundry has automation and analytics that support biological systems engineering. Synthetic biology solutions can be examined for any given challenge. However, building a biofoundry is challenging and has many technical and operational considerations.²⁴ A biofoundry could be built at a university, while distributed manufacturing hubs could be located closer to points-of-need at teaching hospitals or in mobile laboratory/manufacturing units.⁸

The GBA is a worldwide network of institutions sharing knowledge, infrastructure and expertise. The GBA objectives are to:

- "Develop, promote, and support noncommercial biofoundries established around the world."
- "Intensify collaboration and communication among biofoundries."
- "Collectively develop responses to technological, operational, and other types of common challenges."
- "Enhance visibility, impact and sustainability of non-commercial biofoundries."
- "Explore globally relevant and societally



Regulatory medical writing

Figure 1. A schematic diagram showing the variety of documents worked on by medical writers

Reproduced with permission from McIntosh, A. (2009). Broad-spectrum medical writer: Nature or nurture? The Write Stuff, 18, 1, 7– 8. Abbreviations: CSR, Clinical Study Report; PSUR, Periodic Safety Update Report; IB, Investigator Brochure; SmPC, Summary of Product Characteristics; PIL, patient information leaflet; PR, Public Relations impactful grand challenge collaborative projects."

Many successful research and innovation centres and networks in developed countries were built on an idea. The same sorts of centres could be built in places where there is seemingly nothing.

Recently, International Pharmaceutical Quality

EMWA is a writers'

association, and

writing is important

to education.

We learn and share

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we educate others.

coverage of the CASSS WCBP hybrid meeting from January 25– 27, 2022, reported Organon's Christine Moore talking about global regulatory authority solicitations concerning distributed manufacturing, also known as decentralised manufacturing.²⁵ Her comments indicate that distributed manufacturing is becoming a reality as regulators begin to engage in dialogue with industry and the general public.

If you are interested in getting involved with biofoundries, message the GBA directly. Here is a link to their contact page:²⁶ https://biofoundries.org/contact

RNA technology experts are in university molecular biology departments. Look at the GBA members list and consider expanding the alliance to include your chosen university: https://biofoundries.org/members

EMWA is involved in SDG 4 Quality Education

Medical writers work on a spectrum of documents from regulatory medical writing to medical communications (Figure 1).^{27,28}

There will be opportunities for communities to educate their own medical writers and other skilled workers. Have you ever thought about being a medical writer?

EMWA is a writers' association, and writing is important to education. We learn and share knowledge by doing something and writing about it – we educate others. Organisations like

> EMWA provide an opportunity to engage in continuous professional development.

For example, the EMWA Veterinary Special Interest Group

I am a member of the Veterinary Special Interest Group (Vet SIG), so I will use it as an example of education at EMWA. Vet SIG membership

has a wide range of expertise and experience. Vets at EMWA have experience in various biomedical fields, forming their diverse views and opinions. They have developed expertise gained over years of practice. They collaborate with colleagues inside and outside their areas of interest and knowledge.

The EMWA Vet SIG holds meetings for information exchange and education, as do all EMWA SIGs. From July 2020 to July 2021, discussion topics included:

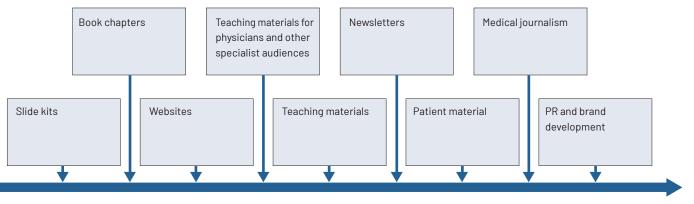
- Self-introduction of participants and exchange of career path histories.
- Introduction to a veterinary regulatory framework for pharmaceuticals, feed, medical devices, cosmetics

- Introduction to VICH (International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products) objectives and overview of guidelines
- Evidence-base for the clinical use of honey in dogs, as an illustration of critique of the evidence
- Writing about pathology
- The 3Rs of replacement, reduction, and refinement of animal experiments in non-clinical research
- Role of veterinarians in the food industry, human health, One Health, and policymaking
- Distributed manufacturing

Topically, a Vet SIG member gave an educational workshop on One Health. The workshop occurred at an EMWA conference in November 2021. This workshop was given virtually because of pandemic restrictions. As an aside, EMWA offers many virtual training opportunities in their virtual learning environment. The goal of the One Health workshop was to provide a foundation level workshop to new and experienced writers to improve their understanding of One Health. Discussion topics included:

- One Health definition and history
- Comparative and translational medicine
- Antimicrobial resistance
- Zoonoses and emerging infectious diseases
- Epidemics and pandemics

In 1964 the father of veterinary epidemiology, Calvin Schwabe, came up with the term One Medicine and considered the relevance of



Medical communications

ecosystem health. However, long before this, in 1858, Rudolf Virchow said, "Between animal and human medicine, there is no dividing line – nor should there be. The object is different, but the experience obtained constitutes the basis of all medicine." These are facts taught during the EMWA One Health workshop.

There are arguments for the SDGs to include One Health.^{29–31} The World Health Organization describes One Health as "an approach to designing and implementing programmes,

policies, legislation and research in which multiple sectors communicate and work together to achieve better public health outcomes."^{32–34} One Health approaches are relevant to zoonoses control. Zoonoses are diseases that can spread between animals

and humans. The World Health Organization refers to Covid-19 as a possible zoonotic disease.³⁵ The World Organisation for Animal Health's Director-General Dr Monique Éloit noted, "The COVID-19 pandemic is a stark reminder that collaboration across sectors is absolutely critical for global health." While France's Minister for Europe and Foreign Affairs, Mr Jean-Yves Le Drian, commented, "The COVID-19 pandemic, whose zoonotic origin is strongly suspected, underlines how closely human, animal and environmental health are linked. It demonstrates the importance of the One Health approach."

Summary

This article has highlighted UN Sustainable Development Goal 4 Quality Education and some things that EMWA members do to support this goal – perhaps without realising. It draws parallels between UN SDG 4 Quality Education, One Health, and a vaccine distributed manufacturing model. Distributed manufacturing is highlighted as a case to empower communities to engage in quality education. Examples illustrate how important improved quality of education is to improved quality of life. By acting on these combined topics, there will be an effect on our health, our future, and our planet. The same examples apply to any under-served community from low-, middle-, and high-income countries.

EMWA members are looking to the EMWA Executive Committee to understand what medical writers can do to support SDG 4.

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The opinions expressed in this article are the author's own and not necessarily shared by her employers or EMWA.

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Author information

Jennifer Bell worked in quality management roles in medical device and pharmaceutical manufacturing, and clinical trial sectors from 2010 to 2018. She holds a PhD in molecular microbiology and an MSc in pharmaceutical manufacturing technology. She is passionate about the potential for biotechnology to improve lives. Today she is a freelance medical writer.

The role of health literacy in the healthcare decision-making process

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Abstract

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Health literacy is defined as "the knowledge, motivation, and competence to access, understand, appraise and apply information to make decisions in terms of healthcare, disease prevention, and health promotion" according to Quaglio et al.⁵ Poor health literacy has direct consequences on the ability to acquire and evaluate information on health issues.⁵ Therefore, strategies should be pursued to improve health literacy, from large-scale policy actions to optimise schooling to interventions targeted at small communities or patient groups. Medical writers and science communicators can play a proactive role in improving health literacy by providing faultless and correct content and drafting clear and understandable documents.

Introduction

0 ne of the Agenda 2030 goals for $S_{\rm eff}$ is $11 - 10^{-10}$ Sustainable Development of the United Nations is the "quality of education to ensure inclusive and equitable quality education and promote lifelong learning opportunities for all".1 A variety of efforts are planned to guarantee literacy and numeracy worldwide, regardless of age or gender, by 2030. For example, the European Union has included health literacy in its Health Development and Improvement Program (EU Regulation 2021/522).²

The principles, strategies, and actions to attain this goal are based on the modern conception of literacy as "a continuum of proficiency levels in a given context", in contrast to the simplistic dichotomy of "literate" versus "illiterate". Its ultimate objective is for individuals to acquire

adequate and recognised competence in both literacy and numeracy, corresponding to that attained through primary education.³

Education is one of the pillars of selfconsciousness and is an essential tool for making informed choices about one's health, wellbeing, work, family, and community. Education depends greatly on literacy and numeracy. Literacy is therefore considered a human right; it is not only a tool of personal awareness and empowerment but also a means for social and human development. Indeed, improving literacy and numeracy can help improve the socioeconomic status of communities and promote

sustainable development at the local, regional, and national levels.³ In 2016, UNESCO stated, "Literacy is a fundamental human right and the foundation for lifelong learning. It is fully essential to social and human development in its ability to transform lives."4

Definition of health literacy

Health literacy is literacy related to health and wellbeing. This concept, which originated in the United States and Canada in the 1970s, has spread around the world and is used to define competencies in a public and personal health context.⁵ More specifically, health literacy is defined as "the knowledge, motivation, and competence to access, understand, appraise and apply

information to make decisions in terms of healthcare, disease prevention, and health promotion".5

Therefore, health literacy provides a level of knowledge, personal skills, and confidence to change lifestyles and living conditions, allowing individuals to improve their and their community's health.5

Nutbeam et al.⁶ describes three dimensions of health literacy:

- Functional health literacy is "the ability to read health information."6 This dimension sometimes includes numeracy (the ability to use mathematics in everyday life).
- Interactive health literacy refers to "more advanced cognitive and literacy skills, which, together with social skills, can be used to participate in everyday situations actively, extract information and derive meaning from different forms of communication, and apply this to changing circumstances".6
- Critical health literacy refers to "more advanced cognitive skills which, together with social skills, can be Health literacy is applied to critically analyse information and use this to exert greater control over life events and situations".6

defined as "the

knowledge,

motivation, and

competence to

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understand,

appraise and

apply

information to

make decisions

in terms of

healthcare,

disease

prevention, and

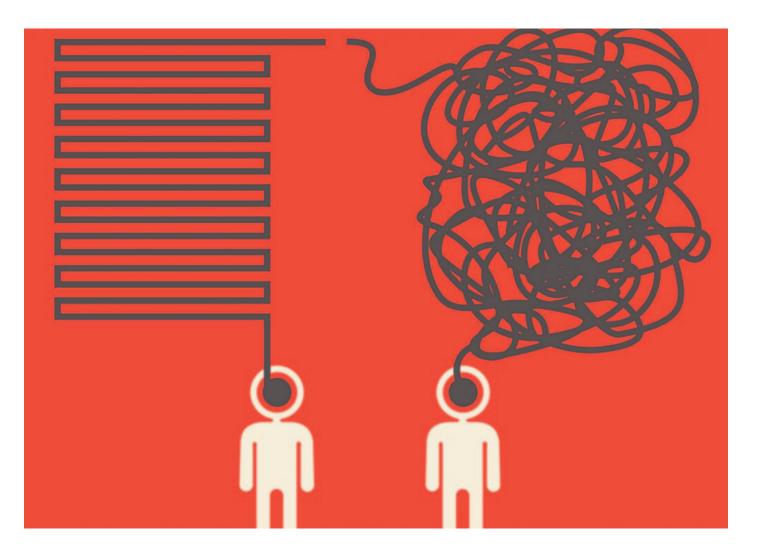
health

promotion".5

To increase health literacy, access to medical information and abilities to evaluate and critically to use it must be improved. Unfortunately, in a vicious circle, health literacy depends upon more general levels of literacy. Therefore, poor literacy can negatively affect health directly not only by limiting personal, social, and cultural development but also by hindering the development of health literacy.

Although health literacy is becoming increasingly important, few studies have systematically determined its level and the factors that determine and affect it.

A 2011 study in Europe by the European Health Literacy Project used the HLS-EU-Q, a multidimensional, comprehensive questionnaire that measures health literacy in the general population.7 The questionnaire uses a broad definition of health promotion as described by the World Health Organization in the Ottawa Charter.⁸ The survey found that more than 10% of all respondents and 1.8-26.9% by country had an inadequate level of health literacy. Furthermore, specific subgroups of the



population had the lowest health literacy, namely, people with poor health status, low socioeconomic status, lower school education, and older age. Financial deprivation was the strongest predictor of low health literacy, followed by social status, education, and age, whereas gender had a minor effect. Although the study included only a few European countries and had a limited sample size, the results should help understand the reasons for deficiencies and disparities in health literacy.⁷ The results also show that health literacy is a public health challenge in some European countries.⁴

Two case studies

Two case studies exemplify how poor health literacy can have direct consequences on the acquisition and evaluation of health-related information and how acquiring good health literacy can help individuals make good choices about their personal health.

Case study 1:

The spread of fake news in Italy about COVID-19 during the pandemic

An Italian study on misinformation about COVID-19 in Italy by Moscadelli et al.⁹ examined the spread of fake news related to eight topics: plot, origin, vitamin C, vitamin D, garlic, 5G, laboratory, and HIV. The study found that fake news accounted for 77.8% of all articles reviewed, indicating that fake news about COVID-19 was more likely to be viewed and shared than real news.⁹

These results illustrate a critical point: health literacy directly influences the sharing of news and information by allowing individuals to filter large amounts of information and discern what is fake. Key factors influencing this include:

- cognitive biases (confirmation bias, "cherrypicking"),
- ii. the willingness to fact check,
- iii. digital literacy, and
- iv. the extent of health literacy.

Thus, improved health literacy may lead to better understanding of scientific information and the ability to distinguish between real and fake news.⁹

Case study 2:

The influence of health literacy on patients' decision-making when enrolling in an oncology clinical trial

The second case study highlights the direct impact of health literacy on health-related decision-making. The study focussed on patients with breast cancer, who are normally involved in many shared decisions during their therapeutic journey. These patients have many choices to make because they often have to decide between numerous treatment options and clinical trials; these decisions may be even more challenging when they have limited health literacy.

In the study, women with breast cancer were invited to enrol in a clinical trial. In accordance with Good Clinical Practice, each woman received an informed consent form to help her weigh the risks and benefits associated with the treatment and decide whether to be enrolled. The study then analysed the relationship between health literacy and enrolment. Patients who were more confident in their decision to enrol perceived a lack of risks associated with the experimental treatment option. Also, those who recalled recurrence as a risk of enrolling in the trial had an average health literacy score higher than the overall cohort.

Of note, participants who understood the risk of recurrence and its weight in the decision-making process also had a better understanding of informed consent.¹⁰ The finding that understanding of informed consent seemed to be related to the level of health literacy suggests that improving health literacy can help improve patients' awareness when making decisions about enrolling in a clinical trial.

What interventions can improve health literacy?

Strategies to improve health literacy range from large-scale policy actions to optimise schooling to interventions targeted at small communities or patient groups. A systematic review analysed the interventions for improving health literacy in Europe between 1995 and 2018. Although firm conclusions about the effectiveness of interventions could not be drawn because of the low quality of the studies included, the type of intervention (group,

individual, community-based) appeared to have little importance. The study suggested that to improve health literacy and thereby improve motivation, empowerment, and self-confidence, inter- ventions should be tailored to the needs of participants, with information and critical skills presented in an appropriate format with correct and engaging language.¹¹ Improving comprehension, acknowledgment, and application of health literacy can support policy action intended to address major public health challenges.⁹

Why should medical writers be interested in health literacy?

Medical writers should not be indifferent to health literacy as they are responsible for writing

clear and understandable documents for the target audience. To create documents for patients, such as an informed consent forms or layperson summaries, that they can use and understand, the writer must consider the reader's health literacy. Good Lay Person Summary Practice¹² suggests keeping in mind the level of health literacy when writing a layperson summary and keeping the language as simple as possible so that it will be accessible to people with primary education or low health literacy

To improve health literacy and thereby improve motivation, empowerment, and selfconfidence, interventions should be tailored to the needs of participants, with information and critical skills presented in an appropriate format with correct and engaging language.

skills. A conversational style can help. The challenge for medical writers, who usually work on scientific or regulatory documents, is to convey complicated messages related to clinical trial results to people with varying levels of health literacy.¹²

On the other hand, medical writers have an opportunity to improve health literacy by communicating science responsibly. Many peer-reviewed journals now require a plain language summary of scientific studies and clinical trials, which may favour direct access to scientific information. Also, patients' associations, cultural associations, and even hospitals and company websites need to produce verified content. A challenge for medical writers in this context is writing text that is rigorous but appealing. When writing for people with varying health literacy levels, we suggest that medical writers remember Italo Calvino, an Italian literate

who, throughout his career, focused on maintaining the reader's attention by using clear, incisive, and memorable visual images along with precise language.¹³

Conclusion

Health literacy is a valuable tool that empowers individuals and communities to improve their health status and achieve sustainable development. Training and educating healthcare professionals, teachers, social workers, and community volunteers about the importance of health literacy and effective health communication is vital. Adequate expertise can be obtained by reviewing materials and processes used by stakeholders and by receiving training in verbal and written communication. Medical writers can play a proactive role by conveying truthful and flawless health information that can be understood by the targeted reader. This means adapting the language and the scientific content to the audience.

Disclosures and conflicts of interest

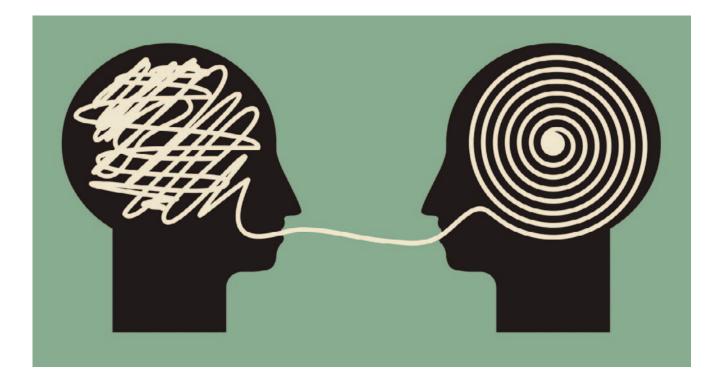
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Disclaimers

The opinions expressed in this article are the authors' own and not necessarily shared by their employers, clients, or EMWA.

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Fake news and vaccination: How the Science Anti-Fake News team in Argentina is fighting the infodemic

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Abstract

At the outset of the pandemic, it became clear that misinformation ("fake news") on COVID-19 was spreading rapidly. In this article, we discuss our efforts to combat misinformation by joining with researchers from various disciplines in Argentina to form the Science Anti-Fake News team. We highlight three examples of fact checks on vaccine misinformation that we conducted from October 2020 to July 2021 and provide evidence of their reach in our social media audiences. The article further discusses the manner in which misinformation spreads and the importance of "democratising" the availability of scientific knowledge in the context of the uncertainty provoked by the COVID-19 pandemic.

Introduction

n Latin America, the concept of "fake news" has been popularised through a literal translation of the English "false information". Fake news is content that does not have an objective basis but is presented as news. Allcott and Gentzkow define it as "news articles that are intentionally and verifiably false, and could mislead readers".¹ Other experts classify it as information specially designed to misinform, deepen prejudices, and cause political damage.² Although there is no unique definition, we define it here as misleading information disseminated through information technologies – such as press, television, radio, websites, and social media – with the aim of misinforming people and even inducing certain opinions and behaviours.

Of note, although it may have been created with the intention of misinforming, some people who are victims of such misinformation unfortunately contribute to its spread.

"Fake news" has increased significantly since the outbreak of the COVID-19 pandemic. Some studies and surveys show an exponential rise in the dissemination of fake news on epidemiological and immunological issues.³ As communication analysts notice, this phenomenon is probably linked to the uncertain context in which we are living. The feeling of vulnerability leads to the search for certainties and truths, which can reinforce previous convictions or what is called "confirmation bias". Fake news contributes to crystallising

individual preferences and prejudices and, especially, to exacerbating negative emotions.⁴ In March 2020, when the COVID-19 pandemic had recently been declared, the World Health Organization (WHO) used the term "infodemic" – coined in 2003 by journalist and political scientist David Rothkopf – to refer to a swift and far-reaching spread of false or misleading information in digital and physical environments. According to the WHO, the infodemic "causes confusion and risk-taking behaviours that can harm health. It also leads to mistrust in health authorities and undermines the public health response".⁵ Thus, scientists, journalists, and governments not only must help to contain the COVID-19 pandemic but also fight against the infodemic and its effects on people's behaviours.

As the term suggests, an infodemic is a worldwide phenomenon that affects diverse countries and regions, including South America.^{6,7} In Argentina, fake news has been disseminated since the COVID-19 pandemic arrived. This fake news includes a panoply of

We define [fake news] as misleading information disseminated through information technologies such as press, television, radio, websites, and social media with the aim of misinforming people and even inducing certain opinions and behaviours.

topics, from misleading information about alternative treatments to cure the disease to conspiracy theories about the supposed dangers of vaccines. It is in this context that the Science Anti-Fake News team was born. Our team developed through the initiative of young researchers from various disciplines who wished to help with the struggle against fake news. This article recounts the experience of the Science Anti-Fake News team.

For this article, we concentrate on some fake news that spread at the beginning of the vaccination campaign in Argentina, more specifically, from October 2020 through July 2021. First, we analyse how misinformation is fabricated and spread, based on a set of fake news items that circulated in

relation to the vaccines available in Argentina during this period. Second, we describe how the team refuted this fake news and how our activities impact on public opinion. Finally, the article highlights the importance of democratising scientific knowledge in the context of the uncertainty unleashed by the COVID-19 pandemic.

What is "Science Anti-Fake News"?

Motivated by a sense of social responsibility and worried about the COVID-19 outbreak and



infodemic, the Science Anti-Fake News team became the first project focused on COVID-19 misinformation that was endorsed by the National Scientific and Technical Research Council of Argentina (known as CONICET, for its name in Spanish, Consejo Nacional de Investigaciones Científicas y Técnicas).⁸ This group aimed to use scientific evidence to counterattack COVID-19 misinformation. The team is composed of 16 young scientific researchers and PhD students originally motivated by the emergence of viral fake news that threatened public and individual health. Dismantling fake news is not an easy task. When questions or fake news related to COVID-19 arrive at our social media accounts, the team checks the veracity of

the concerns by looking for evidence and consensus among scientific societies. Once verified by many members of our team, as if it were a peer-reviewing process, the information must then be written in an accessible language that can be understood by a non-specialist audience. Then, it is published on the ConfiAR website (a platform designed by the Argentine government to display verified information related to COVID-19)9 and in our social media accounts on Instagram, Facebook, Twitter, and YouTube (see Box 1). Believing that good information should be available for everyone throughout our country, the group expanded to include an additional 12 researchers from other disciplines, including social communication,

Box 1. Social media accounts of Science Anti-Fake News

Instagram: https://www.instagram.com/anti__fakenews/
 Facebook: https://www.facebook.com/ciencia.anti.fake.news
 Twitter: https://twitter.com/anti__fakenews?lang=es
 YouTube: https://www.youtube.com/c/anti_fakenews

Note: Science Anti-Fake News has more than 30,000 followers on Instagram, 24,000 followers on Twitter, and 6000 followers on Facebook.

political research, and anthropology, and from locations throughout Argentina. More than 300 checks have been carried out since the beginning of the pandemic.

Fake news and vaccination campaign

Fake news about science often consists of a mix of true and false statements. These items usually include technical language, refer to facts that could be true if considered in isolation, and sometimes include the testimony of public figures. In our experience, it is generally possible to identify those cases in which misinformation is the consequence of an error of interpretation. When this type of erroneous information is issued by the media, it is generally related to poor journalistic practices. The new technologies and the speed of the dissemination of information disrupt journalism work routines, modifying information priorities so that speed is prioritised over quality. We attribute most of the unintentional false information to this factor.

Science Anti-Fake News has endeavoured to counterattack misleading information linked to the vaccination campaign deployed in Argentina since October 2020. For this article, we are highlighting three examples of misinformation that occurred at different moments across the pandemic. These examples were chosen based on the level of social media engagement we saw for our fact checks and the number of requests we received from TV and radio stations for our team to provide clear, accurate (but not technical) scientific information about the topics.

How we dismantled three fake news items on vaccination

When encountering fake news or community concerns on COVID-19, we search for reliable scientific information on that topic. We mainly consult scientific peer-reviewed articles published online, although we may also search manuscripts posted on preprint servers. We use preprint manuscripts cautiously by specifying in our reports that the results have not been subject to peer review. Many times, misinterpretation of preprints have been used by digital media to make a statement that is not proven yet. So, when this is the case, we thoroughly analyse the cited preprint. Platforms such as PubMed, BiorXiv, MedrXiv, and SSRN (formerly known as the Social Science Research Network) are constantly being monitored to stay current with the latest information. We also look for guidelines from the WHO, the US Centers for Disease Control and Prevention (CDC), the European Medicines Agency, and COVID-19 guidelines from our local health authorities, especially on topics such as vaccination and treatments. Basically, we look for scientific consensus.

From our more than 300 fact checks, we selected three examples of fake news items to describe how we work and the impact of our efforts in our social media networks. In October 2020, when the first results of COVID-19 vaccine clinical trials were reported, misinformation began to spread that claimed that vaccines were going to change our DNA. This misinformation



Falso: un 30% de las personas vacunadas con Sputnik V en Argentina desarrolla efectos advertos graves.

False: 30% of people vaccinated with Sputnik V in Argentina developed serious side effects.

was particularly worrying as we were seeing it promoted by a group of health care workers and false experts; one of the interviews done had more than 24,000 plays on the RadioCut app. Not only did they spread misinformation on social media but also on TV and radio, taking advantage of the presenters' lack of knowledge on those topics. We reviewed scientific evidence, especially on WHO and CDC web pages,^{10,11} related to whether there were any possible genetic alterations mediated by the newly developed vaccines.

Later, in December 2020, there was a misinterpretation of statements from Russian health authorities. One of them had suggested that people should not abuse alcohol after vaccination with SputnikV. This was misinterpreted by digital media, which claimed that people should abstain from alcohol for 42 days after the first SputnikV dose. This is an example of fake news that was promoted by digital media with alarmist headlines. When we saw such headlines, we looked for evidence related to vaccines and alcohol consumption and found that moderate alcohol consumption would not affect vaccine efficacy. Moreover, it should be noted that for any vaccines – not just SputnikV – alcohol abuse can suppress the immune response.

Finally, in January 2021, when the vaccination campaign became relevant, misinformation began to spread suggesting that there was a substantial percentage (more than 20%) of severe

Table 1. Social media reach for three fact checks by Science Anti-Fake News

Fake News Item	Date of Publication	Number of Profiles Reached	Likes and Reactions (engagements)
COVID-19 vaccines were developed too quickly to be safe and skipped pre-clinical stages.	October 2020	More than 30,000	More than 2000
You cannot drink alcohol for 42 days after Sputnik-V inoculation.	December 2020	More than 60,000	More than 5000
A huge percentage of severe side effects after COVID-19 vaccination have occurred.	January 2021	More than 50,000	More than 3000

Note: The Science Anti-Fake News team has more than 30,000 followers on Instagram, 24,000 followers on Twitter, and 6000 followers on Facebook.



Falso: las vacunas contra COVID-19 tienen nanochips.

False: The vaccines against COVID-19 have nanochips.

side effects triggered by COVID-19 vaccines. It circulated in the form of viral WhatsApp audio messages and as disturbing headlines on some media. To counteract this fake news, we analysed the results of the clinical trials of COVID-19 vaccines and the epidemiological reports of the Argentine Health Ministry, which show the events presumably attributable to vaccination. These data exposed that severe side events were no more than 1% in trials as well as in the "real world" in people who had been vaccinated in Argentina up to that point.

Once we have gathered accurate information about a topic, our team writes an essay with sources to discredit the fake news. Team members revise the message as needed so that it is in a non-technical language so our target audience can understand the information we are seeking to explain. The fact-checked statement is then shared on the ConfiAR platform and on our social media accounts. Table 1 shows the social media influence of the three fact checks mentioned above.

The case of SputnikV and alcohol deserves a deeper analysis. The misinformation about the need to abstain from alcohol for 42 days brought about many calls and requests from TV and radio shows. So, for example, when we clarified the information regarding alcohol drinking and SputnikV live on one of the most popular Argentine TV channels, the video with the accurate information had 18,427 views on YouTube.¹² We thought about some possible explanations for this phenomenon. Christmas

and New Year's Eve were approaching, there was so much confusion and concerns regarding SputnikV, partly because of the absence of public Phase III results and partly due to a massive campaign against this vaccine elicited by many journals and digital media.¹³⁻¹⁶ We hypothesised that those were the reasons why this fact check went so viral.

Discussion

The researcher Carina Cortassa¹⁷ establishes the Deficit and the Ethnographic Contextual models to best describe the concept of the public communication of science. The Deficit model assumes the lay public to be scientifically illiterate. It emerges from the traditional model of teacher-student. The Ethnographic Contextual model is based on an anthropological conception that contemplates the dialogue and the interests of the audiences and tries to take into account the previous knowledge of the public to enrich the understanding of science. Science Anti-Fake News adheres to the Ethnographic model because it was born from popular experience in the context of a pandemic and of the uncertainty experienced in 2020.

Our project continues. Day after day, we decide which statements to fact check based on social media interaction with our audience and by noticing the topics that are being covered in the news media.

Throughout these 2 years of intensive experience in dismantling false information, it has become clear that fake news also poses a political problem. Science took centre stage around the world due to the coronavirus pandemic and positioned itself as the main guide for public policy in most countries. Stopping the spread of false news contributes to the success of actions aimed at mitigating the damage of a crisis – in this case, the COVID-19 pandemic. So, dismantling fake news implies cooperating with the success of health policies.

Before the pandemic, the impact of the massive spread of fake news by social media on vaccination coverage was already known. The Vaccine Confidence Project showed that Japan



Falso: existen diversas curas para el coronavirus que están ocultando.

False: There are cures for the coronavirus that are being hidden.



Falso: algunas vacunas contra COVID-19 no se probaron en animales y se hicieron ensayos directamente en humanos.

False: Some vaccines against COVID-19 were not tested on animals and were tested directly on humans.

ranked among the countries with the lowest vaccine confidence in the world in 2018.18 The authors suggested that the low confidence there might be linked to safety scares in 2013 regarding the human papillomavirus (HPV) vaccine. This event ended in the suspension of proactive recommendation of the HPV vaccine by the Japanese Ministry of Health. As a result, HPV vaccination coverage decreased approximately 70% in 2 years. Moreover, this news about the Japanese Ministry of Health's actions spread globally by online media and social media networks and was applauded by anti-vaccine groups. Related to this, previous studies showed that vaccine-related social groups can influence the opinion of the population about vaccination, decreasing immunisation rates and in consequence, bringing on disease outbreaks.¹⁹ In the past few years, Pakistan and Nigeria have experienced an increase in poliovirus cases as new waves of misinformation surrounding the polio vaccine have been circulating in both countries.18

Factors more consistently associated with improved vaccine uptake included high confidence in vaccines, trust in healthcare workers as a source for medical and health advice (rather than family, friends, or other nonmedical sources), and higher levels of science education.¹⁸ Another study²⁰ reports that if we ask audiences to focus their attention on the accuracy of the information they receive, instead of the emotions it provokes, the level of spread of misinformation shared online can be reduced. This supports the importance of our work in the fight against fake news.

We would like to emphasise that the fake news discussed in this article were selected based on our social media analysis. We do not know how the fact checks may have affected TV and radio audiences that watched and/or listened to the shows. Moreover, the overall impact on engagement on our social media does not take into consideration that perhaps our Facebook, Twitter, and Instagram accounts share followers, overestimating the social media reach. On the other hand, the Science Anti-Fake News team has demonstrated that it is possible to combat fake news through interdisciplinary hard work and commitment to the sharing of high-quality, wellresearched information.

Given that misinformation affects vaccination rates, we hold that it is essential for scientists to commit to the popularisation of scientific information, especially in contexts of uncertainty and crisis. Science must not be separate from society and can and must offer responses according to the urgency of the context. Our Science Anti-Fake News team was born to persist, and we will keep fighting fake news on further health topics beyond COVID-19.

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The authors declare no conflicts of interest.

Data availability statement

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Race and ethnicity in biomedical literature: A narrative review

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Abstract

Race and ethnicity are not clearly defined in biomedical literature and misaligned with genomics and epigenomic findings; the guidelines for consistent reporting in publications and regulations from health authorities are lacking.

Minority populations are underrepresented in clinical studies; this limits the identification of risk profiles for diseases (which is the main objective of precision medicine) and fuels false beliefs and implicit bias of clinical decisions. This setting hinders interpreting, generalisation of findings, and prevention planning, and increases socioeconomic disparities in healthcare access.

This review outlines recent studies on race and ethnicity and criteria for the proper use of terminology according to evidence, clarity, transparency, and ethics in biomedical documents.

Introduction

or hundreds of years, there has been a vigorous debate about dealing with race and ethnicity categories in studies regarding human health. In particular, how defining and describing race and ethnicity concepts in biomedical literature.¹ In the last century, humans had been classified in the distinct anthropological groups of Caucasoid, Congoloid, Mongoloid, Capoid, and Australoid;² however, these terms have been discarded as new genetic information came to light. In 1994, the Italian geneticist Luigi Luca Cavalli Sforza published the book The History and Geography of Human Genes,³ which summarised and evaluated genetic information and the data of genetic diversity of that time. Stemming from the idea that DNA helps track human origins and history, this book documented the genetic similarities among humans and misleading classifying humans according to any "race" concept to explain phenotypic differences. The human genetic studies and genomics research that followed were more advanced and confirmed overwhelming DNA similarities and the negligible DNA differences among humans.^{4,5} However, genetic variations cannot account entirely for the phenotypic differences among humans. To date,

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as the picture grows in complexity, the debate about race and ethnicity as diversity measures persists in biomedical literature.

The disparity in healthcare access due to race and ethnicity are crucial confounding factors leading to severe consequences. Underrepresented subpopulations in clinical studies can mask the epidemiology of several diseases.^{6–9} Missing data have led to bias; therefore, it is difficult identifying possible connections between socio-demographic and genetic determinants and clinical variables.⁴

This literature review provides

an overview of the concepts and terminology of "race" and "ethnicity" and how they have been applied in the biomedical literature and their implications therein.

Definitions of race and ethnicity

In general dictionaries, "race" is defined as a group of people sharing a common origin, and physical features.¹⁰ "Ancestry" or "ethnicity" refers to categories as having a common descendent or national and cultural traditions.¹⁰ The designations of race and ethnicity or ancestry in the biomedical literature are highly heterogeneous and inconsistent across countries, clinical studies, and clinical genetics practice.^{2,4} Race and ethnicity data in clinical databases and algorithms are often absent, inconsistent, incomplete, or contradictory, which leads to unreliable interpretation of results.^{11,12} For example, discrepant comparison of lung function

between Blacks and Whites still points to the questionable "race correction" of spirometric measurement in the US since the 19th century and has not yet been updated using the scientific approach and modern methods.¹ Race and ethnicity assessed by different criteria fuel the debate around determinants of diseases. These criteria are often US- or EU-centric and should be evaluated with caution. In the present article, the terminology for race and geographic origins are those used by the original authors of the

> articles. Ethnicity and ancestry designations are used interchangeably in the literature, although ancestry usually includes cultural and behavioural features relevant for healthcare.

> American Medical Association (AMA) Style suggestions for harmonised designation of race and ethnicity are reported in the paragraph "Because words matter" of this article.

Genetic variants

Natural selection has contributed to genetic variation of individuals or populations.⁵ The sequence of DNA bases of one gene or a

group of genes can permanently change; DNA modification not linked to disease is named a "genetic variant". Research has highlighted the existence of more genetic variants than sociocultural categories such as race. Genome-wide association studies were performed to stratify populations according to clusters of gene expression and not geographic origin.² Indeed, the percentage of genetic variation between two subpopulations is low by increasing the number of *loci* analysed, and most genetic variations are tracked among subjects belonging to a single population.⁵

Although genetic variants are not typically linked to diseases, some genetic variants may be associated with the risk of some diseases. For example, the incidence of end stage kidney disease (ESKD) is much higher in African Americans than Whites.¹³ ESKD has been associated with polymorphisms at the *APOL1*



locus in non-diabetic people with West African ancestry. This genetic variant was selected because it conferred protection against sleeping sickness common in West Africa due to *Trypanosoma brucei.*⁶ However, polymorphisms do not account for the increased risk of kidney disease and no mechanistic relation has been demonstrated until now.^{6,13}

The phenotypes observed among populations have other sources of diversity; the risk of diseases may be linked to external factors that impact the epigenome; various chromatin and RNA modifications have consequences on health from gestation to death.^{6,14} For example, the low mortality rate of SARS-CoV-2 virus infection in Africa compared to Europe, the US, and Asia can be explained by the differences in environment instead of race. Moreover, clinical laboratories may apply different classifications of genetic data and other parameters suitable for clinical evaluation.⁴

Studies involving South Asian populations living in the US or EU countries (with a high prevalence of type 2 diabetes) lack wellcharacterised genetic and epigenetic profiles.¹⁵ Conversely, the inclusion of subjects with African ancestry identified novel *loci* in obesity, metabolic syndrome, or immune diseases such as multiple sclerosis.⁷

The genetic and epigenetic profiles can help identify subpopulations at risk of syndromes and diseases, which may be fundamental for prevention strategies.

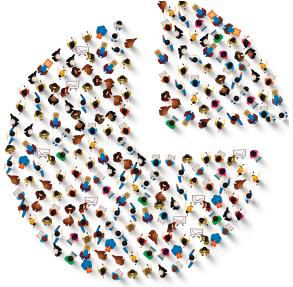
Therefore, limiting inclusion of subjects of various subpopulations prevents targeting the objective of precision medicine. Conversely, including diverse subpopulations in genome-wide association studies may strengthen the research, cast light on genotype-phenotype interactions in diseases, and identify new drug targets.⁶

Race and ethnicity in clinical studies

The persistence of false beliefs in race and ethnicity categories in randomised clinical trials and observational studies may impact clinical decisions.¹⁶ Standardised data in registries favour measuring disparities in healthcare access among different subpopulations. Also, it provides comprehensive epidemiology and prevention strategies in many medical fields.¹⁷ For example, African Americans and Whites with newly diagnosed nonmetastatic prostate cancer and treated with standard healthcare access, after adjusting for demographics, cancer, treatment-related baseline differences, and inverse probability weighting, displayed comparable stage-to-stage prostate-cancer mortality.¹⁸

The Platelet Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) trial compared aspirin plus clopidogrel versus aspirin alone at 90-day follow-up in 4044 US subjects.¹⁹ The subgroups of Black participants (918/4044, 22.7%) had a higher cumulative risk of stroke than White patients. The adjustment for covariates (demographic data, comorbidities, and adherence to aspirin plus clopidogrel treatment) confirmed the higher risk of early recurrence of stroke after minor ischemic stroke or TIA of Black participants.¹⁹ The Reasons for Geographic and Racial Differences in Stroke (REGARDS) study involved 9416 Blacks and 13,091 Whites without a history of CV diseases.²⁰ At 6.1-year follow-up, compared to Whites, Blacks showed a significantly higher risk of sudden cardiac death (SCD), confirmed after adjustments for sociodemographic, comorbidities, health behaviour changes, intervening CV events, and risks of non-SCD mortality causes. However, these variables did not account for the higher incidence of SCD in Black patients.²⁰

The perception of pain is complex and may be influenced by cultural differences. Still, implicit bias about race and ethnicity in pain can increase the burden of pain, blur the assessment and mislead recommendations.¹⁶ In 2017, the National Institute of Health (NIH) supported the OPPERA cohort study on orofacial pain enrolling White, Black/African American, Hispanic, Asian, Native Hawaiian/Pacific Islander, American Indian/Alaskan Native, and other populations subjects. The study did not find any racial differences among the populations in tissue characteristics and nociceptive sensitivity by 34 pressure, mechanical, and thermal pressures.²¹ The NIH study of Reynolds Losin et al. (2020) analysed the pain perception pathways in three ethnic groups by functional



Magnetic Resonance Imaging. This study highlighted similar nociceptive pain processing among the groups, which overturns the influence of races, ethnicity or culture on the complexity of pain perception.²²

Underreporting race and ethnicity data or inconsistent reporting without standardised methods in orthopaedics,²³ surgery,²⁴ real-world data of medical devices,²⁵ anaesthesia,²⁶ or other specialties hinders the possibility to identify differences in treatments, post-intervention outcomes,²³ and real-world evidence.²⁵ Most US and UK healthcare systems usually collect data on race and ethnicity,¹⁷ but most EU countries do not.⁸ Study designs and statistical protocols are essential to highlight, deepen, or confirm clinical similarities or differences among subpopulations. It also eases to evaluate the contribution of socio-demographic variables and comorbidities.

Implications

Limited studies on the health of ethnic minorities can have a negative impact on healthcare expenditure for diseases like diabetes, mental health, or infectious diseases.²⁷ Race and ethnicity (alongside other determinants) seem to account for differences in insulin regulation and glycaemic response to carbohydrates; however, given the scarcity of studies, recommendations on insulin dosing and formulations in more diverse populations is still lacking.²⁸

The *New England Journal of Medicine* editors' team has recently marked the value of inclusion

of various subpopulations in research studies for the generalisability of the findings and the extension of new treatments.9 Subgroup analyses of clinical studies can highlight risk factors or diseases determinants of the diverse subpopulations; they also can increase the equity of the access and provision of healthcare. Moreover, transparency favours the decision of the reviewers and publishers on publishing manuscripts. From January 2022, authors who intend to publish in NEJM will be asked to provide supplementary information tables about the representativeness of the patient populations enrolled in the studies.9

Because words matter

The guidelines for specifying the reasons to use race and ethnicity terms in biomedical publications (e.g., generalisability, disparities in healthcare and expenditure) were published in 2003 when the Human Genome Project was completed.⁴ However, the original five-group anthropologic classification is still used, yet reduced to the three major NIH population ancestries (European/ Caucasians, African, and Asian).² Numerous medical documents may include race and ethnicity terms:

- Regulatory documents such as protocols, case report forms, Summary of Product Characteristics, and leaflets
- In medical communication such as manuscripts for publication in peer-reviewed journals
- Project descriptions for grants or funding proposals

Table 1 summarises the current evaluations and suggestions of the editorial associations for reporting race and ethnicity in biomedical literature.

Recently, the JAMA editorial team has published practical guidelines to improve the quality of reporting race and ethnicity data in regulatory documents or clinical studies.¹⁰ Race and ethnicity designations must always be consistent and justified. As social constructs, the utility of race and ethnicity in biomedical research and practice is limited; however, its pretextual use can help highlight disparities and pitfalls. In this view, the solutions proposed by the AMA Manual of Style committee are continuously under revision according to cultural and social evolution and open to feedback of authors, editors, and readers to enhance the correctness of reporting terms.¹⁰

- Methods: should explain how race and ethnicity or ancestry have been identified (e.g., self-reported or by the investigator or database or other modalities). Data collection on race and ethnicity must be motivated and contextualised according to socio-economic settings relevant as health determinants.
- Results: the ethnic categories can be listed in alphabetic order instead of numerical majority and specified as the "others" group.
- Discussion: structural racism or disparities in healthcare can be highlighted and contextualised. Discussion or Conclusions sections should suggest appropriate studies to identify variables and determinants of health. The terms for defining race and ethnicity have to be specific. For example, "African American"

or "Black" can be substituted by "African descendant" as this term underlines not only the origin but also culture and traditions. However, the "African descendant" designation is questionable if culture and traditions are not practised.

The AMA committee suggests capitalising the name of races or ethnicities, e.g., White, Hispanic, Latino, or Asian. They suggest avoiding categories like "Asians" or "Blacks"; instead, adjectival nouns would be more appropriate (e.g., "Asian women" and "African American patients"). Adding the geographic origin to race and ethnicity definition can be relevant. It can, however, be challenging. The term "Caucasian" refers to the region of Eurasia. Therefore, "Caucasian" should be used only for people from that region and not as a synonym for White people.¹⁰

populations entail a standard designation of race and ethnicity, different protocol measures and suitable calculations methods for sample sizes are required for study designs and proper reporting.¹⁰

Based on the existing International Committee of Medical Journal Editors (ICMJE), the editorial guidelines of the publishers should focus on reporting race and ethnicity data with clear clinical motivations related to the research questions for the biomedical studies. The editorial teams should harmonise recommendations and suggestions in collecting and reporting data. Statements and designations of race and ethnicity should be applied not only by authors but also by publishers and reviewers.

Legislative framework

The primary part of the EU legislation is the treaties and the secondary are laws (Directives). Discrimination based on race and ethnicity is

Since the inclusion criteria of various

Table 1. Current evaluations and suggestions of editorial associations for reporting race and ethnicity in biomedical literature

2019 ICMJE ²⁹	Because the relevance of such variables as age, sex, or ethnicity is not always known at the time of study design, researchers should aim for inclusion of representative populations into all study types and at a minimum provide descriptive data for these and other relevant demographic variables and recommend "Authors should define how they determined race and ethnicity and justify their relevance. Authors should use neutral, precise, and respectful language to describe study participants and avoid the use of terminology that might stigmatise participants". ²⁹
EQUATOR (Enhancing the Quality and Transparency Of health research) network ³⁰	The use of the "race and ethnicity" terms is only partially addressed.
COSORT 2010 ³¹	The "ethnicity" variable has been quoted in the Item 21 paragraph about the generalisability of trials findings in some examples (i.e., in Table 4), but no designation and suggestion about reporting race and ethnicity have been provided.
STROBE ³²	No mention
European Association of Science Editors ³³	"Race" was mentioned only as a variable to be disaggregated.
COPE (Committee on Publication Ethics) ³⁴	Does not provide any specific core practice for reporting in research studies.
CDC (Centers for Disease Control and Prevention) ³⁵	 Acknowledged the problem regarding race and ethnicity and highlighted general principles with different expressions in health communication, such as: Instead of "high risk group" prefer "disproportionately affected groups" Instead of "racial or ethnic groups" prefer "people from racial or ethnic groups" Instead of "minority" prefer "(people from) racial and ethnic minority groups"

banned and is explicitly stated in the Directive 2000/43/EC and treaties. However, the EU legislation lacks non-discrimination laws on access to healthcare. The responsibility of nondiscrimination is held by the national regulations of each EU country that have variably weak legal platforms regarding race and ethnicity (article 168 of the Treaty on the Functioning of the EU Union).³⁶ As reported in cases studies (e.g., the antihypertensive BiDil³⁷), the racialisation of drug regulation has been rising in the US and EU.37 The concept of "racialisation of pharmaceutical regulation" refers to how race and ethnicity have become important to drug testing and evaluation.³⁷ A recent comparison of 397 new drugs approved in the US and Europe

has highlighted the uninterrupted lack of concordance between the pharmaceutical legislations by specific tools like the International Conferences on Harmonisation.³⁷ This comparison has revealed inconsistent designations of race and ethnicity in the labels or "Summary of Product Characteristics" of pharmaceutical products. FDA emphasises the inclusion of race and ethnicity subgroups in the labels more than EMA, but this inclusion and the reported differences are less frequent in clinical trials.³⁷

Pharmaceutical regulations on drug approvals lack data on the different effects of pharmaceutical products in various populations because most of the registrational clinical trials performed during drug development include mostly White patients. For example, given the difference in genetic variants, the algorithm for the dose of warfarin may differ in Whites and African descendants.⁶ To note, health authorities do not require pharmaceutical industries to enrol subjects belonging to minorities in clinical studies, nor in numbers that enable proper analyses and conclusions on drug effectiveness.38 This shortcoming lowers the robustness of meta-analyses,³⁹ limits having a complete pharmacovigilance system of a drug's adverse events, and consequently, risks of knowledge gaps in drugs profiles.

An amendment to the EU legislative framework should be considered essential. In particular, pharmaceutical regulations should require an equitable enrolment of patients in clinical studies.



Conclusions

"Race" and "ethnicity" or "ancestry" are complex terms that need increased knowledge and indepth analysis in biomedical literature. The support of the legislation at EU and local levels could ease the advancement of the scientific evidence with positive implications in healthcare access.

Evidence and evaluations of all the stakeholders can lead to the consistent and specific use of race and ethnicity concepts in regulatory documents and publications and pinpoint their relevance in clinical practice.

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The opinions expressed in this article are the author's own and not necessarily shared by her employer or EMWA.

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The author declares no conflict of interest.

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Update of the Consolidated Health Economic Evaluation Reporting Standards: CHEERS 2022

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Abstract

If economic evaluations are to be used by researchers and healthcare decision makers, they need to be adequately reported. This article discusses the update of the Consolidated Health Economic Evaluation Reporting Standards (CHEERS 2022), the main motivations for the update, the major changes to the CHEERS checklist, and the resources to support its dissemination and use. The update of CHEERS is an important step in increasing transparency in the reporting of economic evaluations. Those in the medical writing community are encouraged to use the CHEERS 2022 guidelines when assisting authors of economic evaluations in communicating their research.

Introduction

ne key element of sustainable healthcare systems is financial sustainability. The budgets for healthcare are under increasing pressure because of the high-level of innovation in medicine. While these innovations have the potential to deliver major benefits to patients, they often come with major costs. Therefore, most high-income countries employ health technology assessment (HTA), of which a major component is the conduct of economic evaluations. In these studies, the benefits of new health technologies (drugs, medical devices, and health interventions more generally) are compared with their costs, to assess whether they provide good value for money.

If economic evaluations are to be used by researchers and healthcare decision makers, they need to be adequately reported. In the recent issue of Medical Writing focusing on medical decision making and health technology assessment, we discussed the development of the Consolidated Health Economic Reporting Standards (CHEERS) and outlined the CHEERS 2013 checklist.¹ At the time, we indicated that the CHEERS checklist was being updated due to developments in economic evaluation methods and changes in the environment in which economic evaluations are conducted and reported. The new CHEERS 2022 statement and checklist were released on January 11, 2022, and co-published in 16 journals.* The new checklist (see Table 1) should now be used instead of the original CHEERS checklist.

It is important that those assisting in the reporting of economic evaluations are aware of the new reporting standards. The purpose of this paper is to outline the new CHEERS 2022

* Journals publishing the CHEERS 2022 Statement are: Applied Health Economics and Health Policy, Brit J Obstet Gynae, BMC Health Services Research, BMC Medicine, BMC Public Health, BMJ, Clinical Therapeutics, Health Policy Open, International Journal of Technology Assessment in Health Care, Journal of Managed Care & Specialty Pharmacy, Journal of Medical Economics, MDM Policy & Practice, Pharmacoeconomics, The European Journal of Health Economics, Value in Health, and Value in Health Regional Issues (in Spanish) checklist, to discuss the rationale behind the main changes, and to make readers aware of some of the resources being made available to support the dissemination and use of CHEERS 2022.

New features of CHEERS 2022

Reflecting developments in methods

There have been several developments in health economic evaluation methods since 2013, and they do not all require changes in reporting guidelines. However, the original CHEERS was criticised for being too focused on costeffectiveness analysis and the measurement and valuation of health benefits in quality-adjusted life-years. Developments in the methods and use of health preference measurement and valuation have mainly occurred in the context of freestanding studies rather than as part of economic



evaluations. Therefore, in the discussion of Item 13 ("Valuation of outcomes") in the CHEERS explanation and elaboration document,² it is now made clear that a range of approaches could be used to value health benefits, including willingness-to-pay³ and discrete choice experiments.⁴

In addition, although the main interest in conducting economic evaluations is increased efficiency (i.e., maximising the total benefits from the use of healthcare resources), there is also interest in how those benefits are distributed.⁵ For example, subgroups of the general population may be differentially impacted by health interventions due to socioeconomic status, ethnicity, geographical location, and disease categories such as disability or severity of illness. Decision makers may be interested in the equity impacts of interventions as well as their efficiency. Therefore, a new reporting item (Item 19) has been added on "Characterising distributional effects" in reporting economic evaluations.

Reflecting the need for more transparency

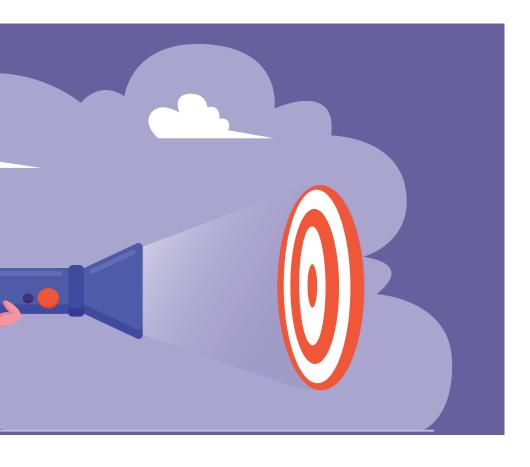
The main objective in improving the reporting of research is to increase transparency and the

ability to replicate an analysis. However, two particular issues have arisen in the context of health economic evaluation.

First, in contrast to clinical trials, where the study protocol and statistical analysis plan is determined in advance and often made public, health economic analysis plans are not very common in economic evaluations.⁶ This has led to concerns that bias could be introduced by the selective reporting of results or analyses. Therefore, Item 4 ("Health economic analysis plan") has been added, asking study authors to report whether a

health economic analysis plan was developed and where it is available.

Secondly, many economic evaluations employ decision-analytic models as a vehicle to synthesise data from several sources. In modelling, there is considerable analyst discretion in the choice of the data and methods used and the assumptions made. Although many of the reporting items in CHEERS ask study authors to



o make these choices transparent, there have been of calls to make the models themselves publicly available so that other researchers

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can fully explore the impact of different analytic choices and conduct analyses of their own.⁷ Therefore, in Item 16 on the "Rationale and description of the model", authors are asked to report if the model is publicly available and where it can be accessed.

Recognising the role of patients and the public

The role of patients and the public in clinical and health services research has increased in recent

years.⁸ In addition, many health technology assessment committees include patient representatives. Therefore, patients and the public are becoming an important audience for health economic evaluations. In the development of CHEERS 2022, a public and patient involvement and engagement (PPIE) group was formed to support and advise the Task Force in the development of its recommendations. This resulted in two new reporting items. One of them (Item 21, "Approach to engagement with patients and others affected by the study") asks authors to report on any approaches to engage patients or service recipients, the general public, communities, or stakeholders (e.g., clinicians or payers) in the design of the study. The other patient-centric addition is Item 25 ("Effect of engagement with patients and others affected by the study"), which asks authors to report on the effect that any engagement had on the approach or findings of the study.

Resources to support the dissemination and use of CHEERS 2022

Several resources are being developed to support the dissemination and use of CHEERS. These can be accessed on the websites for CHEERS (http://ispor.org/cheers) or EQUATOR (https://www.equator-network.org/ reporting-guidelines/cheers/.)

 Several presentations are being developed; some for webinars targeted toward selected audiences, and some for those involved in teaching students or other groups about CHEERS.

Table 1. CHEERS 2022 Checklist

SECTION /Topic	ltem	Guidance for Reporting	Reported in section
TITLE			
Title	1	Identify the study as an economic evaluation and specify the interventions being compared.	
ABSTRACT			
Abstract	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	
INTRODUCTION			
Background and objectives	3	Give the context for the study, the study question and its practical relevance for decision making in policy or practice.	
METHODS			
Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.	
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	
Setting and location	6	Provide relevant contextual information that may influence findings.	
Comparators	7	Describe the interventions or strategies being compared and why chosen.	
Perspective	8	State the perspective(s) adopted by the study and why chosen.	
Time horizon	9	State the time horizon for the study and why appropriate.	
Discount rate	10	Report the discount rate(s) and reason chosen.	
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	
Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.	
Measurement and valuation of resources and costs	14	Describe how costs were valued.	
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.	
Rationale and description of model	16	If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.	
Analytics and assumptions	17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	
Characterizing heterogeneity	18	Describe any methods used for estimating how the results of the study vary for sub-groups.	
Characterizing distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	
Characterizing uncertainty	20	Describe methods to characterize any sources of uncertainty in the analysis.	

SECTION /Topic	ltem	Guidance for Reporting	Reported in section		
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (e.g., clinicians or payers) in the design of the study.			
RESULTS					
Study parameters	22	Report all analytic inputs (e.g., values, ranges, references) including uncertainty or distributional assumptions.			
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure.			
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.			
Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study			
DISCUSSION					
Study findings, limitations, generalisability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could impact patients, policy, or practice.			
OTHER RELEVANT INFORMATIO	N				
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis			
Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.			

This checklist was developed using US English.

- 2. Members of the CHEERS II Task Force have produced a series of videos discussing the rationale behind the various reporting items. These can be accessed as a group or as individual videos if one's interest is in a particular reporting item.
- 3. Downloadable interactive forms have been developed, making it easier to provide responses to the 28 reporting items. These can be accessed on the CHEERS website and https://don-husereau.shinyapps.io/ CHEERS/.
- A users' guide for patients is being developed, explaining the rationale behind the reporting items in lay language, along with a glossary to explain the technical terms.

Conclusions

The update of CHEERS is an important step in increasing transparency in the reporting of economic evaluations. The CHEERS guidelines are one of the EQUATOR series of reporting guidelines. Those in the medical writing community are encouraged to use the CHEERS 2022 guidelines when assisting authors of economic evaluations in communicating their research. The appropriate use of reporting guidelines is intended to lead to more transparent and timely publications.

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Disclosures and conflicts of interest

The authors declare no conflicts of interest.

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Chris Carswell practised as a clinical pharmacist for over 10 years before becoming a medical writer and then a full-time professional journal editor. He is currently Editor in Chief of *PharmacoEconomics* and *The Patient: Patient-Centered Outcomes Research.* He is also Co-Editor in Chief of *Pharmaco-Economics Open*, and the consulting editor of *Applied Health Economics and Health Policy.*



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The September 2022 edition



A virtual workforce

Working remotely/working from home has become the norm these days. This issue will focus on various aspects of working from home - the good, the bad, the ugly. We will have articles on the challenges of writing from home, managing teams and also, on how some of us overcome these challenges and enjoy this opportunity.

Guest Editors: Archana Nagarajan

EMA

A career journey in sustainability:

Three questions for Alex Schuman, Head of Corporate Sustainability and Diversity, Equity, & Inclusion, Schrödinger

any pharmaceutical and medical device companies are making huge environmental, social, and governance (ESG) commitments, such as striving to achieve carbon neutrality, and aiming to reach diversity, equity, and inclusion (DEI) goals. In order to get there, they need corporate sustainability experts to lead, organise, and help implement these initiatives.

We are delighted to have a conversation with one of these experts, Alex Schuman, who has made a successful and fulfilling career in sustainability that spans over a decade. Alex specialises in driving long-term corporate sustainability and ESG strategies, ESG reporting, sustainability communications, philanthropic giving, volunteerism, workplace mental health, and diversity, equity, and inclusion. In 2021, she was named a Sustainability Leader Award Finalist in the inaugural World Sustainability Awards. She is currently the Head of Corporate Sustainability and DEI at Schrödinger.

- Editor-in-Chief

MEW: There are many industry buzzwords and acronyms related to sustainability. One is corporate social responsibility (CSR) and the other is environmental, social, and governance (ESG). Why are these important for companies and the healthcare industry?

Alex Schuman (AS): It is incredible to see how, over the last 18 to 24 months, the general consumer of information is dramatically more aware of concepts and terms like "sustainability", "ESG (environmental, social, and governance)", and "CSR (corporate social responsibility)". I believe that there is an argument that could be made for all of these terms being synonymous, but, based on where expectations are headed, and where the conversation is going, I tend to focus more on sustainability and ESG.

To use a metaphor, to me, ESG is a list of ingredients, and sustainability is the whole pie.



Alex Schuman

Having a really good recipe for your ingredients is going to give you the most delicious pie. My job? To figure out what ingredients exist across the organisation and then develop that perfect recipe.

One of the first things that I do when entering an organisation is aligning on these definitions up front. It is incredibly difficult to develop a comprehensive strategy, one that touches all areas of a business, if those involved are not all using the same words to mean the same thing. It may seem simple, but defining sustainability and ESG are two of the most important things that any organisation can do when developing a strategy and framework in this space. This fact is true regardless of industry, and it can and should help shape all related decisions.

MEW: How did you get into this field? What drives you to excel in what you do?

AS: Coming out of my undergraduate degree, I didn't have a specific vision of success. I was focused on staying in the city where I graduated, and I was lucky enough to get a job at a local medical device company that – unbeknownst to me – would position me to create a career in sustainability.

Through a bit of luck and a lot of proactivity, I ended up being placed on a project that would change the course of my career (or perhaps just provide the direction I had been seeking). My first foray into the world of sustainability was helping the company to create a charitable donation application for local community organisations to apply for funding from the company. What started with an application for hospital galas and local nonprofits, grew into supporting a wide variety of community engagement initiatives. Fast forward a few years and I was helping the company develop its first sustainability report and related function. During this time, I went to business school in the evenings to learn more about how a business worked – I knew that if I didn't understand the ins and outs of a business, I would never be able to ask the right questions.

I consider myself incredibly lucky to have found a career that, not only do I enjoy, but is inherently rooted in helping others. I have always been passionate about positively impacting those around me, and how lucky am I to be able to make a career out of it! The impact of those in the sustainability industry is enormous. I feel grateful to be able to consider myself a member.

MEW: You were one of the finalists at the 2021 World Sustainability Leaders Award. This is an amazing achievement. How did it feel?

AS: Being recognised as a finalist for the first World Sustainability Leaders Awards was a great honour and one that I cherish. Whether it is an award for me individually, my team, or my company, being thought of and recognised for your work is always incredibly validating. There are a lot of sustainability awards that exist these days, and it absolutely feels good to be acknowledged, but what is most important is the work itself. I believe that awards, rankings, and ratings can provide great insight as to what is expected next and may also provide great validation for work done to date. However, they are not the ultimate goal. The goal is to make the most impact possible, wherever possible. That's the real reward.



A medical writing primer for oncology dossiers

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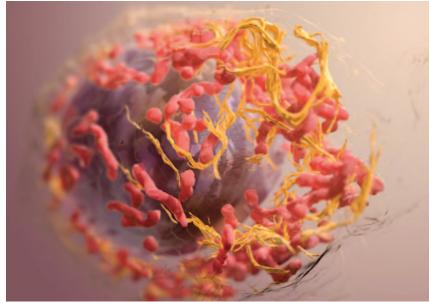
Abstract

Oncology is one of the most common areas of drug development in the pharmaceutical industry. As a medical writer, it is important to be aware of the unique aspects of oncology studies and have some understanding of the principles underlying cancer therapies. This article outlines a number of key hurdles faced with oncology studies and dossiers and guides medical writers through these so they can bring meaningful advice to their dossier team and prepare a high-quality submission dossier.

n 2020, the majority of new drugs approved by the FDA were for cancer treatment.^{1,2} Existing cancer drugs are also regularly approved for multiple indications, which adds to the workload for each drug.² The data needed to prepare the submissions to get these drugs approved come from large numbers of oncology studies taking place all over the world. This means, as a medical writer, you will likely be involved in writing documents for an oncology programme at some point in your career and it is important to be aware of the unique aspects of oncology studies and have some understanding of the principles underlying cancer therapies.

Oncology-specific challenges for medical writers

Coming to terms with the terminology and acronyms as well as the oncology-specific efficacy endpoints (progression-free survival, overall response rate, duration of response) can be challenging when you first get into the oncology arena. Cancer is a disease that is frequently treated over the long term, and even when the



cancer has been eliminated, follow-up continues for years. As a result, the endpoints to assess efficacy tend to look at the effect over time and its endurance, not just a static assessment of whether the disease is cured, as in many other therapeutic areas. The challenges associated with this in the context of submission dossiers arise from the fact that there are often multiple interim study reports, in addition to the final Clinical Study Report, and multiple data cuts over time (sometimes with different data cuts across multiple studies), which can be tricky to explain to the reader of a submission.

Cancer therapy is also a very dynamic area with developments in biotechnology rapidly shifting the approach to treatment. The medical dogma in many cancer types can shift swiftly, which means that the scientific rationale, currently available treatments, and medical-need descriptions often need to be updated frequently – sometimes changing considerably, even within a 12-month period, as new treatment options change the therapeutic landscape.

How to support oncology dossier teams

As medical writers, our role is to collaborate with the clinical experts to understand their vision for the treatment being studied and to crystallise the messaging from the clinical programme. We need to work with them to know where current changes in the medical opinion might need to be reflected in the medical-need discussion and to understand how the product under assessment needs to be positioned in the overall picture of available therapies. Frequently, because the clinical experts are often deeply involved in the research going on in their area, we also need to help get them to look at the big picture for the purpose of registration. It is important that the regulatory documents we write stay focused on what is needed to get regulatory approval of the target product profile (TPP) and not get bogged down and off-target in academic questions (that can be very interesting but should be saved for publications).

To be able to do this effectively, it is essential that submission teams have a clear and well developed TPP from the start of a clinical development programme. Ideally, the programme should be reverse engineered to specifically collect the data that will be needed to support the intended claims of the TPP. At the latest, it should be ready by the time writing on a submission dossier begins. Without the TPP, it can be challenging to know what aspects to focus on in the Module 2 summaries. If written in parallel, it often gets in the way of writing the dossier as the team chases a moving target. Having the TPP ready and agreed on well in advance gives the team clarity on what issues to focus on throughout the clinical programme, in general, and when writing the Module 2 summaries, in particular.

Common hurdles and how to handle them

During an oncology clinical programme, it is not uncommon to have multiple dose modifications as the investigators adapt to manage adverse events and slowly home in on the optimal dose regimen. Early studies can have different dosing regimens than later studies. As a result, treatment groups can be very fragmented, making it very

difficult to interpret the data, particularly in a pooled dataset, because the data cannot be easily compared across different doses. Changes in dosing can also mean that the proposed dose has less exposure time than earlier doses. These problems affect the interpretation of both efficacy and safety and need to be considered carefully when planning how to present the data in the dossier.

Another hurdle that teams often grapple with when writing oncology dossiers is how to handle adverse events of special interest (AESIs). Due to the different organs affected by different cancers, there is often little consistency in the AESIs collected in different studies. This presents a challenge when summarising them across studies in

Module 2.7.4. Do you try to find a consistent grouping of these across studies in different cancer types, or do you just present AESIs from the pivotal trial? In oncology, the AESIs will be driven by the risk factors from the underlying disease (cancer type) and in a large dossier, you will need to find a way to bring some very diverse safety data together. This should be thought about as early as possible when the team begins to plan for the dossier, and it certainly needs to be discussed in the statistical analysis plan (SAP) for the safety summaries.

Useful things to consider

Kaplan-Meier plots are widely used in oncology programmes for the depiction of overall survival as well as the time to onset and time to resolution

While subject matter experts are focused on their particular area of expertise, a medical writer is far enough away from the minute details to be able to add value and guidance to ensure the documents stay focused and fit for purpose.

of adverse events. These plots can be very useful in visualising how much of a difference there is for the duration of survival in patients treated with the drug under assessment vs. other treatment options. Similarly, in the context of adverse events, Kaplan-Meier plots can help make clear the periods of risk for drug-related events. It is helpful for medical writers to understand how Kaplan-Meier plots work, so they can provide useful context when writing about these.

Something else to keep in mind when planning for and writing oncology dossiers is whether there is a likelihood of submitting in other regions (e.g., Japan). If so, have a discussion with the colleagues from those other regions while developing the

SAPs for the efficacy and safety summaries to be sure that all analyses will be planned as required or expected by their local agencies. There is nothing more frustrating than thinking the dossier is fit-for-purpose for a global submission, only to find out that you need additional analyses to be run and incorporated into the files.

Conclusion

Overall, an experienced medical writer can bring meaningful advice and guidance to the dossier team. While subject-matter experts are focused on their particular area of expertise, a medical writer is far enough away from the minute details to be able to add value and guidance to ensure the documents stay focused and fit for purpose. Medical writers often come to the project with a fresh pair of eyes and they can ask the naïve questions that the team may have completely overlooked. With a strong regulatory lead who has a good vision of the target and clinical experts who understand the therapeutic benefits to be gained, a strong medical writer rounds out a dossier team by advising on how to present the information with clarity that will direct agency reviewers to what they are looking for and aid the approval process.

Disclosures and conflicts of interest

The author, Julia Forjanic Klapproth, owns Trilogy Writing & Consulting, a company specialised in providing regulatory medical writing. Maurice Löwens is employed by Trilogy Writing & Consulting. The authors declare no conflicts of interest.

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Julia Forjanic Klapproth, PhD started working as a medical writer in 1997, and she is passionate about the value of good medical writers. In 2002, she co-founded Trilogy Writing & Consulting, a company specialised in providing regulatory medical writing. Julia has been President of the European Medical Writers Association (EMWA) twice (2001-2002, 2007-2009).





Maurice Löwens has over 13 years experience as a medical writer, having worked on numerous types of clinical regulatory documents. In his current role as a Senior Medical Writing Manager at Trilogy Writing & Consulting, he leads teams of writers on a wide variety of regulatory writing projects.

Transparency and public disclosure:

What climate research can learn from clinical research – and vice versa



he healthcare industry is spearheading initiatives for public disclosure, open access, and plain language summaries in biomedical research. These initiatives are being mirrored in other fields of research as well, including climate research. Below we list some parallelisms between biomedical research and environmental research.

Transparency and disclosure

The Carbon Disclosure Project (CDP) is a notfor-profit organisation that runs the global disclosure system for greenhouse gas emissions. CDP drives companies and governments to manage their environmental impacts. "The world's economy looks to CDP as the gold standard of environmental reporting with the richest and most comprehensive dataset on corporate and city action."¹

Based on self-reported data, CDP scores companies and cities based on public disclosure and inventory of emissions, reduction targets, and climate action plans, and comes up with the so-called A list. The City A List 2021 included 95 cities from all continents.

More than 270 made it to the Company A List 2021, but only a disappointing handful of pharmaceutical companies are listed. The CDP A List may be compared to the Good Pharma ScoreCard, which ranks companies on their clinical trial transparency and data-sharing performance.² Pharmaceutical companies should proactively participate in CDP as part their corporate sustainability goals.

Open access

Open access in biomedical research is making headway³ whereas climate research is lagging behind. There is an urgent call for open access to environmental research papers as health and environmental crises converge. "Research that is published open access has a greater impact than research that is locked behind a paywall. It is read more and cited more, and it can be built upon, reproduced, validated, or refuted by other researchers much more easily. It can also be used by members of the public, educators, clinicians, journalists, and policy makers to spread awareness of pressing issues."4

The Electronic Information for Libraries (EIFL), the Scholarly Publishing and Academic Resources Coalition (SPARC), and Creative Commons started a campaign to increase open access to research on climate science and biodiversity. The project goal is to "create a truly global campaign to promote open access, open science and open data as effective enabling strategies to accelerate progress towards solving the climate crisis and preserving global biodiversity".⁵

Lay summaries

Plain language is vital to communicating with the public, and the healthcare industry is leading the pack.⁶ The 2021 United Nations Intergovernmental Panel on Climate Change (IPCC) report⁷ has been criticised for using complex and highly technical terminologies. A recent study⁸ looked at effectiveness of IPCC communications by conducting interviews among members of the general public. The results indicate that use of common climate change terms as listed in the

Table 1. Communicating climate change with plain language

Term	Definition	Suggested improvement
Mitigation	A human intervention to reduce emissions or enhance the sinks of greenhouse gases	"Policies that reduce emissions to stop climate change (from getting worse)." References to specific climate change actions or climate change policies should reduce confusion with other contexts, in which mitigation may have a different meaning.
Carbon neutral	Carbon neutrality is achieved when anthropogenic CO ₂ emissions are balanced globally by anthropogenic CO ₂ removals over a specified period. Carbon neutrality is also referred to as net- zero CO ₂ emission.	Spelling out "carbon dioxide" may avoid any confusion about the type of carbon involved. Referring to "no net increases in carbon dioxide in the air", or to "balance out the carbon dioxide we put into the air" may help to avoid confusion with "zero carbon". To clarity the process, these descriptions may need to include examples of carbon dioxide removal (see below).
Unprecedented transition	Transition: the process of changing from one state to another in a given period of time. Transition can be individuals, firms, cities, regions and nations and can be based on incremental or transformative change. (No definition for 'unprecedented' transition available.)	"Making big changes together to stop climate change." Examples should specify which big changes are required.
Tipping point	A level of change in system properties beyond which a system reorganises, often abruptly, and does not return to the initial state even if the drivers of the change are abated. For the climate system, it refers to a critical threshold when global or regional climate changes from one stable state to another stable state.	Findings suggest a need for descriptions of tipping point that highlights the connection with climate change, the seriousness of the issue at hand, and the role of cascading effects in the climate system. For example, this may include a phrase such as "point at which we can no longer undo climate change (and its effects on)" or "when it is too late to stop climate change (and its effects on)", with specific examples.

IPCC glossary was actually fraught with confusion and misinterpretation. This held true for the climate-concerned, the ambivalence, and climate change doubters. The study proposed some strategies on how the communicate climate change in plain language. Some examples are provided in Table 1,9 reused with permission from *The Anthropocene*.

Conclusions

Knowledge not communicated is knowledge wasted. Regardless of the field of research you are in, transparent communication is of prime importance and clinical research is paving the way. Climate research is playing catch up but seems to be headed in the right direction. Both fields of research can learn from each other.

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Raquel Billiones

News from the EMA

The articles included in this section are a selection from the European Medicines Agency (EMA)'s News and Press Releases archive. More information can be found on the Agency's website: www.ema.europa.eu.

SECTION EDITOR

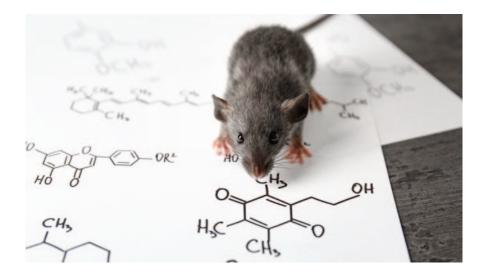


EMA implements new measures to minimise animal testing during medicines development

September 29, 2021

MA is putting in place special support to developers to replace, reduce and refine animal use for the development, manufacturing and testing of human and veterinary medicines. The Agency is promoting these three principles – replace, reduce and refine; commonly referred to as 3Rs – through EMA's Innovation Task Force (ITF). This action will facilitate the development and implementation of New Approach Methodologies (NAMs) that are in line with the European Union legislation on the protection of animals used for scientific purposes.

ITF is a dedicated forum for early dialogue between regulators and developers of medicines to discuss innovative aspects such as emerging therapies, methods and technologies. Set up to



ensure coordination across the Agency, the ITF is a multidisciplinary group that includes scientific, regulatory and legal competences. It will provide an opportunity to discuss 3R-compliant methods and facilitate their integration into the development and evaluation of medicinal products.

The ITF's service is free of charge and any NAMs adhering to the 3Rs principles that can be used to fulfil testing requirements are eligible for consideration.

Alternative approaches to animal models, such as improved tests based on human and animal cells, organoids, organ-on-chips, and in silico modelling, provide opportunities to develop better and more predictive scientific tools to protect human and animal health as well as the environment.

Opening the ITF platform to discussions of 3Rs-compliant methodologies is expected to encourage prioritising and speeding up the integration of alternative methods into the regulatory framework. This action supports the reduction of animal use and is in line with EMA's Regulatory Science Strategy to 2025 aiming to build a more adaptive regulatory system that will encourage innovation in human and veterinary medicine.

First-in-class medicine to treat aggressive form of breast cancer

October 15, 2021

MA has recommended granting a marketing authorisation in the European Union (EU) for Trodelvy (from Gilead Sciences Ireland UC), a first-in-class medicine to treat adult patients with unresectable (cannot be removed by surgery) or metastatic triple-negative breast cancer who have received two or more prior systemic therapies, at least one of them for advanced disease.

Triple-negative breast cancer is an

aggressive type of breast cancer that does not have the usual receptors (targets) which other targeted cancer medicines act on.

Currently, chemotherapy remains the standard treatment for patients with metastatic triple-negative breast cancer. However, it is estimated that only 10 to 15% of patients with this type of cancer respond to this treatment and the time without their disease worsening is only 2 to 3 months. Therefore, there is a high unmet

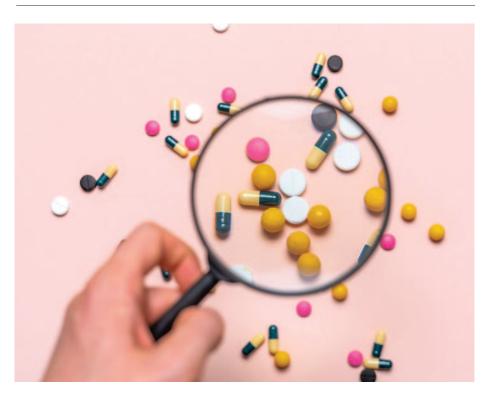
medical need for new treatments that improve the outlook for patients.

Trodelvy's active ingredient is sacituzumab govitecan. It combines a humanised antibody (a type of protein) designed to recognise and attach to the Trop-2 receptor with a type of an antineoplastic agent called topoisomerase I inhibitor. This is intended to inhibit the cancer to grow, divide, and spread.

EMA's human medicines committee (CHMP) reviewed the application for marketing authorisation under an accelerated timetable to

Generating high-quality evidence from registry-based studies

October 26, 2021



MA has published guidance to provide key methods and good regulatory practices to pharmaceutical organisations on the planning and conduct of registry-based studies.

A patient registry is an organised system that collects uniform data over time on patients who are diagnosed with a particular disease or condition, or who receive particular medicines. A registry-based study is a clinical trial or a noninterventional study that investigates a research question using the data collection infrastructure or the patient population of one or several patient registries.

Medicine regulators may sometimes suggest that pharmaceutical companies use the data collection infrastructure or population of a patient registry to exploit information from clinical use and to monitor the safety and effectiveness of authorised medicines when used in the real-world setting. There can be significant differences in requirements for types, structures, and processing of data across existing registries. These often present challenges in the assessment of the suitability of existing registries to be used in clinical studies.

This guideline aims to help those involved in registry-based studies to better define study populations and design study protocols; it provides further guidance on data collection, data quality management, and data analysis to achieve higher quality evidence. This in turn will facilitate EU regulators' assessment of the safety and effectiveness of medicines, for the benefit of public health.

As patient registries are key to conducting registry-based studies, the guidance includes an annex with good practices in the establishment and management of patient registries and their use for other regulatory purposes.

This guideline will facilitate a more datadriven, robust regulation of medicines, as foreseen in the Big Data Steering Group Workplan that implements the Network Strategy to 2025. It is based on a discussion paper on methodological and operational aspects for use in patient registries for regulatory purposes, which was available for public consultation and generated almost 1,000 comments from 68 stakeholder organisations. Experience gained from EMA's human medicines committee (CHMP) qualification opinions for two networks of registries, and input collected during five workshops on specific patient registries organised by the Agency also fed into the final guidance.

enable faster patient access to this medicine.

The CHMP based its recommendation on data from a Phase 3, multicentre, open-label, randomised clinical trial. The study investigated the safety and efficacy of Trodelvy in 529 patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC). All patients enrolled had relapsed after at least two prior chemotherapies for breast cancer. Participants were randomised (1:1) to receive sacituzumab govitecan 10 mg/kg as an intravenous infusion on days 1 and 8 of a 21-day cycle or treatment of physician's choice (eribulin, vinorelbine, gemcitabine, or capecitabine).

The medicine prolonged the overall survival (i.e. how long patients live) by approximately 5 months (11.8 months for sacituzumab govitecan compared to 6.9 months for treatment of physician's choice) and the progression-free survival (i.e. how long patients live without their disease getting worse) by about 3 months (4.8 months for sacituzumab govitecan compared to 1.7 months for treatment of physician's choice).

The most common side effects with Trodelvy in clinical trials included diarrhoea, nausea, neutropenia, fatigue, alopecia, anaemia, vomiting, constipation, decreased appetite, cough, and abdominal pain.

The opinion adopted by the CHMP is an intermediary step on Trodelvy's path to patient access. The opinion will now be sent to the European Commission for the adoption of a decision on an EU-wide marketing authorisation. Once a marketing authorisation has been granted, decisions about price and reimbursement will take place at the level of each Member State, taking into account the potential role/use of this medicine in the context of the national health system of that country.



Repurposing of authorised medicines: pilot to support not-for-profit organisations and academia

October 28, 2021

MA and the Heads of Medicines Agencies (HMA) are launching a pilot project to support the repurposing of medicines as a followup to the European Commission's Expert Group on Safe and Timely Access to Medicines for Patients (STAMP) discussions on a proposal for a medicines repurposing framework.

The aim of this initiative is to support notfor-profit organisations and academia to gather or generate sufficient evidence on the use of an established medicine in a new indication with the view to have this new use formally authorised by a regulatory authority. This is a way of making new treatment options available to patients.

As part of the pilot, EMA and the national medicines agencies will provide regulatory support, primarily scientific advice, to help these stakeholders generate a data package robust enough to support a future application by a pharmaceutical company.

Conditions for which no or few medicines are currently authorised, or which are associated with high morbidity and/or mortality despite available medicines, will be the focus of the pilot. Candidate medicines for the pilot should fulfil the following criteria:

- contain a well-established active substance;
- be an authorised medicine (containing the concerned active substance) out of data exclusivity and market protection periods and out of basic patent/supplementary protection certificate (SPC) protection;
- target an indication in a condition distinct from the currently authorised indication(s);
- target an indication in an area where important public health benefits are likely to be achieved.

While marketing authorisation holders may develop medicines for uses in other indications, sometimes they lack the incentives or the commercial interest to pursue the necessary research and development and complete the regulatory process needed for the authorisation of a new indication for old medicines which are no longer protected by a patent or data exclusivity. This could be a wasted opportunity for public health. At the same time, academic institutions and/or patient organisations may be interested in carrying out this development for the benefit of public health. However, they may not have the necessary regulatory experience and have no intention of becoming a marketing authorisation holder themselves.

The pilot will run until the completion of

scientific advice for the selected repurposing candidate projects and optimally until the filing of an application by a pharmaceutical company for the new indication. A report will be published after the pilot.

The medicines repurposing framework proposal was developed by the European Commission's STAMP Expert Group composed of representatives of EU Member States together with EMA and stakeholders from not-for-profit organisations, patients, healthcare professionals, industry, health technology assessment bodies, and payers.

EMA proposes to support the development and implementation of a repurposing framework in its Regulatory Science Strategy to 2025, which is its plan for advancing engagement with regulatory science over the next five to ten years.

Repurposing of medicines for COVID-19 falls outside the scope of this pilot project. The development and authorisation of treatments for COVID-19 is coordinated by the COVID-19 EMA pandemic Task Force (COVID-ETF) and should follow the steps outlined in the following document: PDF icon EMA initiatives for acceleration of development support and evaluation procedures for COVID-19 treatments and vaccines. Repurposing programmes for medicines intended for COVID-19 will therefore not be considered for this pilot.

2011-2020: More than 40% decrease in sales of antimicrobials for use in animals

November 23, 2021

he annual report on the European Т Surveillance of Veterinary Antimicrobial Consumption (ESVAC) published by EMA shows that European countries have substantially reduced the use of antimicrobials in animals. According to data from the 25 countries that provided input for the full 2011–2020 period, overall sales of veterinary antimicrobials in European countries were 43% lower in 2020 than in 2011. While an increase of 6% in overall sales for the 25 countries in 2020 compared to 2019 was registered, data for the next years are necessary to better understand this observation. These data show that "EU policy initiatives combined with guidance and national campaigns promoting prudent use of antimicrobials in animals are having a positive effect," said Ivo Claassen, Head of EMA's Veterinary Medicines Division.

Sales of those antimicrobials that are considered critically important in human medicine, decreased noticeably between 2011 and 2020 and accounted for only 6% of total sales in 2020. In particular, sales of third- and fourthgeneration cephalosporins dropped by 33%, polymyxins by 76%, fluoroquinolones by 13% and sales of other quinolones dropped by 85%. These classes include antimicrobials used to treat serious infections in humans that are caused by bacteria resistant to most other antimicrobial treatments. In animals, they should be used with restrictions in order to preserve their effectiveness and mitigate the risk to public health, as indicated in the Antimicrobial Advice Ad Hoc Expert Group (AMEG) categorisation.

The eleventh ESVAC report presents data from 30 EU/EEA countries (including the UK as an EU Member State during the calendar years covered in the report) and Switzerland. All participating countries voluntarily provided information on sales of veterinary antimicrobial medicinal products. In order to present more recent data, and in preparation for the timelines for the reporting of sales and use data for antimicrobials in animals as required by Regulation (EU) 2019/6, data for both 2019 and 2020 were collected and presented in this ESVAC report.

For each of the participating countries there is a separate section presenting sales trends by

antimicrobial class. Some countries have described their main activities to combat antimicrobial resistance and how these activities have contributed to the observed changes in sales in their country. These measures include national action plans, national campaigns for prudent use of antimicrobials in animals, restrictions on use of certain antimicrobials in food-producing animals, or measures to control prescription of antimicrobials in animals.

The ESVAC project was launched by EMA in September 2009 following a request from the European Commission. Since then, the Agency has coordinated and supported European countries in establishing the standardised and harmonised reporting on the volume of sales of veterinary antimicrobial medicinal products. The ESVAC report is published annually and is used as a reference source of information for scientists, veterinarians and other health professionals, risk assessors, and policy makers in the EU Member States on the topic of antimicrobial resistance. Under Regulation (EU) 2019/6, reporting of sales and use data for antimicrobials in animals will become a legal obligation for EU Member States and the Agency. The new requirements will apply to data from 2023 onwards.



A vision for use of real-world evidence in EU medicines regulation

November 24, 2021

nabling the use of real-world evidence (RWE) and establishing its value for regulatory decision-making on the development, authorisation, and supervision of medicines in Europe by 2025: this is the vision of European regulators as outlined in an article from Peter Arlett, Head of Data Analytics and Methods at EMA, Jesper Kjær, Director

of Data Analytics Centre at the Danish Medicines Agency, Karl Broich, President of the Federal Institute for Drugs and Medical Devices (BfArM), and Emer Cooke, EMA's Executive Director, published in Clinical Pharmacology & Therapeutics.

The authors emphasise that delivering this vision, anchored in the Network Strategy to 2025, will support the development and use of better medicines for patients.

The creation of the Data Analytics and Real-World Interrogation Network (DARWIN EU) will be key to delivering this vision. This EU-wide network will allow to access and analyse healthcare data from across the EU. It will be launched in early 2022 with the establishment of a coordination centre to on-board data partners and to drive the conduct of studies requested by medicines regulators and, at a later stage, also requested by other stakeholders.

The article explains plans to establish methods and standards for high-quality collection and use of RWE, in cooperation with stakeholders including patients, healthcare profes-

sionals, industry, regulatory and public health agencies, health technology assessment bodies, payers, and academia.

According to the authors, it will be important to advance the debate on the value of RWE compared to randomised clinical trials (RCTs), the gold standard to demonstrate efficacy of a medicine. The vision is that RWE and RCTs should be seen as complementary, each having strengths and weaknesses, with their relative importance depending on the regulatory question. A rigorous and systematic approach to learning from doing will help to identify and establish the use-cases in regulatory decision-making for which RWE will add most value.

In this context, EMA has also contributed to an article that examines when and how RWE was

used to support marketing authorisation applications for new products and extensions of indications, submitted to the Agency in 2018 and 2019. The retrospective analysis shows that 40% of initial marketing authorisation applications and 18% of applications for extension of indication for products currently on the market contained RWE. The article describes the characteristics of RWE included in these applications and identifies areas where further research is required.

Both articles aim to support transformation to data-driven regulatory decision-making and to advance patient-centred access to better medicines. They are available through open access:

- Arlett, P., Kjær, J., Broich, K. and Cooke, E. Real-World Evidence in EU Medicines Regulation: Enabling Use and Establishing Value. Clin. Pharmacol. Ther. 2022; 111:21-23.
- Flynn, R., Plueschke, K., Quinten, C., Strassmann, V., Duijnhoven, R.G., Gordillo-Marañon, et al. Marketing Authorization Applications Made to the European Medicines Agency in 2018–2019: What was the Contribution of Real-World Evidence?. Clin. Pharmacol. Ther., 2022; 111:90-97.



New treatment for sickle cell disease

December 17, 2021

MA has recommended granting a marketing authorisation in the EU for Oxbryta (from Global Blood Therapeutics Netherlands B.V.) for the treatment of haemolytic anaemia (excessive breakdown of red blood cells) due to sickle cell disease in patients 12 years of age and older. Oxbryta is to be used on its own or in combination with hydroxycarbamide (also known as hydroxyurea).

Sickle cell disease is a genetic condition in which the red blood cells become rigid and sticky and change from being disc-shaped to being crescent-shaped (like a sickle). The change in shape is caused by the presence of an abnormal form of haemoglobin (the protein in red blood cells that carries oxygen around the body).

In patients with sickle cell anaemia, the abnormal sickle shaped red blood cells block the blood vessels, restricting the flow of blood to organs, such as the heart, lungs and spleen. This situation causes episodes of acute pain called vaso-occlusive crisis (VOC). Furthermore, these abnormal red blood cells are destroyed at a faster rate than normal, leading to a condition called haemolytic anaemia. Vaso-occlusive crisis and haemolytic anaemia are the most common complications of sickle cell disease and are frequent causes of visits to emergency departments and hospitalisation.

Currently, most patients with sickle cell disease are treated with hydroxyurea and crizanlizumab, medicines for preventing VOC. However, there is a high unmet need for medicines to treat haemolytic anaemia, which is experienced to various degrees by all patients. Available treatment options are limited to blood transfusions and allogenic haematopoietic stem cell transplantation (a procedure where the patient receives stem cells to help the bone marrow produce healthy blood cells). Therefore, new medicines for this manifestation of the disease are needed.

The active substance of Oxbryta is voxelotor, a small molecule which attaches to and stabilises haemoglobin, preventing haemoglobin polymerisation (i.e. formation of abnormal haemoglobin) that causes the red blood cells to become sickle shaped.

The main study that EMA's recommendation is based on was a Phase 3, randomised, double blind, placebo-controlled, multicentre study. The study investigated the safety and efficacy of voxelotor in 274 patients with sickle cell disease aged 12 to 65 years. Patients enrolled in the clinical trial had a baseline haemoglobin level between 5.5 and 10.5 g/dL. Ninety patients received 1500 mg of voxelotor, 92 patients received 900 mg of voxelotor and 92 patients received a placebo. After 24 weeks of treatment, 51.1% of patients treated with 1500 mg of voxelotor had a greater than 1 g/dl increase in their haemoglobin levels compared to 6.5% of those receiving placebo. These results were observed when Oxbryta was used on its own or in combination with hydroxyurea, which is the standard treatment for patients with sickle cell disease. The most common side effects reported in clinical trials for Oxbryta included headache, diarrhoe, and abdominal pain.

Oxbryta was supported through EMA's Priority Medicines (PRIME) scheme, which provides early and enhanced scientific and regulatory support for promising medicines with a potential to address unmet medical needs. Representatives of patient organisations were also consulted during the assessment of benefits and risks of Oxbryta to share their unique reallife perspectives and ensure that patients' needs are taken into account in the regulatory decisionmaking process.



This is called the hash, pound, or number character. A hashtag is a keyword or set of keywords that is preceded by the # character. It is used in social media to create a thread of conversations around a specific theme or topic conveyed in short texts or microblogs. It is commonly used in Twitter, Instagram, YouTube, Pinterest, etc.

A dictionary of most common hashtags can be found at https://www.hashtags.org/definition/~h/. For your info, EMWA is compiling a list of standarised hashtags for our social media use.

This is called the "at" sign or symbol. The @ sign is part of email addresses and social media user names ("handles"). Our EMWA handles are as follows: @Official_EMWA (Twitter), @EMWA (LinkedIn), and @europeanmedicalwritersassociation (Facebook)

The two most important keys on your keyboard

Medical Communications and Writing for Patients

Editorial

Dear All,

Happy New Year! Welcome to the first issue of 2022's *Medical Writing*. I hope that you and your loved ones are all managing to stay as safe and sane as possible, and I hope that you all had a wonderful Christmas break.

In this edition of *Medical Writing,* I'm delighted to present TWO articles. Both are time sensitive, so we took the unusual decision of running two pieces in this section rather than wait and space them out.

The first piece is a summary of the excellent work just completed by the Med Comms SIG. They have devised, run, and collated the results of a survey on predatory publishing. Predatory publishing is an issue that should be of grave concern to the medical writing, clinical development, and academic communities, and so it is very important that we not only establish awareness and the extent of the problem, but also raise the issue for continued discussion and to keep awareness high.

The second piece is an update from the Med Comms SIG's second Meet and Share session, which took place in November 2021. The session was titled *Ethics in Publishing*, and covered the practical issues surrounding data integrity and authorship eligibility when writing manuscripts for clients. As always with Meet and Share sessions, it was an excellent exchange of knowledge and experience, and members were

SECTION EDITOR



able to provide examples of key processes that could help to avoid misunderstandings and future disagreements. If you missed the session, this article is a great way to catch up on all of the discussions!

I hope that you enjoy both articles as much as I have, and see you in the next issue!

> Bestest, Lisa

Predatory practices posing problems

n Autumn 2021, a survey was sent out to all EMWA members on behalf of the Medical Communications Special Interest Group (MedComms SIG) to help it better understand the issues presented by predatory publishing practices. Expert and SIG member Simon Linacre analysed the results and suggests here some practical steps for medical writers to follow

to mitigate the pitfalls of predatory journals [Full disclosure: Simon Linacre was formerly marketing director at Cabells, a scholarly analytics firm which sells products and services that help counteract predatory publishing].

Predatory journals are a major concern for medical writers, with a significant impact on all healthcare stakeholders – that is the overall finding from EMWA's member survey conducted in the second half of 2021. With 128 respondents – drawn mostly from EMWA but also ISMPP and AMWA

members - the results paint a picture of highlevels of awareness, but also express concerns about how predatory journals and conferences are permeating medical communications and public policy.

Predatory activities – mainly featuring journals and conferences, but also including books, author services and journal indexes – tend to focus on deceiving authors into thinking they are paying for a service that is not delivered. For

Predatory activities – mainly featuring journals and conferences, but also including books, author services and journal indexes – tend to focus on deceiving authors into thinking they are paying for a service that is not delivered. example, an author will pay a fee to a journal to make their article open access when published, with the fee intended to cover costs such as peer review, copyediting, proof reading, and search engine optimisation (SEO). In the predatory world, none of these costs are incurred as they don't happen, with articles published without any form of independent check and potentially catastrophic results for any other researchers using the published research in good faith.

Simon Linacre

EMWA MedComms SIG committee member slinacre@gmail.com

Background

The survey was sent out in October 2021 following the high levels of interest and engagement in seminars hosted by EMWA in recent years on the topic of predatory journals. Predatory journals have been a hot topic of conversation since 2009 when librarian Jeffrey Beall first coined the term and highlighted their practices. Since then, the numbers of journals identified as predatory have grown rapidly, with spam emails soliciting papers for predatory journals and conferences appearing regularly in researchers' inboxes.

The apparent increase in predatory activity and potential for harm to medical communications, together with interest in the subject from EMWA members, provided a catalyst for the MedComms Special Interest Group to put together a survey to understand more about how it was affecting those in the industry. The survey was issued by EMWA Head Office, and also sent through to other medical communications bodies to garner as many responses as possible.



Figure 1. Word cloud showing open-ended responses from members of EMWA regarding how best the association can support members

Key findings

The key themes the survey uncovered can be summarised in the following ways:

- Awareness: Overall, there is huge awareness of the predatory phenomenon, with 97% of respondents saying they had heard of the terms associated with it. Similarly, 78% had themselves come across predatory activity, and 70% knew of the joint statement by COPE-ISMPP-AMWA on predatory publishing (https://www.emwa.org/about-us/ position-statements/joint-positionstatement-on-predatory-publishing/). However, in a trait that is seen across the survey, a significant minority (25%) had not heard of the joint statement at all.
- Identification: For the 78% of respondents who had come across predatory activity, there were some follow up questions on how they were able to identify this. Personal experience was the main factor (70%), with resources also proving useful for identification (36%). More worryingly, a large number of people

had been solicited directly (76%) to contribute to a predatory journal or conference, with 11% admitting they had inadvertently submitted a journal or paper. In addition, 20% of people didn't know if they had been solicited or if they had submitted anything, representing the significant minority again who appear to be unable to differentiate predatory journals and conferences from legitimate enterprises.

• Impact: There is little doubt medical writers believe predatory activities to be a big problem for medical communications, with 86% (journals) and 78% (conferences) thinking they have a major impact. Four in five don't believe it is just a problem affecting academics – although one in 10 do think it is just their problem – and 78% believe these activities can lead to disinformation in public policy. Perhaps the strongest result when it comes to impact is that one of the highest positive responses in the survey of 91% was reserved for those agreeing that there was a wider impact on all health stakeholders such as medical professionals and patients.

• **Resources**: In terms of tackling the problem, given that the majority of respondents said they could identify predatory journals and conferences from experience and a third by using resources, developing programmes that build on these two factors would seem sensible. Specific resources used included the long-defunct Beall's List (54%), the Committee on Publications Ethics (https://publicationethics.org/resources/ discussion-documents/predatory-publishing - 46%), the Think. Check. Submit. website (https://thinkchecksubmit.org/ - 32%) and Cabells' Predatory Reports database (https://www2.cabells.com/aboutpredatory - 22%). Demand for such resources appears to be high, with 84% of people agreeing that further resources provided by EMWA would be useful for their work.

Interpreting these results, the responses appear to hold for most constituents in medical writing. It was distributed through aligned organisations as well as EMWA, which meant that while 68% of respondents were from Europe, a fifth were from North America. There was also a wide range of experience represented, with the most typical cohorts having 11 to 20 years experience (28%) and aged between 40–49 years old (35%).

Implications

One of the questions in the survey was an open one, which asked respondents how they would like to see EMWA support its members [see Figure 1]. There were many practical recommendations suggested by respondents, including education programmes available to all medical writers, a single website including all relevant information, a new list available for anyone to check journal titles against, and the continued rollout of webinars and talks on the subject from organisations such as EMWA.

All of these recommendations for action will be taken on board by EMWA as it determines where to focus on its activities to support members and the wider medical communications community in the future. When it comes to predatory journals and conferences, it is clear that while most medical writers are aware of the problem and feel relatively confident in dealing with it, many others are either unaware or quite uncertain about identifying and avoiding being lured by predatory operators.

Acknowledgements

The author would like to thank EMWA Head Office for their assistance with the survey, as well as members of EMWA, AMWA, ISMPP, and the Australian and New Zealand medical writers association who responded to the survey.

Disclosures and conflicts of interest

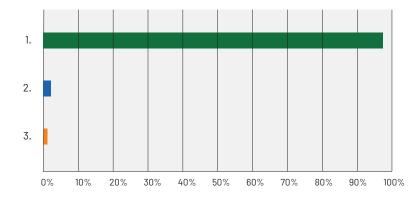
The author was formerly employed by Cabells, which sells products and services to combat predatory publishing activities.

Data availability statement

For inquiries about data and other supplemental information, please contact the corresponding author.

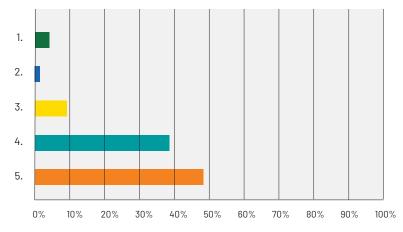
Results of the Survey

Question 1: Have you heard the term "predatory publisher", "predatory journal" or "predatory conference" ?



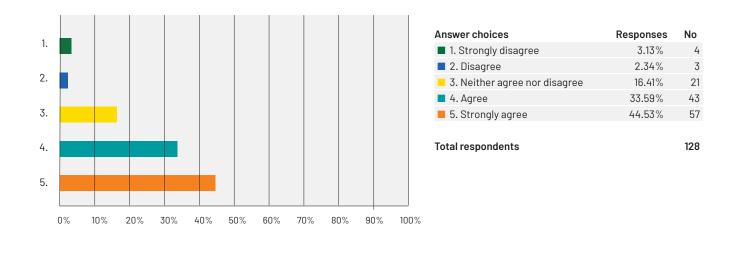
Answer choices	Responses	No
1. Yes	96.88%	124
2. No	2.34%	3
3. Not sure	0.78%	1
Total respondents		128

Question 2: Do you agree predatory journals impact the work of medical writers and medical communicators?

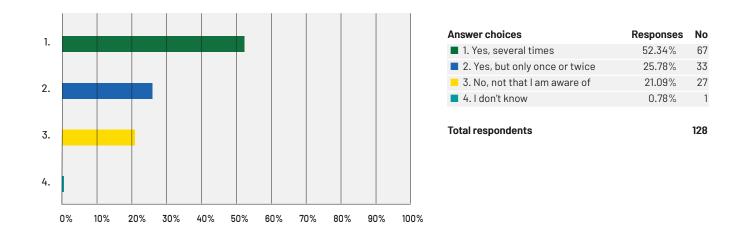


Answer choices	Responses	No
1. Strongly disagree	3.13%	4
2. Disagree	1.56%	2
3. Neither agree nor disagree	9.38%	12
4. Agree	38.28%	49
5. Strongly agree	47.66%	61
Total respondents		128

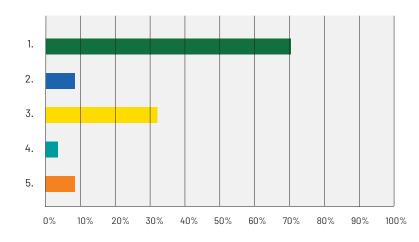
Question 3: Do you agree predatory conferences/events impact the work of medical writers and medical communicators?



Question 4. Have you ever come across predatory publishing or predatory conference activities in the course of your work?

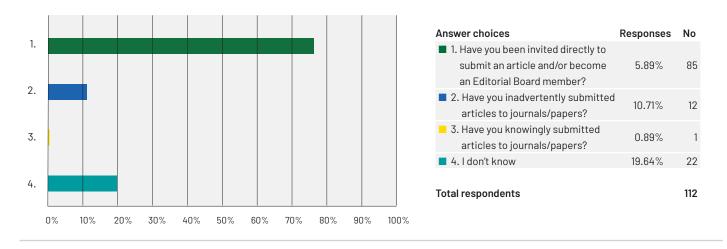




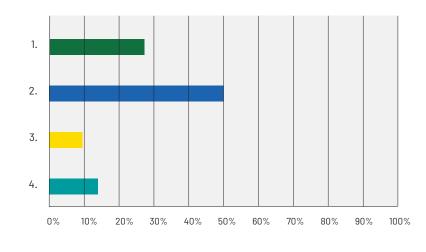


Answer choices R	Responses	No
1. It was clear from my own experience	70.34%	83
 2. It was pointed out to me by someone else 	8.47%	10
3. I used a resource to help me	32.20%	38
4. I only found out after I had used the source	3.39%	4
5. I don't know	8.47%	10
Total respondents		118

Question 6: If you have answered "1" or "2" to Q.4, regarding your direct experience of predatory journals/conferences: [all that apply]

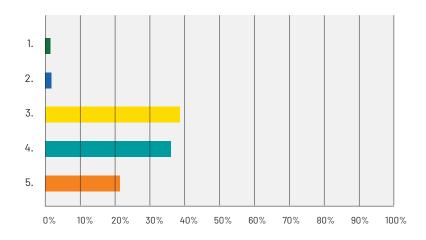


Question 7: If you have answered "1" or "2" to Q.4, how often do you receive unsolicited emails from suspected predatory journals or conferences?



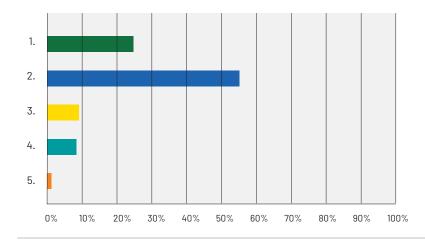
Answer choices	Responses	No
1. Never	27.19%	31
2. Once a month	50.00%	57
3. Once a week	9.65%	11
4. More than once a week	14.04%	16
Total respondents		114

Question 8: If you have answered "1" or "2" to Q.4, do you agree predatory solicitations are becoming more common?



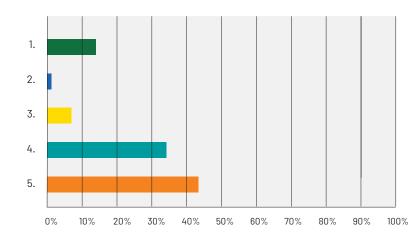
Answer choices	Responses	No
1. Strongly disagree	1.72%	2
2. Disagree	1.72%	2
3. Neither agree nor disagree	38.79%	45
4. Agree	36.21%	42
5. Strongly agree	21.55%	25
Total respondents		116

Question 9: Do you agree with this statement: "Predatory publishing practices are an academic problem and they don't impact me or my work"?



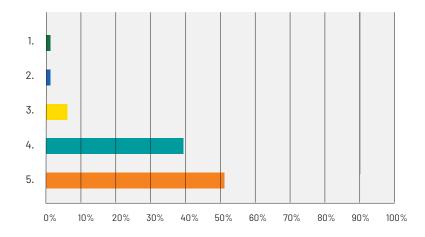
Answer choices	Responses	No
1. Strongly disagree	25.00%	32
2. Disagree	55.47%	71
3. Neither agree nor disagree	9.38%	12
4. Agree	8.59%	11
5. Strongly agree	1.56%	2
Total respondents		128

Question 10: "If left unchallenged ... predatory practices could fuel disinformation in public policy". Do you agree with this statement?



Answer choices	Responses	No
1. Strongly disagree	14.06%	18
2. Disagree	1.56%	2
3. Neither agree nor disagree	7.03%	9
4. Agree	34.38%	44
5. Strongly agree	43.75%	56
Total respondents		128

Question 11: Do you agree predatory publishing practices could impact significantly on medical professionals, patients and other related stakeholders?

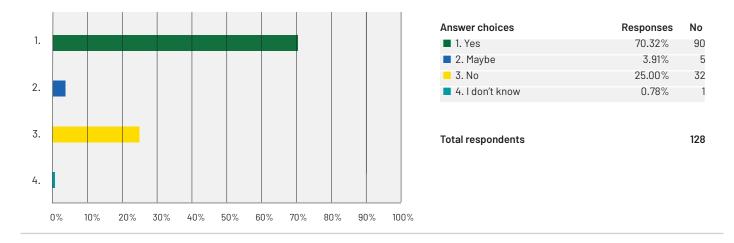


Answer choices	Responses	No
1. Strongly disagree	1.56%	2
2. Disagree	1.56%	2
3. Neither agree nor disagree	6.25%	8
4. Agree	39.84%	51
5. Strongly agree	51.56%	66
Total respondents		128

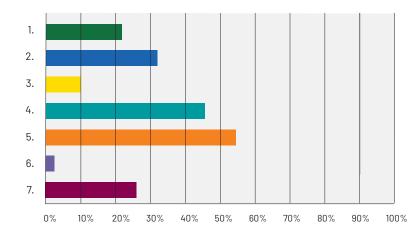
www.emwa.org

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Question 12: Are you aware of the EMWA-ISMPP-AMWA Joint Position Statement on Predatory Publishing https://www.emwa.org/news/amwa-emwa-ismppjoint-position-statement-on-predatory-publishing/ and other related stakeholders?

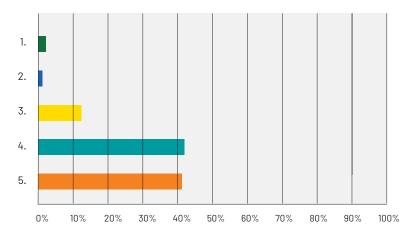


Question 13: Have you heard of the following resources developed to counter predatory practices? [all that apply]



Answer choices	Responses	No
1. Cabells Predatory Reports	22.05%	28
2. Think. Check. Submit.	32.28%	41
3. Think. Check. Attend.	10.24%	13
4. COPE principles of transparency	45.67%	58
5. Beall's List	54.33%	69
6. Dolos list	2.36%	3
7. None of the above	25.98%	33
Total respondents		127

Question 14: EMWA is thinking of developing further resources for members to support them in dealing with predatory journals, books, conferences and author services. Do you agree such resources would be for your work?

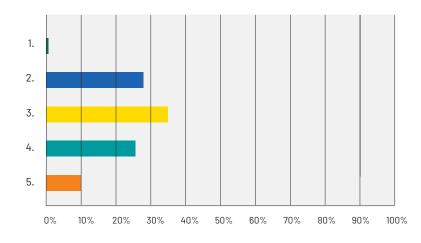


Answer choices	Responses	No
1. Strongly disagree	2.34%	3
2. Disagree	1.56%	2
3. Neither agree nor disagree	12.50%	16
4. Agree	42.19%	54
5. Strongly agree	41.41%	53
Total respondents		128

Question 15: If you have any ideas on how EMWA can support its members with regard to predatory publishing activities or if you have any comments, please add them below.

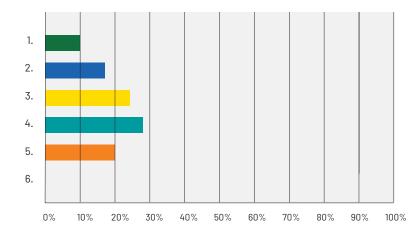


Question 16: How old are you?



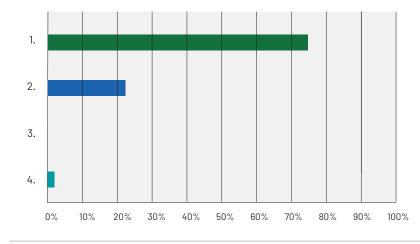
Answer choices	Responses	No
1. Under 30	0.78%	1
2.30-39	28.13%	36
3.40-49	35.16%	45
4.50-59	25.78%	33
5 . Over 60	10.16%	13
Total respondents		128

Question 17: How many years' experience do you have as a medical writer/communicator?



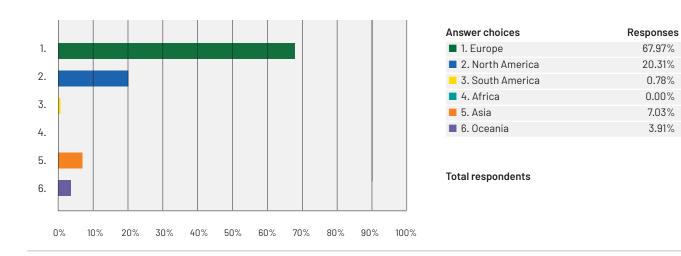
Answer choices	Responses	No
1. 0-2 years	10.16%	13
2. 3-5 years	17.19%	22
3. 6-10 years	24.22%	31
4. 11-20 years	28.13%	36
5 . 21+ years	20.31%	26
 6. I have no experience as a medical writer/ communicator 	0.00%	0
Total respondents		128

EMWA

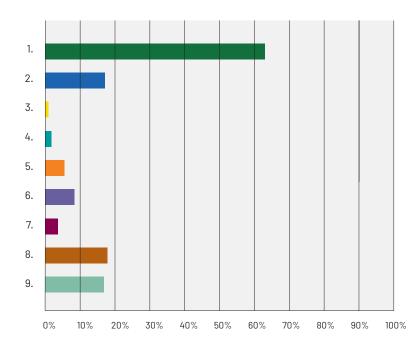


Answer choices	Responses	No
1. Female	75%%	96
2. Male	22.66%	29
3. Non-binary	0%	0
4. Prefer not to say	2.34%	3
Total respondents		128

Question 19: In which region did you live in August 2021?



Question 20: Which of the following departments is your function assigned to in your company? (Do not answer if freelancer)



ponses	No
63.81%	67
17.14%	18
0.95%	1
1.90%	2
5.71%	6
8.57%	9
3.81%	4
18.10%	19
17.14%	18
	1.90% 5.71% 8.57%

Total respondents

105

No

87

26

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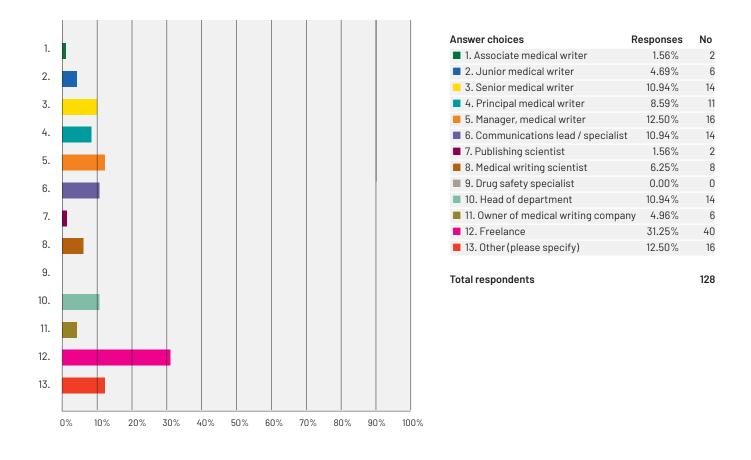
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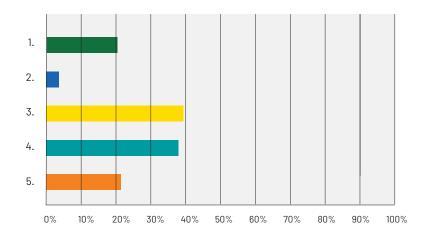
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Question 18: Which of the following best describes you?

Question 21: Which of the following best describes your job title?



Question 22: Are you a member of one of the following organisations?



Answer choices	Responses	No
■ 1. AMWA	20.25%	16
2. AMWA (Aus / NZ)	3.80%	3
3. ISMPP	39.24%	31
4. EMWA	37.97%	30
5. Other (please specify)	21.52%	17

Total respondents

79



Ethics in publishing: Second Meet and Share session of the Medical Communications Special Interest Group (MedComm SIG)

n the second Meet and Share session, which took place in November 2021, we discussed practical ways to handle issues surrounding data integrity and authorship eligibility that we may encounter when developing manuscripts for our clients. It was a stimulating exchange of various points of view,

We may, at times,

discover that the

conclusions are

exaggerated, data

analysis is

problematic, or data

quality is poor.

from experienced writers sharing their strategies on working with uninformed clients to publication professionals providing examples of key processes that could help avoid misunderstandings and future disagreements.

When we begin the process of developing a manuscript, we cast our fresh eyes over the data

and critically assess its quality and validity. We

may, at times, discover that the conclusions are exaggerated, data analysis is problematic, or data quality is poor. We may find that authors are not contributing sufficiently enough to merit a byline. Also, we may face illegitimate authorship requests at the time of article submission. During this session, the following recommendations

were made to help navigate these tricky situations:

• **Communicate risk:** When conclusions are inflated, alert the sponsor of the risks they face if they lose their audience's trust. A loss of reputation would affect brand and market value. Although such discussions are more difficult with clients who

feel personally involved in the study, it is

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worth highlighting the good faith under which scientific research is conducted.

- Communicate politely and clearly:
 - Clients would be more open to discussing data integrity problems and altering their perceptions if our tone was helpful, respectful, and humble. So, lead the discussion by asking questions and request clarifications.
 - Offer actionable suggestions, e.g. performing root cause analyses if the primary outcome analysis yielded disappointing results.

- We should not let imposter syndrome silence our doubts. This advice is especially pertinent to junior writers. The experienced writers in the group assured that voicing concerns is welcomed by most publication teams, provided it is done in an inoffensive and humble way. The clients' reactions to such behaviour can also help the writers assess if they would consider working with these clients again. The consensus was that it is better to lose a few business prospects in the short term in order to attract the right type of client.
- As we are the first line of control to ensure that all authors listed in a manuscript have fulfilled the authorship criteria, we could get "silent" authors to take ownership of the manuscript's content by asking them direct questions that require detailed answers.
- We should be clear about the author inclusion and exclusion criteria with the authors and sponsors early in the publication development. The prospective authors must be made aware of the International Committee of Medical Journal Editors (ICMJE) and Good Publication Practice (GPP3) guidelines.^{1,2} Marketing efforts may be affected when an author who is prominent in their field is removed from the author list; therefore, we must aim for open and clear alignment of processes with all impacted departments. We agreed that medical writers should not succumb to commercial pressures.
- Do our own calculations: We should check if the reported limits of data ranges seem sensible, if units are accurate, and if basic calculations are correct. While it is helpful to have basic statistical knowledge to check data quality, our meticulous nature can also help us identify errors in the data. For instance, we could look at the minimum and maximum values to detect outliers within a dataset.
- Make it less personal: In addition to referring the clients to best practice guidelines for ethical writing, we could highlight that our concerns will eventually be voiced by other groups who will be reviewing the data, e.g. regulatory authorities, peer reviewers, and journal editors. It would help to pose some challenging questions to the client to help them think deeply about the data and reassess their strategy, such as:
 - What questions do you not want to be asked by the regulator?

- Is there data in here that could embarrass you?
- Are we working with a verified dataset or reviewed report?
- What do you think the editor or peer reviewer will say?

• Share responsibility:

- With editors and reviewers: Following writing guidelines requires us to explain the limitations of the data clearly in the manuscript. We should also mention any concerns that impact the conclusions of the study. This will help the journal editors and peer reviewers correctly assess the quality of the study.
- With statisticians: It would be helpful to have statisticians take ownership of the data quality and analyses. We agreed that their contributions merit an authorship. A colleague with knowledge of the scholarly publishing industry shared that editorial boards and peer reviewers are sceptical of the data analysis if they do not find a statistician listed as an author. This could be a good argument to convince the client to use and credit a statistician.
- With authors: We could present the issues to the lead author and ask for their support.
- Have a process-driven approach for assessing authorship eligibility: Using a detailed authorship eligibility form based on the Contributor Roles Taxonomy (CRediT) terms for contributorship may be helpful.³ Ideally, it should be filled in and agreed to already at the kick-off meeting. It would need to be updated throughout the publication development process and finalised at the time of submission. To convince all parties to complete the form, use the following rationales:
 - The information contained within could be used to justify authorship eligibility to the journal editor and to settle any internal disputes that may arise later.
 - At the time of an audit, the form could be used to provide evidence of contributions. Using publication planning software tool, like Datavision,⁴ can also help keep detailed records that could be useful if an audit were requested.
- Walk away: If the issues are not resolved despite all our efforts, then we should consider stepping back from the project and requesting that our names be removed from the acknowledgements section.

Overall, we learnt that having confidence, using positive and clear communication strategies, and sharing accountability would help us reach our ethical objectives as medical writers. The MedComm SIG is grateful to all participants for their openness. This forum, which is open to all EMWA members, continues to be a judgmentfree space to learn from and lend support to other medical writers.

Acknowledgements

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Getting Your Foot in the Door

SECTION EDITOR



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"Do your homework, knowledge is power!" my teachers used to say. Yes, we learn a lot during our education, respect the rules of the system, and we rely on that knowledge. However, once that stage is over, we are overwhelmed with possibilities and stare at job ads. Different perspectives, experiences, and ideas can help a lot. In this section, Peter Morgan, Jean-Régis Humbert, and Elodie Pauwels share their stories on how they embarked on their medical writing careers. Stijn Staes gives us the insight that we are not limited by our degrees or experiences. These stories are just a reminder to follow your passion and your path will unfold when you least expect it.

Ivana

From a survivor to a creator and a freelancer in just 10 lessons

t took me more than 25 years and a lot of different professional roles in all parts of the world to arrive at a stage of inner freedom where I wanted to be since I was born. In this article, I'll write about my personal quest in 10 lessons. Lean back and get ready for a bumpy ride! These lessons and experiences ultimately changed my life and personality in a way that I never could have imagined. The least I can do now is to share my life experience, inspiration, and energy, which you can use for your own personal development.

Freedom has been my deepest aspiration since I was a child. I was raised in a small town in Belgium which I perceived as some kind of imprisonment, and I always wanted to break out. One day, I decided to explore the world outside of my small town. There, I discovered the vibrant and foreign city of Maastricht at the age of 12 without my parent's permission. Every week I used to risk my life riding a bicycle in heavy traffic and on unsafe roads just to be in Maastricht.

There I had a sense of freedom and would listen to strangers talking in an unusual Dutch accent. I enjoyed the city vibes and found the most extraordinary gadgets in shops that had only been existing in my dreams.

Lesson #1 was I learned to go out and explore. Take risks if you want to have adventure in life and encounter new opportunities. That's the recipe for an exciting and fulfilling life.

Following rules and society's expectations were never my cup of tea. During my whole life I've balanced between the attraction of a safe golden cage and my unstoppable hunger for adventure and freedom.

Looking back, it all started with the choice of my studies. I truly liked to perform and to be on stage. I had a vision to become a famous actor which did not suit my parents' expectations, as these kinds of jobs were socially not acceptable and would not provide a stable financial income according to their perspective. Additionally, on a personal level I was struggling with my sexual orientation. When I saw a gay man in a famous TV hospital soap opera for the first time, it brought me hope and relief. Not being out yet was a valid reason for me to go into nursing school in the belief that I will get the confidence needed to break the silence. My two major challenges were Looking back, seemingly solved.

However, I discovered that hospitals were a classic example of strict hierarchy and obedience such as of a nurse to a doctor in those days. Moreover, I didn't find a suitable match and my hunger for knowledge was not yet

fulfilled. Getting a master's degree was a logical choice as it would open doors, so I was told. I enrolled in master's studies in hospital management and graduated with distinction through my perseverance and belief that I can succeed, even when it did not match my dreams.

Lesson #2: Never regret a single choice in your life. It will bring you to your next, unknown destination. Remember to look back at what you have achieved and give yourself credit.

Still, I was not ready to settle down for a 9 to 5 job. So, I decided to undertake a pilgrimage of one year backpacking to South and Central Stijn Staes Executive Coach and Podcaster Ghent, Belgium stijn@stappenmetstijn.be

America. This journey unlocked my passion for travelling and interest for other cultures. Furthermore, I learned to be independent and make a network of friends all over the world. Many times I felt lonely there but it could not compete with the beauty of the travel. Lesson #3: Being alone gives you the opportunity to get to

I realise that life is

full of opportunities,

you only have to see

and seize them.

know yourself in the deepest ways possible!

Back home I decided to get an education in Tropical Medicine in Antwerp to work for Doctors without Borders. It was the perfect combination of my passion for people and travel. At the same time, it was a great solution for "my wrong

choice of study". I was kidnapped, shot at, and survived heavy bombings. During that time, I had discovered the most isolated areas of Africa to cure diseases and help thousands of people in the most dire circumstances. I learned about living in poverty among the poorest and starving cultures/places of this planet. I still vividly remember how I appreciated a small, salty potato as a full meal. This experience changed me forever, showed me to be humble, and made me grateful for all that I have, which would be Lesson # 4.

The poppy fields of Afghanistan and the

religious battles of Indonesia taught me that everyone has his own truth. It is just a matter of being respectful and being able to truly listen. That's the recipe for building a peaceful society. **Therein lay Lesson #5: to always face people and situations with an open mind and to see it as an opportunity.** It is the only way to help others, experience joy and make true friendships and relationships.

When I came back home, I felt like an outcast in Western society. I needed some sort of structure and found a fixed term position in Belgium. I discovered all the advantages of a fixed income, long term-working relationships, and stability. **Sometimes it is good to settle down for a while, and just go with the flow of life (Lesson # 6).**

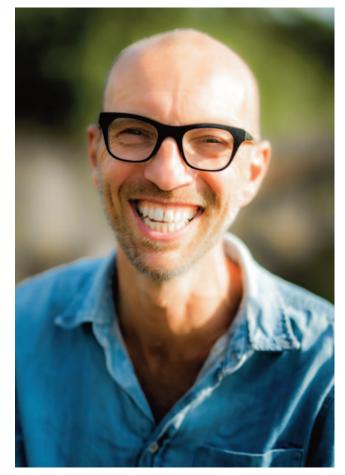
Downside ... I had to start back at the bottom as an HR-consultant before reaching the top again as my foreign experience was not fully validated. Ten years and three promotions later, I found myself in the role of general manager of the biggest juvenile detention centre in Belgium. Lesson #7: sometimes you have to start from scratch in order to climb the ladder again.

At the age of 45, I was a successful manager with a nice salary and a great pension forecast. These are the perfect circumstances that 95% of people long for. Lifetime job security! Yet I was to be faced with hunger for my freedom again.

One day sitting at my laptop, I couldn't stop asking myself why I was actually doing this job. I opened a new campus, and employed 100 very passionate and engaged personalities. Together we made the biggest reorganisation in the history of the detention centre. We turned it from an old prison into a holistic, youngster-oriented institution. Yet, after three successful years, I found myself completely bored and in a golden cage!

My struggles intensified and time brought changes; a new boss did not bring the solution or quell my discontent. Major quarrels and discussions were part of the daily routine which tore me up completely. It was crystal clear that I had to leave the job. Yet I didn't have the courage to do so, and as a consequence, I was fired unexpectedly. **Therefore, Lesson #8, if you don't make your own decisions, someone else will make it for you and be assured it won't be to your benefit.**

A turbulent period in my life started. The



Stijn Staes

union organised a strike, my case was on the national news and even the Minister of Health got involved. In parallel, my father was diagnosed with final stage cancer. I felt my life was taken over by others and negativity.

I found myself at a crossroads and had to choose between prosecuting the government and taking care of my father. I followed the choice of my heart and took care of my father. Those moments I will never forget as they are the most important in life. Remember, moments in life are transient, as well the people we love. They will never come back once they are gone (Lesson #9).

I was so devastated when my father passed away that I decided to take a sabbatical. The remote areas of South Africa and Norway gave me new perspectives and the inspiring idea to become a consultant in the private sector. A small voice inside me whispered that this was not the right job to apply for. Despite my struggles I accepted a very tempting offer as I needed the money. When I was at the beginning of my new role my boss announced to me that the company was broke. This moment was the confirmation of my inner voice. At that stage I realised that money won't make you happy and you should always follow your intuition. That was my most valuable lesson, Lesson #10.

I considered this unforseen dismissal as a fresh start. Strangely I felt blessed. I could finally create my own company, my coaching and HR business. In my coaching sessions, which I often organise outside in nature, I see people turning around their lives, and performing at their best. It is a true blessing that I can be a part of their transformation process.

Furthermore, I've been discovering a beautiful talent of mine, interviewing Belgian top leaders in my podcast, *Studio Stijn, Inspirational Leadership.* I've started yoga classes, horseback riding, singing, and recently, I finished my first painting! It makes me happy to encounter so many inspirational human beings every day and it is a fulfilling, daily life.

To wrap up my life lessons for you: Speaking out in an authentic way has always, in my experience, brought me love and joy. Hiding my true self, accepting or living up to other people's standards and norms have never given me satisfaction or fulfilment.

I still have many dreams to pursue; I want to write a book about my podcast,

have an exhibition of my paintings, and a house in nature. But there is no more urge, no more need to prove myself. I just feel and look at life, take it as it comes. Looking back, I realise that life is full of opportunities, you only have to see and seize them. Enjoy your ride!

Disclaimers

The opinions expressed in this article are the author's own and not necessarily shared by his employer or EMWA.

Author information

Stijn Staes, Executive Coach and Podcaster, worked as a manager for Doctors Without Borders all over the world and in different executive positions in HR and management in Belgium. Today he works with leaders and organisations to optimise their performance and wellbeing. He is the host of the podcast *Studio Stijn: Inspirational Leadership* where he interviews Belgian and international leaders.

Perseverance is the key to success

Finding your way can take time

EAN-RÉGIS: When I completed my master's degree in therapeutic research in 2016 at the University of Picardie Jules Verne, Amiens, France, I had no idea that one day, I would embark on a career in medical writing. At that time, I was passionate about biomedical research, and I really had the ambition to pursue a PhD. Unfortunately, I quickly understood how difficult it is to get funding for a project and to get a steady job at the university. I even had become disillusioned with the profession when I had a discussion with post-docs struggling to get a permanent position in my research unit, despite their skills and their level of experience.

After pondering my career, I decided to embark on a professional reorientation. My goal was to become a teacher in Life and Earth Sciences in public high schools. At first I applied to teach as a contractual teacher but the French Department for Education could not offer me a position. Instead, I accepted a position as a contractual laboratory assistant, which was the opportunity to prepare for the competitive examination to become a teacher, while working directly with adolescents and supporting teachers in different schools. I successfully passed the

written test but not the oral exam. I had held my position of a lab assistant for three years in several high schools, but I was discouraged both by the pupils' behaviour and the difficulty of passing the very selective examination. In addition, my contractual position was precarious employment, and was not sustainable. In the end, I felt too far from my real

motivation, which is working in the health sector. However, my professional reorientation allowed me to finance a new career change: I wanted to leave the public sector, without undertaking another long period of university studies. In January 2020, I applied to the Catholic University of Lyon (UCLy), France, which offers holders of a master's degree or a PhD a one-year professional training course (Biotechnologies Manager IPROB5) with the aim to work in the pharmaceutical industry. While searching on the internet for a profession that could match my scientific knowledge, my skills and my personality, the position of regulatory medical writer piqued my interest. I thought that this may be the job that suits my criteria. I understood what the job could be about as I had the opportunity to be trained on guidelines and regulations of clinical trials during my master's degree. Besides, my master's project was a translational study of patients admitted for vascular and cardiothoracic surgery. These experiences encouraged me further to become a medical writer, which seemed to be the best compromise between my passion for the clinical field and my fondness for writing and languages.

One day, whilst I was browsing the website of the Bernard Gregory Association¹ I came across the interview of Elodie, a medical writer since 2013. The way she described her profession was very engaging to me,² but I didn't know that our paths would cross one day.

A providential encounter in a partly confined world

In January 2021, I started to look for an internship when teleworking was strongly advised in this period of restrictions due to the Covid-19 pandemic. As I was the very first student in UCLy's course to specialise in scientific writing, I had difficulties finding a company that would accept my application, despite UCLy's extensive professional network. Constantly on the lookout

Good organisation is paramount because these reports are long and you have to manage a lot of data and files. for internship offers on LinkedIn, I finally contacted Elodie at 4Clinics. She was kind enough to forward my application to the Director of Medical Writing and Regulatory Affairs and, if successful, would train me in the profession, even remotely. After I had a call in English with the director, 4Clinics eventually agreed to welcome me in late

April for an entirely home-based 6-month internship. The distance did not hinder my learning or my motivation, and this internship confirmed my professional choice.

I mainly worked on adapting international documents to French regulations (summary protocols, informed consent forms, etc.). These are certainly the projects I enjoyed the most – as I said before, I am passionate about languages and medicine. I like the possibility of switching between English and French, and to constantly acquire new knowledge in a wide range of therapeutic areas. The documents may be the same, but their content is always different. Doing quality control had a major influence in my work

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and my training, as I saw the documents from a different perspective. It is a great way to learn from more experienced writers.

I didn't have the opportunity to write a clinical study report for a client, but I wrote one as a training. This was the most challenging part of my internship. Good organisation is paramount because these reports are long and you have to manage a lot of data and files. I also had to familiarise myself with the very specific style of regulatory writing: neutral, accurate, and concise. It was somewhat baffling to analyse my draft after Elodie's review, but this is all part of the learning process.

I also understood the importance of being a team player and communication between team members. I would not have progressed as much without the support of my colleagues and without Elodie's investment. Her advice, comments, corrections, working methods, and her support have contributed to my development.

I am extremely grateful to 4Clinics for allowing me to gain this first experience in medical writing. At the end of my internship, I was offered a permanent contract at 4Clinics. In addition to rewarding my efforts and my personal investment in my professional integration process, this offer has shown me that perseverance is the key to success, and is the beginning of my career in a fascinating field.

If others are still hesitating to embark on this career, I can only advise them to undertake a professional training course to allow them to do an internship. It is the best way to test their own motivation and to gain initial experience before applying for a job. Applying directly as a junior medical writer can be tricky because recruiters often demand a certain level of experience. This kind of training course is a good way to create a professional network and acquire experience to add to your CV.

LODIE: When Jean-Régis contacted me in February 2021, we discussed the feasibility of a remote internship. We knew it would be a challenge for both of us. I had a transparent approach, telling him I had never mentored a trainee in medical writing (approximately 8 years had passed since I last mentored a trainee, in a lab, and supervising is



Elodie Pauwels and Jean-Régis Humbert, after Jean-Regis' internship defense in Lyon, France

quite easy when you share a bench!). Luckily, information technology tools are now well developed, and we could mimic being in a shared office whenever needed so that I could answer orally any question, and even see whether Jean-Régis was struggling with a task or happily focused on it. Communication is the key, even more when you are far away. I briefed Jean-Régis on several types of regulatory documents and we had regular meetings during his assigned tasks (quality control or writing) to discuss different topics, such as writing style, localisation of source

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Jean-Régis Humbert has been a medical writer at 4Clinics France since April 2021.

data, interpretation, or the way of presenting things. I reviewed and made comments on all documents he wrote as exercises and was available to discuss my findings. Supervising Jean-Régis has been rewarding for me (as well) as I saw his competence grow month after month. Jean-Régis had been attentive to comments and tips and implemented them in a timely manner. He became an integral part of our team prior to the end of his internship and we are now lucky to have him on board. May your career as a medical writer be successful, Jean-Régis!

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- Founded in 1980, the Association Bernard Gregory (ABG) works for the professional development of PhDs, the capacity of companies to innovate and the improvement of skills resulting from education through research.
- Association Bernard Gregory. The ABG perspective; Career paths and professions. Medical writing according to Elodie Pauwels, PhD in genetics [published 2018 Nov]. Available from:

https://www.abg.asso.fr/en/ vue/careerpaths-and-professions

Elodie Pauwels has been a medical writer in several clinical research organisations since October 2013.

Finding my path from academia to medical writing

ooking back now, I can trace the origins of my medical writing career to the final year of my master's degree: a year-long research project that had turned into a disaster. My experiments had failed, I had virtually no data, and in my attempts to salvage something, I had left writing my thesis to the very last minute. Then, when I sat down to write, I had the sinking realisation that I didn't really know how. Not that I couldn't write per se, it was only that faced with a blank page I had no idea how to go about it. What should I say, how should I organise it, what was good and what was bad writing? I felt completely overwhelmed and paralyzed by my indecision, constantly second guessing myself. Panicked and under pressure, I threw what I

could together, and submitted it at the last moment. The result was, as you might expect, disappointing.

It is perhaps somewhat paradoxical, then, or maybe masochistic, that after taking time to reflect on this experience my conclusions were: 1) that I wanted to do a PhD, and 2) that I kind of liked writing, and wanted to learn to do it well. I took some confidence from a few positive comments on my thesis, which aligned with areas where I felt things had actually clicked, and seeing my own view confirmed gave me the belief that I had the ability to write, even if my last attempt had gone down in flames.

After some searching, I eventually found a PhD position in Germany, which I followed with

Peter Morgan Associate Medical Writer Azur Health Science peter@azurhealthscience.com

post-docs in the Netherlands and France. I enjoyed research. I did experiments (some of which worked!), I supervised students, I wrote research papers. Being a student and post-doc was fun and an adventure, living and working in different countries and cultures. But now I had to decide the next phase of my career, and life as an academic held little appeal for me. I liked science, but I didn't feel any particular need to be the one making discoveries, and a career in one little niche felt too claustrophobic.

Medical writing had been lingering at the back of my mind ever since I'd heard about it as a PhD student, and the more I thought about it, the more it seemed like the ideal career for me. I had thought a lot about writing since my master's thesis disaster, and writing papers had been one of my favourite parts of the job. Going into medical writing seemed the natural direction, one where I could continue to use my scientific knowledge and further develop as a writer. And so, when my last post-doc came to an end, with my work published and my research career neatly wrapped up, I took the plunge and left academia.

Entering the job market

To start with, I took a little time to decompress and get my bearings. It was liberating, but at the same time, daunting. I had no network outside of academia and no real understanding of how the job market works. Naturally, therefore, I set about searching the easiest and least effective way possible – job adverts.

I applied to many job postings with little success. Responses, when they came, were typically of the thanks-but-nothanks variety. There were many reasons why this might have been the case, and setting out I had been prepared for a trial and error approach, but without feedback I was left guessing. Translating my academic experience to an industry CV was not

straightforward. Many of the relevant skills I had developed were not easily quantifiable, and it was difficult to convey the value I gained from my

research experience in short, neat bullet points. Deciphering job adverts was also new to me, and I was unsure how to tailor my applications in a meaningful way. But the most obvious problem was my lack of industry experience, as even for 'entry-level' positions almost all employers were asking for 2 to 3 years of experience (sometimes going so far as to mark this out in bold font as *mandatory*). On top of this, my years as a post-doc were also a worry, as

I'd read several interviews with hiring managers commenting how they were the death of candidates, how post-docs were too old, overeducated, and under-experienced. All told, it was



Peter Morgan

clear I needed a different approach, and to get anywhere I would need to heed the advice given in big, flashing lights to all jobseekers – network, network, network.

Networking

Through

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as a medical writer.

I was a hesitant networker. Being more of an introverted type, networking sounded intimidating. How do I approach total strangers without any context, other than needing a job? What did I have to offer in return? And there was also the slight problem of being in the midst of the COVID pandemic, and with the world having effectively ground to a halt, formal networking

opportunities seemed pretty limited.

I needed help. I searched around and reached out to Sarah Tilly, of Azur Health Science and Sarah Tilly Mentoring, to ask for advice. On her invitation, I joined a Zoom get together of medical writers in France. Although I didn't have much to contribute, it was interesting and informative to listen in, and I also saw that I was not the only one trying to break into medical writing (yes, perhaps this should have been obvious given the competition for entry-level positions, but it was a lightbulb moment for me). This got me thinking that, as others were presumably looking for advice just like me, it might be good to organise a Q&A where jobseekers could pose questions to experienced medical writers on exactly this problem. It was just the type of event I would like to attend, so why not make it happen?

I proposed the idea to Sarah, and she agreed and asked me to help organise it. A few months later, we did the Q&A as a livestream over Zoom, where we posed questions to a panel of experts. The panellists were helpful and full of insight, and from their answers I gained a better understanding of how employers approach hiring, what they are looking for, and what I could do to improve my chances of success (read: correct all the mistakes I had been making). However, by this point I had gone through the interview process with Sarah and was poised to join Azur Health Science, so I never needed to

put my newfound knowledge to use. Still, the recording is available on the Sarah Tilly Mentoring website for others to hopefully benefit from!

Reflections

With hindsight, I can see there were many things I could have done to make the process smoother. But, through perseverance and a willingness to learn from my mistakes, I eventually found the perfect job for me, and can now look forward to an exciting new career as a medical writer. My advice to you would be to be proactive, and to keep looking forward. Getting your first industry job can be hard, with repeated knockbacks and rejection, but by getting to know people and finding ways to demonstrate your abilities, you'll have every chance to find your ideal job.

Peter Morgan has been a medical writer with Azur Health Science since October 2021.

EMWA is a member-run organisation

When you volunteer to assist EMWA in any capacity, you are furthering the development of our association.

You can choose how you want to get involved: in a very limited way or as part of a larger project. The choice is yours, and everyone shares the benefits.

EMWA members can volunteer in the following areas:

Conference

- Planning committee
- Advertising

Finance

Journal

- Contributions
- Editorial Board

Website

- Contributions
- Web Team

Freelance Business Group

Social Media Team

Training

- Leading workshops
- Professional Developmen
- Webinar contributions
- Webinar Team



Special Interest Groups

- Business Development
- Communicating with the Public
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Veterinary Medical Writing

SECTION EDITORS



Louisa Marcombes louisa@boudimedi.fr Jennifer Bell JenBellWS@outlook.com

Editorial

For this special Sustainability issue of Medical Writing, the editorial team at Veterinary Medical Writing has decided to focus on One Health. As the global society adjusts to adopting a sustainable lifestyle, whether voluntarily or kicking and screaming, assuming a One Health mindset must go hand-in-hand with sustainable living. One Health and sustainable practice are already being incorporated into veterinary school curricula. The clinicians of the near future and many currently in practice are using One Health Medicine to help decision-making and guide sustainable choices for themselves and their animal-owning clients. Medical writers are ideally positioned to propagate One Health thinking; however, to do this, they must incorporate it into their own practice and be comfortable with communicating what is, for many, an abstract concept.

Our contributor to this issue, Dr Deborah Thomson, has pioneered teaching the One Health concept, and she is the founder of One Health Lessons. She is also a veterinarian, an educator, and she was previously a science policy adviser in the United States Senate. Her extensive experience teaching science to a diverse audience has conferred to her unique insights into science communication, which she has shared in her book, The Art of Science Communication, published last year. With an excerpt from her book, Dr Thomson discusses a method to communicate controversial scientific concepts to a sceptical audience. Dr Thomson here imagines the vaccine-hesitant in her excerpt . However, this approach could also be adopted when communicating sustainability and One Health concepts, which may be equally controversial in some quarters. Dr Thomson's methods, which complement those detailed by Michelle Guillemard in her recent Medical Writing article: Addressing vaccine hesitancy in medical writing¹, focus on verbal persuasion. Both strategies are based on empathy, clarity and validation of the audiences'

hesitancy, whether it is based on flawed facts or not.

And we have kept with the One Health theme for this edition of From the Horse's Mouth, with news that a study on pet-owner microbial exchange has been green-lighted and that, in December 2021, the UK recorded the country's largest outbreak of highly pathogenic Avian Influenza. A reminder that, with the backdrop of an ongoing COVID pandemic, the threat of zoonotic disease is constant. So, whilst this is our first foray into One Health medicine, it most certainly will not be our last.

Louisa Marcombes and Jennifer Bell

1. Guillemard M. Addressing vaccine hesitancy in medical writing: How has COVID-19 changed hesitancy communication, and what works? Medical Writing. 2021;30(4):12-6.

The need for clear health communication: From COVID-19 vaccines to the malaria vaccine

here is no such thing as a silver bullet in Τ medicine because medicine is dependent on nature and nature evolves over time. This has been seen most recently with the development and spread of variants of SARS-CoV-2. News of the most recent variant, with its record-breaking number of mutations on the external spike protein, has sparked renewed panic and debate across our small planet. People are wondering -What happens if this pandemic never ends?

In October 2021, the cacophony of the COVID-19 pandemic drowned out the news of a scientific breakthrough: the development of and access to the malaria vaccine for children. According to the World Health Organization, the vaccine's impact is expected to save 1 life for every 200 children vaccinated. This was a historic

event, celebrated by scientists and humanitarians around the world, but now the most important question comes to fruition: How will the public view the malaria vaccine, especially if there is vaccine hesitancy in the community?

The healthcare world has seen this concern time and again, particularly since the various COVID-19 vaccines have been developed and distributed. The simple answer to the aforementioned seemingly complex question is: education. Public education is vital. However, it must be done in a way where the public is not only aware of the science, but also understands and is encouraged to act based on the science. How can that happen when there are people who are hesitant to vaccinate either themselves or their children?

So which strategies can medical communi-

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cators use to bring accepted biomedical science to an audience who may be sceptical about the message conveyed? Below is an excerpt from my book, The Art of Science Communication: Sharing Knowledge with Students, the Public, and Policymakers,1 which details how communication techniques, extrapolated from the fields of business and leadership, can be adopted by medical writers to increase the effectiveness of medical science communication.

Four steps to change the minds of others (an excerpt)

From my personal experiences in the classroom, at the animal hospital, and in a congressional office, I will describe an effective way to not only change people's minds but also to inspire them to accept the change:

Step 1: Respect comfort zones

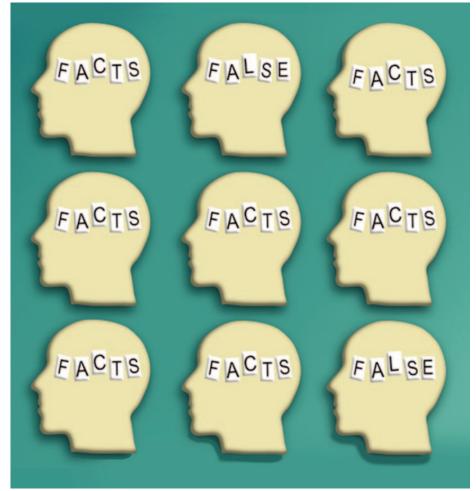
It may sound counterintuitive, but the first step to changing the minds of people is to talk about the inherent benefits of not changing. Recognise that not changing will be much simpler, and people generally take comfort in the status quo. Plus, not changing requires a lot less from people – less energy, less worry, less potential struggle.

Let's use an example of speaking with a vaccine-hesitant person. During your conversation with this person, listen to *why* they distrust the science that legitimises vaccine development and administration. In 2021, despite people being affected by the COVID-19 pandemic for over twelve months, a substantial portion of the American population has refused the COVID-19 vaccine. Instead of becoming angry and/or frustrated, scientists need to be empathetic and listen. Once a person feels heard by another, there is more opportunity to build trust in the relationship. Therefore, the first step is to actively listen and see the world from their perspective.

Step 2: Talk about the costs of changing one's mind

This also may sound counterintuitive. Why would you want to voice concerns about the cost(s) of change? (Costs can include a person's energy investment of moving outside of their comfort zone and being open to both unlearning and then learning new information.) The simple answer, that you may not want to hear is that your audience is thinking about this cost anyway, so you may as well get the topic out in the open. This also demonstrates that you share the same thoughts as your listener. Building upon the first step, this move provides you an added layer of intimacy and makes you appear more relatable.

Taking the vaccine-hesitant conversation one step further, the cost of changing would equate to having the vaccine-hesitant person actually receive the COVID-19 vaccine. It is worth voicing that the vaccine was created in record time, which is both impressive and mystifying to many. Even though the basic science behind the creation of the mRNA vaccine has been around for decades (for more information, search online for Katalin Karikó), there wasn't enough funding to complete the development of mRNA vaccines until the



Vaccine side effects

can happen and

are worth

acknowledging.

Transparency is key.

COVID-19 pandemic flipped the world upside down.

The cost of changing (or, in this case, of getting the COVID-19 vaccine) would address the fact that it is possible to have one or more vaccine reactions such as feeling

ill for a few days to a few weeks, contingent on a person's immune system.

Depending on what type of vaccines are available, there is a chance a booster is needed. This booster further challenges the immune system and improves

its strength to fight the actual virus that causes COVID-19 (SARS-CoV-2). The timing of the booster vaccine is of vital importance as well. If the person (or animal) receiving vaccines is not receiving the booster in a time period that is deemed acceptable for that particular vaccine, they may need to restart the series because of the way the immune system functions. This point bears repeating: the need to restart the vaccine series is not the fault of the vaccine; instead, it is due to the nature of the immune system. The importance of timing of vaccines and their boosters should be discussed so that nobody feels a false sense of security and takes unnecessary risks to their own health. In addition, it is important to review those vaccines are designed to strengthen the immune system but the person

> (or animal receiving the vaccine) could still technically become infected and sick by the pathogen. They just likely won't die from the disease. Again, vaccine side effects can happen and are worth acknowledging. Transparency is key.

Step 3: Address the costs of not changing

Once empathy and trust are established, advance to this step. The goal is to cajole the listener to say "that's right" at least once. Focus on the possible lost opportunities with inaction during this step.

Furthering the COVID-19 vaccine conversation, review how the world changed from 2019 to 2020. Share a story about one or several missed opportunities. Talk about what your expected future would be if not enough people got vaccinated. Would much change for

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the overwhelmed hospitals and, particularly, the first responders and essential workers found in them? (Tip: Emphasising people rather than systems or buildings strengthens the message).

Review that vaccinated people could likely still catch a virus, but they would be less likely to die from the virus. Ask what the vaccine-hesitant

person thinks of this idea. Talk about why you had decided to wear your mask and socially distance yourself from others outside your home for many months. Ask them why they took (or didn't take) certain actions during the pandemic. Talk about why you are tired of

being afraid of a deadly virus and staying away from loved ones in order to protect them. Ask the hesitant person how they are feeling. Talk about how the only way you can stop being afraid is if more people get vaccinated. Talk about how you are tired of seeing sad news reports of the total daily COVID-19 death count. Ask them how we all can get through this together.

(At the time of writing this book, health experts say that the answer is to continue wearing face masks that cover a person's nose and mouth, keep good personal hygiene habits, and vaccinate more people.) Once you hear the vaccinehesitant person say "that's right" at least once, you can move on to the final step.

Step 4: End on a high note

This step brings hope. This is when you speak about the benefits of change. By now, the listener is in agreement with you. It is time to talk about the future in a positive light.

For the COVID-19 conversation, this is where you would ideally hear the other person volunteer to say that they will get the vaccine. However, the world

is far from ideal. Therefore, it is your job to

end the conversation on a high note. Say that you live in less fear since you have been vaccinated because you know that you have strengthened your immune

system in case you encountered the deadly virus. You can now see your fully vaccinated family and friends with less worry. You can now start to imagine your future beyond the pandemic, thanks to your strengthened immune system, which ultimately resulted from your decision to receive your vaccine(s).

In summary

The audience must feel immediately respected, both intellectually and personally, in order to have them exchange the favour and listen to you later in the conversation. Of course, for the medical and veterinary writing community, communication to the audience is through the written, rather than the spoken word. Nevertheless, the principles detailed in this approach can, with a little imagination, infuse medical communications with an empathy that is essential for successfully communicating biomedical science to a hesitant or sceptical audience. Whilst not forgetting to use language appropriate for the audience: the Centers for Disease Control website has an excellent plain language summary of mRNA vaccines.² It is important to remember that a scientist can immediately appear more relatable once they acknowledge their audience's concerns. In addition, acknowledging the future opportunity cost of remaining at the status quo will shift the attention from the vaccine topic today to the projected future. Lastly, leave a positive message that provides hope if the audience does decide to change their mind, and in this case, become vaccinated and encourages others to become vaccinated as well.

Disclaimers

The opinions expressed in this article are the author's own and not necessarily shared by her/their employer or EMWA.

Disclosures and conflicts of interest

Dr Thomson is the author of *The Art of Science Communication: Sharing Knowledge with Students, the Public, and Policymakers.*



From the Horse's Mouth

The quarterly pick of the news from the veterinary world

A research grant has been awarded to the University of Pennsylvania's School of Veterinary Medicine (Penn Vet) to study the clinical significance of microbial exchanges between pets and their owners, it was reported by the *Humanimal Hub* on December 20, 2021. The grant, which has been awarded by the Human Animal Bond Research Institute (HABRI), is titled "Sharing is caring: can pets protect their owners against antibioticassociated disruption of the gut microbiome?" Disruption of the gut microbiome is a commonly encountered complication for antibiotic treatment. It can range from mild diarrhoea to *Clostridioides difficile* infection, and older patients are at higher risk. The study, led by, Assistant Professor of Epidemiology Dr Laurel Redding at Penn Vet, will test the hypothesis that contact with a pet can ameliorate the clinical signs associated with the owner's disrupted gut microbiome. The study will follow a cohort of pet-owning patients over 60 years of age who are on antibiotic treatment following dental implant surgery. Any beneficial effects demonstrated would provide direct evidence of a therapeutic effect of petowner microbial exchange. Although, as noted by the *Humanimal Hub*, it remains to be seen if the researchers adopt a One Health approach and look for a similar effect on antibioticassociated disruption of the gut biome in pets.

A new, free online resource has been launched as a one-stop-shop for veterinary journal publications, it was reported in the *Veterinary Times* on December 23, 2021.

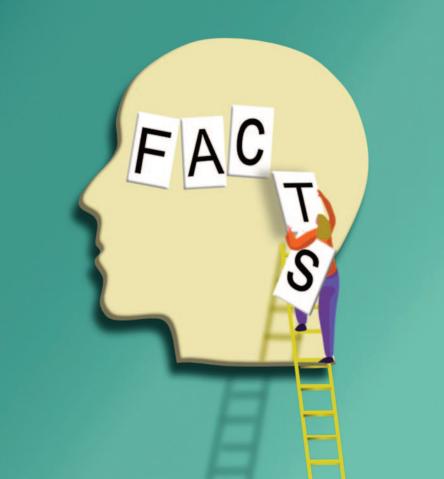
Emphasising people rather than systems or buildings strengthens the message.

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Author information

Dr Deborah Thomson is a veterinarian, educator, previous science policy adviser in the US Senate, One Health consultant, internationally acclaimed speaker, and founder of One Health Lessons, a global organisation that inspires children and adults to value the interconnection between human health and the health of the environment, plants, and animals. She is the Chair of the World Veterinary Association's One Health Education Subgroup, which provides guidance to veterinary schools worldwide in their One Health educational programmes.



Graphic: Louisa Marcombes

The website, vet-lit.org, created by Dr Simon Cook, a lecturer in Veterinary Emergency and Critical Care at the Royal Veterinary College, UK, is a one-stop-shop for users to access information about the latest articles from the foremost veterinary publications. With clinical disciplines and species divided into different areas for easy navigation, there is also an openaccess section, where users can access publications directly. The website features journals such as the Journal of Veterinary Internal Medicine, The Journal of Small Animal Practice, and Veterinary Surgery. However, the selection of journals is based on the reading list for clinical speciality, so the choice of journals drawn upon bears a clinical bias. Nevertheless, it promises to be a valuable resource for readers interested in keeping updated with the veterinary literature.

ublic Health Veterinarians in the UK Ρ were dealing with the "biggest ever" outbreak of Avian Influenza (AI), according to the UK's Animal & Plant Health Agency's Blog on December 16, 2021. At the time of writing, 55 cases of high pathogenicity H5N1 had been confirmed across various regions of Great Britain. A nationwide AI prevention zone was implemented on November 3. From November 29, all birds were required to be kept indoors (wryly dubbed "Flockdown" by the bird-keeping community). AI outbreaks in the UK are usually linked to the arrival of migratory birds during the winter months, and cases in wild birds are first seen in late autumn. However, epidemiologists have observed that the first cases this year were found at the end of October, much earlier than usual. This, along with a greater scale of disease burden in wild birds, resulted in an elevated risk for

domesticated birds, which translated to the large number of cases recorded by the end of 2021. Bird keepers, whether commercial or hobbyists, have been ordered to adopt strict biosecurity measures, which were expected to be in place for several months. The public at large were asked to report the discovery of dead wild birds, particularly target species such as ducks, geese, swans, gulls, and raptors. This is against a background of high pathogenicity AI outbreaks confirmed in 41 countries from different regions since May 1, 2021, as reported by the World Organisation for Animal Health (OIE). Highly pathogenic H5N1 is a zoonotic disease and needs to be tackled under a One Health approach and as a priority of the OIE-FAO-WHO tripartite alliance. As the COVID-19 pandemic rumbles on, this outbreak is a timely reminder of the threat that other viral zoonotic diseases pose to public health.

Lingua Franca and Beyond

How to make our life easier?

It was my pleasure to invite my colleagues from the European Association of Science Editors (EASE) to share their editorial experience with us medical writers. By doing this, we can improve our writing, which will facilitate more successful submissions. The first article to open this collaboration is by Sylwia Ufnalska, who writes about *Help Scientists Save Time*, a campaign launched by her and successfully run by the EASE. During this campaign, the *EASE Quick-Check Table for Submissions* and the *EASE Guidelines for Authors and Translators of Scientific Articles*, were promoted, and I hope that you will find these interesting and helpful.

Maria

SECTION EDITOR

Maria Kołtowska-Häggström, MD PhD maria.koltowska-haggstrom@ propermedicalwriting.com

What can we do to promote more efficient and ethical communication of research results?

Certainly, as medical

writers and

translators, we play a

crucial role now and

the results of our

work affect the

future of societies.

A sale s a long-term member of the European Association of Science Editors (EASE) and the EASE Council (2009–2021), I initiated and coordinated the publication of many resources for science editors, scientists, and science translators. In October 2020, I launched a campaign called Help Scientists Save Time,^{1,2} which promotes simplification of the editorial requirements for initial manuscript submission. Together with Alison Terry, we developed the EASE Quick-Check Table for Submissions (Table 1) for journals to include at the beginning

of their instructions for authors, 3,4 to facilitate searching for basic information needed for submission. A short guide to constructing such a table (updated version 3.1) has already been translated into 15 languages and is available as DOCX files from the EASE website.³

Communication of research results can also be improved by

using the EASE Guidelines for Authors and Translators of Scientific Articles, which explain how to write complete, concise, and clear manuscripts.⁵ The main part of the guidelines is freely available in 30 languages. The Italian Chapter of EASE has decided to translate also its appendices (Abstracts, Ambiguity, Cohesion, Ethics, Plurals, Simplicity, Spelling, and Texttables) and additional information, to aid further streamlining of the publishing process. Recently, Golden Rules for Scholarly Journal Editors⁶ and other helpful EASE publications for scientists, science translators, and editors have been briefly presented in bilingual slides at a webinar for the Ukrainian Chapter of EASE⁷ (and later translated into Japanese).⁸ Many other authors have also suggested interesting improvements in scientific communication. These include changing the IMRAD to BOMRAD⁹ (that is, replacing the Introduction by two sections: Background and Objectives), complete elimination of presubmission formatting and cover letters,¹⁰

> creation of centralised websites that serve many journals, to allow swift resubmission from one journal to the next,¹¹ and publishing full-text scientific articles in HTML (not just PDF) to facilitate machine translation.¹²

As medical writers or science translators, or both, we have a limited influence on the decisions of manuscript authors

and journal editors affecting research waste and editorial procedures; however, we can still refer to international standards in our correspondence with them. Our role in raising awareness about ethical issues is also essential, as explained in the EMWA guidelines on the role of medical writers, e.g. "The writer should also ensure that conclusions are fully supported by the data and that publications do not contain unjustified claims. [...] Medical writers should also draw Sylwia Ufnalska Science translator and editor

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attention to any limitations of the study in the discussion section. [...] If a writer is aware of good quality evidence that contradicts a point being made in a review, or in the discussion section of a primary publication, the writer should attempt to ensure that this research is cited."¹³

All this can contribute to improving the efficiency and quality of scientific communication worldwide and, consequently, to solving urgent problems. These include serious questions related to syringe disposal after vaccination, indoor air pollution during the COVID-19 pandemic,14 the widespread fever phobia, longterm stress and limited physical activity, as they lower our natural immunity and increase the risk of many serious diseases.^{15,16} Certainly, as medical writers and translators, we play a crucial role now and the results of our work affect the future of societies. Our attempts to prevent misinformation and make medical publications more reliable are very much appreciated. I strongly believe that collectively we can make a real change for the better.



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Table 1. Brief introduction to the EASE Quick-Check Table (version 3.1, https://doi.org/10.20316/quick.3.1)

It is intended to make life easier for both authors and editors. When preparing such a table, editors can delete or add some rows if they wish.

Example journal: Quick check for submissions

The following table is provided as an example of how the details in this form may be presented. BASIC INFORMATION FOR AUTHORS

GENERAL GUIDELINES	Manuscripts should be COMPLETE, CONCISE and CLEAR (see <i>EASE Guidelines</i> , ¹ available in many languages). Follow the appropriate reporting guideline, ² if applicable
WORD LIMITS, etc.	

Body text	≤ X words (justified exceptions allowed)
Abstract	\leq X words; structured for original research (BACKGROUND, OBJECTIVES, METHODS, RESULTS, and CONCLUSIONS)
Keywords	\leq X terms, singular, separated with commas; lowercase except proper names; avoid abbreviations
Highlights (below the abstract)	X-Y bullet points (\leq X words each, describing the study in lay terms)
Tables/figures	\leq X tables/figures in total. Their description (captions, values, units, etc.) should be consistent and informative, with all abbreviations explained

TITLE PAGE INFORMATION

Title	\leq X characters, with a description of the study type, if relevant
Short running title	\leq X characters
Author names	Full name: given name(s) first, family name last
Affiliation info required	Department, institution, postal address, email
Corresponding author contact details	Indicate with an asterisk, supply phone number
Persistent identifiers of author(s), etc.	$ORCID \underline{iD}(s)$, ³ identifiers of research project(s), if applicable

STRUCTURE OF BODY TEXT, END MATTER, REFERENCES

Typical headings	Introduction (background and objectives), Methods, Results, Discussion (with a concluding paragraph)
Subheadings	\leq X levels of subheadings, not numbered
Specific wording required for any section	Methods section must include usual ethical approval for human and animal studies (Helsinki/Institutional Review Board compliance, informed consent) and subsection "Statistical analysis", identifying the variables and methods used
End matter (e.g. authorship contributions)	Identify authors by initials in the authorship contributions section (consider using CRediT) ⁴ and add information about funding, if received
References: maximum number	Not limited (with DOIs, URN, PURL, etc. if applicable)
Referencing style	X style required after acceptance (not for initial submission); for more details and examples, see <url>. Endnote style can be downloaded here <url>. Make sure that each citation is complete and accurate</url></url>

FORMATTING

Spelling	UK or US, if consistent
General style	Numbers ≥ 2 as numerals (for exceptions, see <i>EASE Guidelines</i>) ¹ Statistics: $p \leq 0.001$, $n = ##$

SUBMISSION NOTES

Cover letter required? Specific content?	Not required but text field in the online submission system allows for comments to the editorial office. Inform if the study was presented elsewhere
Links to all required author forms: needed at submission or after acceptance? Signed by all authors or by submitting author?	 EASE Ethics Checklist⁵ signed by corresponding author, at submission EASE Form⁶ and/or ICMJE COI forms⁷ signed by all authors, at submission
Proposed reviewers: optional/mandatory? How many? What details are required?	Optional: suggest/oppose up to 3 potential reviewers (full name, email, institution). Consider diverse peer reviewers in terms of sex/gender, ethnicity and geographical distribution
Tables: separate files?	Include at the end of the manuscript (separate pages)
Figures: separate files? Any formats preferred?	For initial submission, figures can be embedded in the manuscript. If it is accepted, high-resolution files (EPS/TIFF/RAW) will be required
Supplementary files?	Upload any supporting data or other required files for review
Fees for open access, colour, etc.?	Publication fee X. Colour free online but X per figure for print

JOURNAL POLICIES, ETC.

Publication model*	Open access, licence X; fee structure: <url></url>
Preprint and prepublication	Articles already available on preprint servers or published in another language can be accepted but this must be declared at the time of submission
Data sharing	Recommended repositories: Clinical trials must include a data sharing statement; other studies may also do so
Peer review**	External, double-blind review usually by X reviewers. Editors make the final decision
Manuscript acceptance rate and average times	About X% submitted manuscripts are accepted. Average time from submission to first decision after peer review: X months

Abbreviations: EASE, European Association of Science Editors; ORCID iD, persistent digital identifier of researchers and contributors (to distinguish between those with the same names); CRediT, Contributor Roles Taxonomy; DOI, digital object identifier; URN, Uniform Resource Name; PURL, persistent uniform resource locator; ICMJE, International Committee of Medical Journal Editors; COI, conflict of interest.

* Publication models: subscription, hybrid (open access optional for a fee) or open access.

** Peer review systems: open, single-blind (authors do not know the identity of review not know the identity of authors), triple-bind (also editors do not know the identity of authors/institution).

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My First Medical Writing

Editorial

I am pleased to share an article by an aspiring medical writer from Poland. Hanna Kurlanda-Witek finished her PhD in geoscience at the University of Edinburgh, specialising in microbiology. After working in an environmental consultancy for a few years, she became a freelance science writer, writing about a variety of topics, from radioactivity, to viruses, to plastics. She has now started a career in medical SECTION EDITOR



Evguenia Alechine ealechine@gmail.com

writing, contributing here with an insightful article on biofilms aimed at creating awareness on the infections they may cause. Hope you enjoy this reading.

Evguenia

Gooey and resilient: Biofilms in a clinical setting

hey clog up pipes, coat your teeth, and flourish on benchtops. These communities of microorganisms, known as biofilms, are a cause for concern in the healthcare industry. In Europe, infections caused by biofilms in hospitals alone affect over 4 million patients per year, leading to 37,000 attributable deaths and contributing to an additional 110,000.¹ In the United States, the Centers for Disease Control and Prevention (CDC) estimated that at any given time, 1 in 31 hospital patients has a

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contributing to an

additional 110,000.

healthcare-associated infection (HAI).² These numbers are not the consequence of a disregard for hygiene by hospital staff, instead they indicate how ubiquitous biofilms are and how difficult it is to eliminate them. Like most bacterial colonies, biofilms thrive on wet surfaces. which is why they are easily found on implants, catheters, and wound dressings. However, biofilms are also perfectly able to survive in dry conditions. One study demonstrated that dry surface biofilms were found on 95% of disinfected items in hospitals.³ The last two decades

have seen extensive research carried out on biofilms, yet they still have the upper hand in hospitals and clinics, and pose a significant medical challenge.

The perfect community

Biofilms can be described as 3D bacterial communities, often consisting of many types of microorganisms. It is estimated that 99% of

bacteria on Earth live in a biofilm.⁴ In fact, most of the actual biofilm is made up of exopolysaccharides (EPS), the slimy substance that bacteria secrete. The EPS creates an ideal microbial ecosystem by neutralising harmful conditions, aiding in gene transfer and nutrient exchange, keeping enzymes close to bacteria, and providing a means of intracellular communication known as quorum sensing. As the biofilm matures, pieces of it detach and colonise other areas. Non-attached biofilm aggregates have

> also been associated with chronic infections, such as cystic fibrosis, a genetic disease characterised by biofilm infections in the lungs.⁵

> Biofilms are by no means uniform, accommodating bacteria at different stages of growth and varied metabolic phases. Typically, the bacteria at the outer edges of the biofilm are most active, as they have plenty of accessible oxygen and nutrients. But it is the dormant, slow-growing bacteria in nutrient- and oxygen-depleted zones within the biofilm that are key to its success. Antibiotics

and other antimicrobial agents attack the outer layers of the biofilm, leaving the deeper layers intact. Considering how often antibiotics are used in healthcare, the bacteria become increasingly tolerant to ever-rising concentrations. Under laboratory conditions, bacteria in biofilms were demonstrated to be 100 to 1000 times more resistant to antibiotics than "freeliving" planktonic bacteria.⁶ Hanna Kurlanda-Witek Warsaw, Poland h.kurlanda@gmail.com

The biofilm-fighting toolbox

The tolerance to drugs is a particular threat in treating patients, as increasing dosage of antimicrobials or biocide strength may result in unfavourable side effects. Also, in terms of



medical devices and instruments, the use of strong oxidisers for an extended amount of time is not often possible. The current approach is to use multi-targeted therapies to combat biofilms. Their complex structure results in a no "one size fits all" method of reversing biofilm growth, similar to the modern-day treatment of tumours.⁷

One way of disrupting biofilm structure is to use physical methods, such as high-velocity sprays, which may contain antibiotics or other common biocides. As an at-home example, the use of a dental water jet has proved to be very effective at removing oral plaque biofilm.8 Coating the surface of medical implants or impregnating wound dressings with, for example, silver nanoparticles, is a method of discouraging biofilm growth before it begins. A similar approach is to re-engineer the surfaces of implants and catheters to make them antiadherent to bacterial colonisation; changing surface charge, increasing surface roughness by etching nanoscale-structures, or making the surface more hydrophobic are just some ideas for preventing bacteria from sticking to medical devices.9

Once a biofilm has grown, the use of EPStargeting substances is a beneficial technique for breaking up the biofilm. The EPS components can be hydrolysed using enzymes or mechanically disrupted with lasers or ultrasound treatment. Using these methods in combination with antimicrobials is crucial in preventing biofilm regrowth. 7

Making the leap from basic science

Many solutions for limiting biofilms in health facilities are still at the laboratory stage. The results are convincing, but there are far fewer follow-up experiments in vivo or with the use of human cell models, which is why very little new strategies for combating biofilms advance to clinical trials. Of the clinical trials that are being conducted, most concern oral biofilms, while biofilms in healthcare-associated infections (HAIs) or in chronic diseases are underrepresented.¹⁰ Also, despite the amount of research conducted on biofilms (over 40,000 papers as of the end of 2019¹⁰), many studies still focus on growing bacteria in Petri dishes, or even on analysing planktonic forms of bacteria, instead of focussing on real-life scenarios in the biofilm world. A multidisciplinary approach to biofilm research is essential to fill the void between studies in molecular biology and medicine. Teaming up with start-ups that aim to bring antibiofilm products to market is also a means of pushing basic science forward and fueling innovation in this field. The "more research is needed" attitude is not enough; it is integrative research on biofilms in healthcare settings that

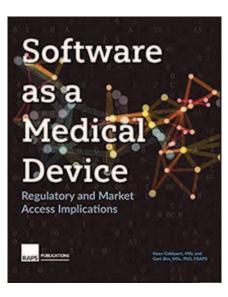


will ultimately decrease the likelihood of infection.

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In the Bookstores



Software as a Medical Device

Regulatory and Market Access Implications

By Koen Cobbaert, Gert Bos, Gloria Hall (editor) Regulatory Affairs Professionals Society (RAPS) Publications 2021 (eBook); 2021 (paperback) ISBN: 978-1-947493-62-9 (eBook) \$175.00 (non-member); 240 pages

s the authors of this book, Koen Cobbaert and Gert Bos, state "software joins the dots, by connecting patients with healthcare professionals and breaking down the boundaries between everyday objects, medical devices, and medicine."

As a medical writer drafting clinical evaluation reports for medical devices and related regulatory documentation, it is extremely important to be fully aware of the implications of medical devices software evaluations. In today's medical devices, software is becoming more and more present, and very often, software is integrated into hardware devices to enable them to achieve their medical purpose. In late 2019, I attended a thorough training course called Software as a Medical Device which helped me understand how complex the field of health software is becoming.

Very helpfully, in Spring 2021, the Regulatory Affairs Professionals Society (RAPS) published Software as a Medical Device, Regulatory and *Market Access Implications*, a comprehensive manual covering this complex regulatory landscape. Subject matter experts in the field have collaborated and contributed different chapters to the book.

The book can either be read in hard copy or as an eBook. The eBook version is particularly useful considering the length (240 pages) and the fact that this version allows the reader to run "searches" on the text. After a preface, the book is divided into 15 chapters, each one addressing a different and specific topic on software, from classification to clinical evaluation, risk management, and usability engineering, among others.

Chapter 1 navigates the reader through an introduction to the field, and Chapter 2 defines what "Software as a Medical Device" is. If you do not know the difference between medical device software (MDSW), software as a medical device (SaMD), software in a medical device (SiMD), software modules, wearables, and software as an accessory, both from a conceptual and from a regulatory point of view, this chapter will really help you navigate through those differences. There are significant variations in how different regulatory jurisdictions consider software in the scope of their medical device legislation, and this is something medical writers should be aware of. Chapter 2 will

If you do not know the difference between medical device software (MDSW), software as a medical device (SaMD), software in a medical device (SiMD), software modules, wearables, and software as an accessory ... this will really help you navigate through those differences.

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text helps the reader fully understand the regulatory definitions and draws attention to the differences and peculiarities.

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After a manufacturer establishes that a product is within the scope of the EU Medical Devices Regulation (MDR), it needs to be classified. Classification rules rely on various regulatory concepts that a manufacturer needs to learn before classifying their products. Chapter 4 covers "Classification of Medical Device

Software" and provides a broad insight into this topic.

Chapter 5 on "Clinical Evaluation of Software" addresses one of the areas in which regulatory medical writers are most often involved: drafting the Clinical Evaluation Report and related documentation. On one hand, there is the drive to foster innovation, and on the other, a need to protect patient safety. Clinical evaluation ensures that the standards on safety and performance are guaranteed. However, the rapid development of software as medical device applications brings both opportunities and challenges. The book has a series of chapters addressing the risks of medical device software.

definitely help readers understand these contrasts.

Chapter 3 defines what constitutes "Software as an In-Vitro Diagnostic Device", describing qualifying in-vitro diagnostic software in the EU, the US, and Canada. Again, various jurisdictions may apply slightly different definitions. These three chapters are the foundation upon which a medical writer may build further knowledge. The The "Safety and Risk Management of Software" is covered in Chapter 6, and "Security Risk Management" in Chapter 7.

Some rather technical chapters follow that address the development phase of devices: "Software Development" (Chapter 8), "Open Source and Third-Party Software Components" (Chapter 9), "Software Usability Engineering" (Chapter 10), and finally, "Artificial Intelligence" (Chapter 11). These chapters are highly technical and may not be suited to all medical writers.

The quality and reliability of health apps is fundamental to having physicians prescribe them. The quality and reliability of a health app may be judged on nuances such as the app's privacy settings, use of patient data, and ethics. Physicians need to have the certainty that a given app fulfils a set of quality and reliability parameters to feel at ease prescribing it. Each of these aspects is addressed in Chapter 12, "Quality and Reliability of Health Apps".

It is no wonder that the digital distribution of health apps is rather complex. Regulatory guidance has addressed physical product distribution, and the digital path proves to be challenging. There are many economic operators involved, and contractual nuances do not make the task easy. Guidance on regulatory implications of digital distribution models is reviewed in Chapter 13.

Manufacturers, and more experienced medical writer colleagues, frequently use medical

device acronyms without necessarily defining them. Medical writers who are new to the field may find the list of acronyms used in the book and presented at the end very helpful as they build up their knowledge in this area of medical writing.

Personally, I found the figures and tables in the book very useful. The authors use these to summarise complex or lengthy concepts. The index at the beginning of the book is well designed and will help the reader find what they need at a glance.

This book presents an updated overview of the topic. Still, it should also be considered that medical device software is a continuously evolving topic. New guidance documents may be released at any moment, particularly on artificial intelligence and online distribution, which are two current hot topics. However, given there are few books available covering this topic it makes this a unique book and an excellent source of information.

Finally, some considerations on the

technicality of the book. Medical writers new to the field will find the first five chapters interesting and helpful and may not feel that their lack of prior knowledge is a limit to their understanding. Seasoned medical writers with experience in this field will still find a lot of useful information in these and subsequent chapters (Chapters 6 to 9, particularly). Additional chapters (Chapters 10 to 15) provide advanced and rather technical information, which may not be immediately applicable to the daily writing projects of medical writers. These last chapters are definitely too technical for medical writers with no experience of medical devices.

Overall, the book goes into much detail and can get rather complex for a medical writer entering the field for the first time. A careful and thorough read is needed to profit from its content entirely. If you are among those writers who would benefit, you might consider using the book as a reference manual of where to go to answer queries, but not as a book to be read from A to Z.



Good Writing Practice

SECTION EDITORS

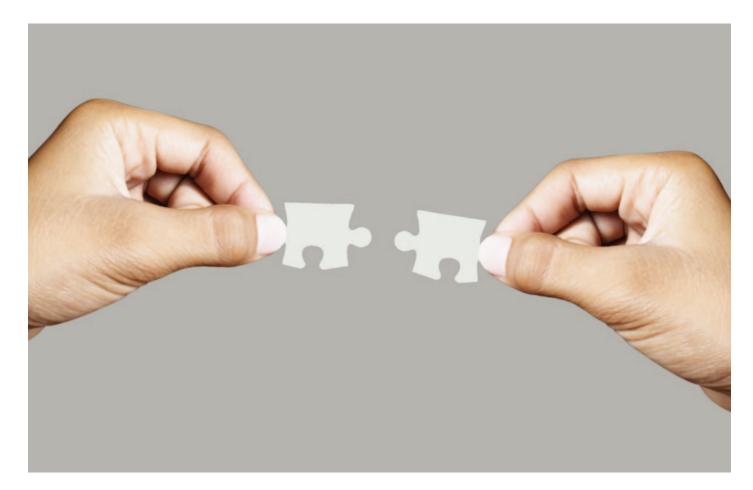


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Grammatical misagreement in function:

Participial phrases (present, past)



Introduction

he present participle using and the past participle based on, both traditionally adjectivals, ostensibly misfunction without a noun to modify (a modifee). The frequency of their usage and misusage in research writing justifies a separate article for analysis and revision.

Experimental sections

Part 1 - Materials and Methods section: method

Example: Present participle

Ascorbic acid was determined colorimetrically using a,a-dipyridyl.

Revision 1

Ascorbic acid was determined colorimetrically with a,a-dipyridyl.

Revision 2

Ascorbic acid was determined colorimetrically by using a,a-dipyridyl.

Notes

A participle dangles either before or after an independent clause without an obvious modifee. In the Example, because ascorbic acid is not using anything, the participle dangles. This dangling results from usage of the passive voice of the following active voice sentence: Using a,adipyridyl, we colorimetrically determined ascorbic

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acid. However, it would be an unnecessary usage of the personal pronoun we in a Materials and Methods section, where we is a narrative focus on the agent rather than the thematic (*ascorbic acid*).

In Revision 1, the usage of the preposition with supports the hypothesis that using may function as a preposition, for which there seems no dictionary support.

In Revision 2, the preposition-gerund phrase

by using functions adverbially by structure and position (i.e., close to the verb phrase modifee *was determined*).

To require consistent usage of *by using* may seem a hypercorrection and pedantic, because *using* alone is so common. However, *by using* is unmistakably adverbial, whereas *using* is not.

Part 2- Materials and Methods section: method

Example: Present participle

The emulsion was forced through a Lipex extruder (Lipex Biomembranes) containing polycarbonate membranes (Nucleopore) at a pressure of 300 PSI using argon gas.

Revision

The emulsion was forced (**300 PSI**, argon gas) through a Lipex extruder (Lipex Biomembranes) containing polycarbonate membranes (Nucleopore).

Notes

This Example is presented to include another type of revision of the adverbial *using*, namely syntactic reduction. In this Revision, the details of the gas used to force the emulsion through the extruder can be embedded as the noun phrase appositional secondary detail (*300 PSI*, *argon gas*). Such secondary detail is deemphasised (by length and parentheses) rather than being over-stated as the sentence-ending phrase *using argon gas*.

Contextual Sections

Part 1 - Discussion section: research results consequence

Example: Past participle

Based on this mechanism, <u>we</u> formulated a model that illustrates the dynamics of holographic grating formation.

Revision 1

Based on this mechanism, **a model was** formulated that illustrates the dynamics of holographic grating formation.

Revision 2

A mechanism-based **model was** formulated that illustrates the dynamics of holographic grating formation.

Notes

The participial phrase *based on this mechanism* traditionally functions adjectivally modifying a contiguous noun, which is not *we* in the Example, but *model*, as in Revision 1.

In Revision 1, there is a contiguous placement of modifier to modifee by transformation into the passive voice *a model was formulated*, thereby resolving any apparent misfunction and eliminating the non-thematic focus on *we*.

In Revision 2, the orienting phrase and subject are melded as a test of modifier-modifee relation.

An adverbial equivalent of based on may be the

phrase on the basis of (or according to this mechanism) which as an adverbial prepositional phrase modifies *formulated*. Being adverbial, such modifiers need not be contiguous to their modifee, but such contiguity would reinforce a structure-function pattern.

Summary

Dissonance results from the adjectival and adverbial misfunction of *using* and *based on*. Revision options: the adjectival function of the present participle *using* and the past participle *based on* either can be transposed contiguously to a modifee or transformed to a decidedly adverbial form such as *by using* or replaced with an adverbial unit such as *according to*.

Experimental sections

- Adverbial misfunction with a dangling present participial phrase: Ascorbic acid was determined colorimetrically using a,α-dipyridyl.
- Over statement of the sentence-ending phrase: The emulsion was forced through a Lipex extruder (Lipex Biomembranes) containing polycarbonate membranes (Nucleopore) at a pressure of 300 PSI using argon gas.

Contextual sections

 Adverbial misfunction with non-contiguous placement of modifier to modifee: Based on this mechanism, we formulated a model that describes the dynamics of holographic grating formation.



The Crofter: Sustainable Communications

SECTION EDITOR

Kimi Uegaki kimi@iwrite.nu

Editorial

Greetings from the croft! As a member of the EMWA's Sustainability Special Interest Group (SUS-SIG), I'm excited about this issue of *Medical Writing* focusing on sustainability. There are so many aspects of sustainability and recently, the link to the word "sustenance" hit me. And it got me thinking about what crofters might cook in their kitchens, and that it would be fun to share easy, nourishing recipes with each other.

I imagine crofters cooking – as much as possible – with locally grown, organic foodstuffs that are produced on a small-scale, and in this way, eating meals that sustain both their health and environment. Winwin!

In this issue, I'd like to share a recipe for a quick and easy two-bean chilli, a handy go-to when you're faced with a document deadline at the end of the day. And for ideas on where you can source organic, local, and environmentally friendly foodstuffs in your region, please check out the directory link in this issue's Your sustainable lifestyle journey infographic by Kate Silverthorne and Louisa Marcombes on page 36

If any of you have favourite plantbased recipes that you would like to share in future issues, please send them to me. Also, if you know of helpful websites to add to the sustainability directory, please send them to Kate Silverthorne at kate@silverthorne.im. Thanks in advance and happy reading and eating! Best, Kimi



TWO-BEAN CHILLI

ADAPTED FROM THE VANCOUVER SUN 6 O'CLOCK SOLUTIONS COOKBOOK

INGREDIENTS

- 2 tbsp (30 mL) vegetable oil
- 3 medium onion, chopped
- 1 tsp (5 mL) cumin seeds
- 2 green bell peppers, chopped
- 3 garlic cloves, chopped fine
- · 2 cans (398 mL) chopped tomatoes
- 1/2 cup (125 mL) water
- 1 tbsp (15 mL) unsweetened cocoa
 powder
- 1 can (398 mL) red kidney beans in chilli sauce
- 1 can (398 mL) black beans, drained and rinsed
- 2 cups (500 mL) fresh, canned or frozen whole corn kernels
- salt and pepper to taste
- extra chilli powder and cayenne powder (optional)
- chopped fresh cilantro
- 1 avocado, sliced

DIRECTIONS

1. Heat oil in a large heavy saucepan over medium heat.

2. Add onions and cumin seeds; sauté for 5 minutes or until the onions are translucent.

3. Add green peppers and garlic; sauté for 1 minute.

4. Add canned tomatoes, cocoa, and water; bring to a boil.

5. Add chilli kidney beans, black beans, and corn. Turn down the heat and simmer, uncovered, for 15 minutes.

6. Add salt and pepper to taste.

7. Serve with a sprinkle of cilantro and slices of avocado on top.

Can also serve with a dollop of yogurt or sour cream, or grated cheddar cheese. Goes well with nachos and (Mexican) rice. Other side dish ideas: grilled corn and sweet potato fries.

Note: I often prepare this in the morning; it's a nice break from sitting at the computer and the flavours get a chance to meld.

PREP TIME: 15 MINS COOK TIME: 25 MINS TOTAL TIME: 40 MINS

Biotechnology

Editorial

This is the first *Medical Writing* Biotechnology regular section. Biotechnology is a broad subject. It can be defined by the use of biological systems and living organisms in production processes. Biotechnology has been around for thousands of years. Think of yeast to make bread. In more recent years, we have used biomolecules and living organisms to make medical treatments.

I am pleased to begin this section with an

article written by Vanessa Zaiatz Bittencourt and Sheng-Chih Chang. Their article is about animal testing and discussions concerning alternatives that are in development. It has a balanced view as one author works in a company that uses animal experiment technology, and the other works in a company that manufactures non-animal experiment technology.

Biotechnology is used to develop defined animal gene lines, e.g., humanised mice. It is also used to develop *in vitro* and *in silico* alternatives

SECTION EDITOR

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to animal testing like an organ-on-a-chip.

This *Medical Writing* issue is about sustainability and Vanessa and Sheng-Chih highlight some of the waste that occurs during drug development.

The subject of biotechnology is so broad that no one person can be an expert on all of it. I want to thank Vanessa and Sheng-Chih for opening my eyes wider.

Jennifer Bell

Non-animal alternatives for research and development are gaining popularity

o guarantee drug safety and efficacy, regulatory agencies recommend testing drugs and other chemicals in two different animal species. Testing is initially done in a rodent and then in a larger, non-rodent mammal. Most research laboratories rely on mice experiments. Mice have a similar genome to humans, are relatively cheap, have a fast reproductive rate, and a short life span. Therefore, they are considered a suitable animal model for initial trials in drug discovery.

Dogs are usually the second species selected for safety assessments of new medicines. A dog's metabolism and response to drugs is closer to human responses.

However, what happens when a drug experiment succeeds in one animal model but fails in the other? Are animal models a fit-forpurpose strategy for advancing drug discovery? With the recent reduced success rates in drug development, how can we deal with a last-minute revelation that a particular animal was not the ideal model to study a specific drug? These are just some circumstances that make us question if our scientific process is sound.

The importance of animals in research

Animals have played a vital role in many medical and scientific advances of the past century. Due to the role of animals, insulin, penicillin, and the polio vaccine have been discovered, just to name a few examples. Scientists can reproduce human disorders in distinct animal models and reproduce manifestations, mimic pathophysiology, and use drugs to cure the condition.¹ The use of animal models in research is a very complex and an important topic to be discussed between scientists and also with school children.²

To guarantee drug safety and efficacy, regulatory agencies recommend testing drugs and other chemicals in animals and submitting a document with all the relevant information collected. The final study report must disclose all details of the study (study raw data and conclusions, name of the researchers, signatures, dates) and a summary. The document should, among other things:³

- Discuss the number of animal studies conducted
- Specify the number of animals used
- Justify the rationale for the model selected
- Describe the similarities of the selected replac model compared to humans and the scient methodology used
 Animals have

Grant applications also require detailed disclosure of research on animals. The applicant must demonstrate that the animal facility is adequately equipped and trained staff is available. Methods and Research Design sections must

discuss how the animals will be treated and justify the selected species and number of animals that will be used.⁴

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Sheng-Chih Chang

Medical Technologist Taihoya Corporation Kaohsiung, Taiwan

Ethics in animal research has increased significantly over the past few years. Yet approval of new technologies for animal substitution is growing slowly. There are a lot of arguments by scientists who are familiar with traditional methods and are still not convinced by the benefits of new technologies. Scientists want – rightly – further validation to justify animal replacement. By doing research on animals, scientists avoid risking human lives in the initial

> phases of drug discovery. Initial experiments are invasive and could result in human death. There is a safety risk even after animal testing, but scientists argue that this risk is significantly higher if we do not test on animals first.

> The European Animal Research Association describes forty reasons

why animals are needed for biomedical research.⁵ Briefly, many important scientific findings, such as development of vaccines and drugs, relied on

played a vital role

in many medical

and scientific

advances of the

past century.



animal data suggesting that these findings would never happen without animal research. Another reason is that animals and humans are very similar physiologically and perform tasks in a similar way.⁵

An open letter from the Confederation of Spanish Scientific Societies exists detailing why animals cannot be substituted in the fabrication of antibodies.⁶ The authors argue that by using animals, scientists can generate antibodies with higher affinity and specificity than those generated using other methods and that substitution of traditional technologies requires further scientific validation.⁶

Animal experiments can only be conducted after a harm-benefit analysis and approved by authorities. European and American committees have created guides to guarantee that the animal experiment is scientifically, technically, and humanely appropriate.⁷ When planning animal experiments, scientists should apply the 3Rs principle (replacement, reduction and refinement) (see Table 1).⁸

Drug development challenges

Drug development has stagnated for years, mostly because costs and time required for discovery are increasing. Pharmaceutical companies deal with many challenges during new drug identification, such as not knowing the cause and mechanism of many human disorders and the lack of good models of human disease.^{9,} 10

Research for a new drug begins in the laboratory with *in vitro* experiments (e.g. using commercially available cell lines) and animal

testing to answer basic questions and to understand diseases. However, humans are complex organisms. We differ greatly from single cells cultured in a plastic dish or mice, dogs, or any other animal used for scientific experiments.

Scientists are investing in improving mice models to best reflect human responses. These models are called "humanised" mice.11 Despite the capability of circulation of human-derived cells in these novel models, mice organs, central nervous system, and muscles are not altered. The question that arises is: why should we spend money and years of research improving an animal model that will never develop and respond to diseases exactly the same as humans? A missing gene, protein, or enzyme in an animal model could ruin drug discovery and innovation. While these models are useful and have contributed to a better understanding of disease mechanisms, science needs additional innovation to complement or even substitute animal models to advance drug discovery.

Agencies like the European Union Reference Laboratory for Alternatives to Animal Testing and other research laboratories and centres around the world are doing critical work showing that we have plenty of options to substitute

Table 1. The 3Rs principle

3Rs	Definition	
Replacement	Methods that avoid or replace the use of animals	
Reduction Methods that minimise the number of animals used per experiment		
Refinement	Methods that minimise animal suffering and improve welfare	

Table adapted from⁸

animals in research with better results when compared to animal models.^{12,13} We need more laboratories implementing these new techniques, to show the specificity and reproducibility of the results until these novel approaches are fully accepted by the scientific field, especially government agencies.1

Experiment reproducibility in animal research

Concerns on the low reproducibility rate between different laboratories of pre-clinical results exist. It does not necessarily mean that the original finding was wrong but raises questions of what is correct.^{14,15} There are many reasons why an experiment is not reproducible, from laboratories not sharing the complete list of research materials used, to poor research design, to differences in Animal studies animal experiments.¹⁵ A survey alone can lead carried out by Nature in 2016 found that more than 70% of scientists have failed at reprovaluable drugs. ducing other scientists' experiments.¹⁶ When scientists

around the world can obtain the same results, this gives strength to the original work. Therefore, to standardise result reports, development of principles and guidelines for reporting preclinical research has been developed by governmental agencies like the National Institutes of Health.14

Like us, animals are directly impacted by their surroundings. Availability and type of food and habitat can impact our behaviour and response to treatments. Animals created at distinct research centres are fed and treated in different ways, which impacts how animals develop a disease and respond to treatment.¹⁷

Mice have higher anxiety when picked up by their tails, which is the most common method of mice capture and handling. This can significantly influence experimental results. Therefore, research groups are investigating the best way to hold mice so they are not stressed during an experiment. Using acrylic tunnels to carry the mice without direct human contact or allowing the mice to freely walk on the handler's open hand without restraining favours less stressed mice during experiments.¹⁸ This indicates that if a researcher is not careful on a particular day and holds the animals in an inappropriate manner, this may lead to different results when compared to someone that handles the animals with care.¹⁹

Important genetic differences between humans and animals

Humans constitute the taxonomic order primates, which include lemurs, lorises, tarsiers, monkeys, and apes. Humans are well known for being social, smart, communicative, and to have a remarkable cognitive ability. We have distinct anatomy, physiology, and cognitive behaviour. Our closest living relatives are chimpanzees. The genetic difference between individual humans is around 0.1%, and when compared to chimpanzees, this difference jumps to 1%. Still, nonhuman primates only account for 0.28% of all laboratory animals used in research in the USA. 90% of the animals used in research are mice, rats and other rodents, from which our genetic difference can reach up to 2.5%.²⁰

Due to evolution, almost every gene found in humans is found in a similar format in other mammals, making them models for studying disease and researching new drugs. Other

> animals like fish, flies, parasites - in some respects - also have similarities to humans, allowing novel findings in science. Large variation of specific gene families can be identified between humans and other animals.²¹ This is natural, it is evolution, and it

highlights our differences.

to loss of

Animals have different absorption, distribution, metabolism, and excretion (i.e. pharmacokinetics) of drugs when compared to humans.^{22,23} Curiously, pharmacokinetics, together with toxicology and safety are the main reasons for drugs failure in clinical trials.²⁴ The Encyclopaedia of DNA Elements (ENCODE) (www.encodeproject.org) Project allows scientists to compare the differences and similarities between human and mouse genomes.²¹ By doing a direct comparison, scientists can pinpoint differences in the metabolism or immune system between species

at the genome level and decide based on these differences if a murine model is indeed the best model to support their research, and this can help to reduce animals in research in a meaningful way.²¹

Drug molecule and experimental animal waste

An overall estimate of global animal use in scientific procedures is around 80 million animals for

2015 alone.²⁵ Potential drug candidates do not progress into clinical studies usually because of animal toxicity, while other approved drugs are later identified as potentially hazardous for human health, which causes drugs to be either relabelled or removed from the market. Animal

studies alone can lead to loss of valuable drugs and subsequently waste of animals.²³ This is one reason why we need regulatory agencies and private organisations to invest in non-animal alternatives to complement or replace animals in research.

A simple practical example is that dogs cannot eat grapes, and we still are not sure why. Grapes can cause severe reactions, lead to kidney failure, and ultimately the dog's death. Similar danger is observed when dogs are fed chocolate.

Let us pretend that chocolate is a new drug and regulatory agencies request proof that this novel compound is safe for human consumption. Scientists decide to test it on dogs as their metabolism is close to humans. After a few trials, it was identified that dogs presented panting, vomiting, tremor, hyperthermia, tachycardia, hypokalaemia, elevation of different enzymes, etc. Even after decontamination, 98% of the dogs that presented these symptoms died.²⁶ The company ends up writing a detailed report with all the acquired data and reasons why chocolate could potentially be harmful to humans and, therefore, should not be sold. Further investigation into the chocolate chemical structure would also be considered during development of new products as a warning of possible toxicity and exclusion of new drugs with similar structures at the early stage of discovery.

The future of non-clinical testing in drug discovery

We understand more about mouse biology than our own human biology. Therefore, it is difficult to identify hidden threats and missed opportunities during research using animal models. Indeed, we cannot rely on ex-vivo experiments alone either, we need more options.

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using animal

models.

We need to generate robust data that reflects how the human body works and that can he systematically extracted, analysed, and applied in a specific field of research. Generation of in silico data combined with accurate in vitro data is one of the solutions. We should focus on improving our biotechnology devices and techniques. Dynamic culture,27 bioprinters,28 organoids,29 organon-a-chip,³⁰ to name just a few. We

also need to take advantage of advances in computing to upgrade in silico technology.31

New technologies for antibody production that do not require animals have been proven to be a powerful animal substitute allowing generation of antibodies that would be extremely

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difficult if using animals.³² The generation of antibodies that do not derive from mice has been shown to have increased therapeutic efficacy and can avoid detrimental consequences e.g. development of allergic reactions against mice generated antibodies.³³ Phage display technology, an *in vitro* antibody selection method, has been used to isolate antibody candidates to treat different diseases. Many antibodies developed by phage display technology have been recently approved by the FDA to treat different diseases like cancer. For instance, the PD-L1 inhibitor atezolizumab was approved in 2016 for bladder cancer and is currently in different clinical trials of other tumour types.³³

Our intention with this article is to acknowledge we still have a long way to go to completely stop using animals in research as we are still adapting.⁵ The scientific community upholds the highest scientific and ethical standards, and this article offers a perspective on that. Many countries around the globe have already established national centres dedicated to the development and validation of alternative methods, while government agencies are concurrently investing heavily in legislation and strategic roadmaps to allow drug approvals using in vitro and in silico methods.^{13,34,35} We have a tremendous amount of data from OMICS (genomics, transcriptomics, proteomics, metabolomics) and tools at our disposal to make scientific research cheaper, faster, and more relevant to human physiology, we just need more support from the scientific field.

Government agencies are concurrently investing heavily in legislation and strategic roadmaps to allow drug approvals using *in vitro* and *in silico* methods.

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The opinions expressed in this article are the authors' own and not necessarily shared by their employers or EMWA.

Disclosures and conflicts of interest

One of the authors works for a company that manufactures non-animal experiment technology. One of the authors works for a company that uses animal experiment technology.

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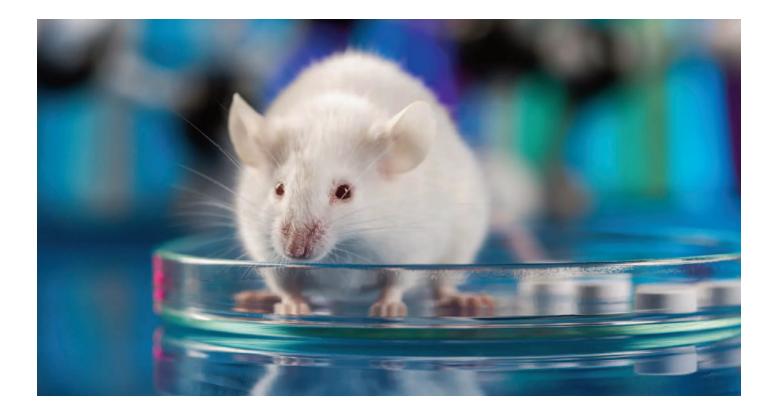
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Pharmacovigilance

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Editorial

The Pharmacovigilance section of this issue is related to the first Meet & Share online event held in December 2021 by the EMWA Pharmacovigilance Special Interest Group (PV SIG) with more than 70 attendees!

Subject matter experts shared their experience and thoughts on the impact of recent guidance, e.g. the Clinical Trials

Regulation in the European Union (EU-CTR), the British Medicines and Healthcare products Regulatory Agency (MHRA) guidance, Japanese and Chinese requirements on development safety update reports (DSURs), and on Japan's Sakigake approach (first-in-class first-in-world accelerated approval). Stefanie Rechtsteiner was one of the presenters in the online event, and here shares with our readers some of the topics

and thoughts that were discussed there.

If you have experience with the topics, or questions or comments related to the article, please contact the PV SIG at info@emwa.org. We hope to have further discussions and learn more together in our next meeting!

> Happy reading, Tiziana

Guidance impact on Development Safety Update Reports

regulations,

directives, or

guidance

documents

the DSUR.

he Development Safety Update Report Т (DSUR) guidance, issued by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH),¹ was introduced in 2011. ICH E2F has not been updated since implementation, unlike other safety guidances, such as Good Pharmacovigilance Practices (GVP) Modules V or VII. Nevertheless, the DSUR has been keeping

safety writers on their toes. This is not only because this concise and well-structured document covers a broad spectrum of topics and both the pre- and post-marketing life-phase of a drug, but also because of its alliance to other documents, such as the Risk Management Plan (RMP), the Periodic Benefit Risk Evaluation Report (PBRER), or the Investigator's Brochure (IB).

The DSUR summarises important safety information from

clinical trials. It is submitted to health authorities across the ICH region and therefore addresses requirements and needs of recipients across the world and brings all of them to the same level of knowledge about a drug under development. It seems natural that new or updated regulations, directives, or guidance documents associated with clinical trials will potentially impact the DSUR.

Recent guidances are the Clinical Trial Facilitation Group (CTFG) Question & Answer (Q&A) document,² the latest Clinical Trials Regulation in the European Union (EU-CTR) No 536/2014 Q&A,3 and guidance text released by the British Medicines and Healthcare products Regulatory Agency (MHRA)⁴ and by the MHRA together with Health Canada (HC).5 CTFG and EU-CTR are EU initiatives to

harmonise the preparation, It seems natural that submission, and review of clinical trial applications, and new or updated the conduct of clinical trials. Among many other topics, they describe which Reference Safety Information (RSI) should be used for determining the expected terms in the cumuassociated with lative summary tabulation of clinical trials will serious adverse reactions potentially impact (SAR) that is provided as an appendix of the DSUR. The RSI, i.e. usually a specific subsection of the IB,² is used for

> determining the expectedness of SARs. If a serious event is considered related to the investigational drug and the serious reaction is not included in the RSI, it is categorised as a suspected unexpected serious adverse reaction (SUSAR) and must be reported to health authorities (and possibly ethics committees) as per statutory timelines. The ICH E2F guideline1 does not go into this level of detail and simply

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By Stefanie Rechtsteiner

states that the RSI (here the IB in general) that is effective at the beginning of the reporting interval should be used for the assessment of new safety information.

Unfortunately, the definition of the RSI version to be used for the DSUR in the new EU guidance seems to be in conflict with the guidance provided in ICH E2F in 2011. This conflict has resulted in confusion and discussion within companies responsible for writing DSURs, and between these companies and health authorities outside the EU.

CTFG 0&A document on RSI

The CTFG updated their Q&A on the RSI in November 2017 and advised sponsors that the primary purpose of the RSI is to serve as the basis for expectedness assessment for expedited reporting of SUSARs and for annual safety reporting. This had an impact on the version of the RSI that was used for the identification of expected SARs in the DSUR cumulative summary tabulation of SARs. The instructions for update, submission, and applicable version of the RSI for the DSUR are summarised in Table 1.

CTFG determines that the most recently approved RSI is the relevant one for the DSUR.

	CTFG Q&A	EU-CTR Q&A	MHRA Inspectorate blog
When to update RSI?	The RSI should only be updated once a year.	Recommendation to update the RSI once a year, in alignment with the DSUR.	-
When to submit updated RSI?	The RSI should be submitted together with the DSUR, "on the same day or shortly thereafter".	The updated RSI should be submitted in parallel to the DSUR, or at the latest within one month of submission.	The MHRA refers to the instructions provided in the CTFG Q&A document, according to which the RSI should be submitted in parallel with the DSUR (on the same day or shortly thereafter). ²
Which RSI version is relevant for the DSUR?	For the identification of SUSARs in the "Cumulative summary tabulation of serious adverse reactions", the version of the RSI most recently approved in all member states should be used. This most recently approved version should at the same time be considered as the "RSI in effect at the start of the annual reporting period".	For the identification of SUSARs in the "Cumulative summary tabulation of serious adverse reactions", the RSI in effect at the start of the annual reporting period should be used. The RSI in effect at the start of the annual reporting period should be the version of the RSI in the IB most recently approved in at least one member state in which clinical trials are ongoing with the investigational drug.	For DSURs for trials in the United Kingdom and also other EU countries, MHRA requires sponsors to use the RSI that was approved at the beginning of the reporting period by both the MHRA and European member states.

Source: CTFG Q&A, EU-CI'R Q&A, MHRA Inspectorate blog2-4

Abbreviations: CTFG, Clinical Trial Facilitation Group; DSUR, Development Safety Update Report; EU-CTR, Clinical Trials Regulation in the European Union; IB, Investigator Brochure; MHRA, Medicine and Healthcare products Regulatory Agency; RSI, Reference Safety Information; SUSAR, Suspected unexpected serious adverse reaction

If the RSI is updated and submitted with a DSUR, and approved some time afterwards, then this newly approved RSI would be the most recently approved for the next DSUR. Since after RSI submission the previous RSI remains in effect until the new one is approved, the RSI in effect at the start of the annual DSUR reporting period would not be the same as the one most recently approved. Figure 1 is from the CTFG Q&A document and illustrates which RSI version is relevant for the DSUR.

Figure 1 shows that for the purpose of identifying unexpected terms in the cumulative SAR tabulation of the current DSUR, the version of the RSI created at the time of the last DSUR (DSUR no. 9, IB no. 6) and submitted in parallel (or shortly thereafter) should be used. Consequently, it would be the RSI version in effect at the end of the DSUR reporting period (IB no. 6) and not the one in effect at the beginning of the DSUR reporting period (IB no. 5) that is relevant for determining the expectedness of terms. This seems to be contradictory to ICH E2F.¹ The CTFG resolved this contradiction by determining that the RSI

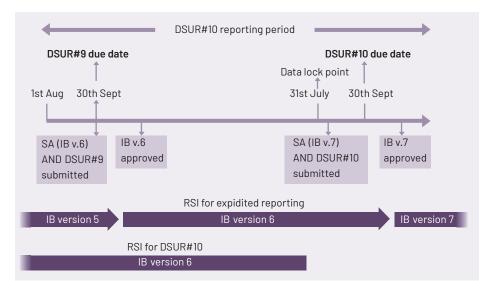


Figure 1. CTFG Q&A - DSUR and RSI version

Source: https://www.hma.eu/fileadmin/dateien/ Human_Medicines/01-About_HMA/

Working_Groups/CTFG/2017_11_ CTFG_Question_and_Answer_on_ Reference_Safety_Information_2017.pdf



most recently approved in all member states "should be considered to be the 'RSI in effect at the start of the annual reporting period'".^{1,2}

Regulation (EU) No 536/2014 Q&A on RSI

The new EU-CTR 536/2014 (Regulation [EU] No 536/2014 of the European Parliament and of the Council of April 16, 2014 on Clinical Trials on Medicinal Products for Human Use, and repealing Directive 2001/20/EC) was issued in May 2014. Since December 2014, the related Q&A document has been discussed progressively, and the final version (version 5) was released in January 2022.³ The regulation also came into effect on January 31, 2022.

The EU-CTR Q&A guidance requests the RSI in effect at the start of the annual reporting period to be used for SUSAR identification in the DSUR.³ This would be in line with ICH E2F. However, in the sentence that follows it is defined that the "'RSI in effect at the start of the annual reporting period' should be the version of the RSI in the IB most recently approved [...]".³ So the CTFG and EU-CTR Q&A documents use almost the same wording, just in changed order. Both documents refer to ICH E2F. Both require sponsors to use the latest approved RSI version, and at the same time consider this latest approved version to be the one that was also in

effect at the start of the DSUR reporting period. The EU-CTR Q&A even shows the same figure as the CTFG Q&A to illustrate which version of the RSI is relevant for which DSUR. Both guidance documents have resolved what could be seen as a contradiction with ICH E2F, by stating that the most recently approved RSI should be considered as the one in effect at the start of the annual reporting period.

MHRA "Inspectorate" blog on RSI

In February 2021, the MHRA released an article in its "MHRA Inspectorate" blog⁴ in which the authors describe common findings in inspections and how to avoid these, and which also addressed the RSI.

In the section on the DSUR, one of the findings that the blog article describes is that "the RSI used for the DSUR listings is not the same RSI in place at the start of the reporting period".⁴ The authors point this out, even with an exclamation mark at the end of their sentence: "Please remember that for the purpose of writing the

... for the purpose of identifying unexpected terms in the cumulative SAR tabulation of the current DSUR, the version of the RSI created at the time of the last DSUR [...] and submitted in parallel (or shortly thereafter) should be used.

DSUR for trials conducted in the UK, as well as other EU countries, you need to use the RSI that was approved at the beginning of the reporting period by both the MHRA and European member states!"⁴ If cases are presented in the DSUR listings with their expectedness based on a version of the RSI different from that approved at the beginning of the DSUR reporting period,

> the MHRA will consider this as incorrect - following ICH E2F with this decision.^{1,4} Consequently, SARs in the DSUR should be presented as unexpected if they are not included in the RSI valid at the beginning of the DSUR reporting period. This rule should be adhered to even if the next version of the RSI (the one submitted with the previous DSUR, which comes into effect during the current DSUR's reporting period and is therefore the latest one approved) does include this SAR. The MHRA considers the RSI "to be fixed at the start of the reporting period in order to set a baseline for review of all safety data received in comparison with this".4

The MHRA has announced that after the EU-CTR transition phase (January 31, 2022, to January 31, 2025) they will publish United Kingdom (UK) specific guidance to clarify whether elements of the EU-CTR will apply also for the UK.

For the time being, sponsors will have to decide whether to follow ICH E2F and at the same time fulfil the MHRA's request for using the RSI in effect at the beginning of the reporting period, or to concur with the logic of the CTFG and EU-CTR instructions and use the RSI version that was most recently approved. One view that was brought up at the Meet & Share event was that it makes sense that the data cut-off for the DSUR and the RSI are the same. This is an argument in favour of using the latest RSI version approved, because it is the one that was submitted with the previous DSUR, with analyses performed at the same level of knowledge and using the same data status. The RSI version in effect at the start of the DSUR reporting period has a data cut-off that is one year older.

We continue to see a contradiction between "in effect at the start of the reporting period" and "the version of the RSI most recently approved", even after many discussions and continuous efforts to find the logic in equating the one with the other, as is done in CTFG and EU-CTR.

MHRA, HC, and EU-CTR on safety signals

The RSI topic caused extensive discussions and continues to do so. Two further topics that are included in a guidance document released by the MHRA and HC⁵ and that are also included in the new EU-CTR, are likely less controversial, but will also have visible implications for the DSUR. Sponsors are requested to transparently describe their safety review process,^{3,5} i.e., they should "explain how they performed their due diligence during the reporting period".5 This description, as per EU-CTR, should provide information on "their surveillance processes for reviewing and identifying potential new safety signals and updating existing safety signals, including but not limited to how often data is reviewed and by whom, what type of data source/format is reviewed, and what potential action may arise as a result of the surveillance process".³ Additionally, the criteria used for adding or deleting expected terms in the RSI should be described. All of this should be included in a region-specific appendix (EU-CTR)³ or in the region-specific information section of the DSUR (MHRA/HC).5 The EU-CTR and MHRA/HC also require that the outcome of the signal process is presented in the DSUR, and for both the format used in the

PBRER is acceptable, but not mandatory. The EU-CTR even acknowledges that signal evaluation for clinical trials may not always be possible or appropriate, and that a justification for not including this information should in such a case be provided instead.³

EU CTR on study ID, case ID, and subject ID in the DSUR

One more change for the DSUR will come with the new EU-CTR for those sponsors that so far included the subject ID in the document. The DSUR appendices contain listings and tabulations, like the interval and cumulative SARs, cumulative SAEs, a list of fatal cases, or of subjects who dropped out of a trial because of adverse events. Some of these data appendices use identifiers for the cases that are presented. So far, depending on the processes and systems established and used by a sponsor, these identifiers would be study ID, case ID, and/or subject ID. To ensure that patient's rights are protected, the new EU-CTR now clarifies that the subject ID should not be used for this purpose: "[...] SARs in the line listing should be identified by case ID and study ID without including subject ID in this document".3 For the DSUR as well as for any potential investigation any authority will initiate, for example on a specific SAR, sponsors are asked to provide the corresponding data in anonymised manner and without revealing the subject ID.

Conclusion

As we have seen, there is quite some change on the horizon and the appearance of the DSUR will most visibly change by the additional signal presentation, with an additional regional appendix required for this purpose. But once the safety review process is described and the description transferred into template boilerplates, this will cause no additional work for future DSURs, and neither will the presentation of the actual signals, at least for those drugs that are on the market and for which a PBRER is available, from which this can be copied. It is the seemingly small changes, like avoiding the subject ID in line listings, that can cause quite some technical effort or can require substantial process changes, depending on a sponsor's database and established processes. And the presentation of expectedness in the cumulative SAR tabulation by applicable RSI version can be a tricky task remember, it should be the one that was in effect at the start of the DSUR reporting period and the latest one approved, and only experience (and authority feedback) will show whether this indeed is the contradiction we perceive it to be.

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The author would like to thank Tiziana von Bruchhausen and Sven Schirp for constructive discussions and valuable feedback.

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Protection of the environment is part of Good Clinical Practice (GCP)

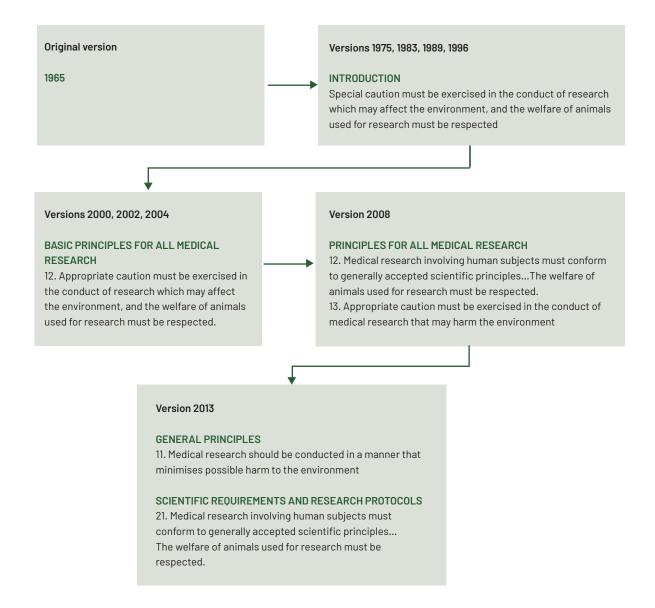
id you know that the Declaration of Helsinki¹ does not only cover the protection of human subjects, it also provides for the protection of the environment and animals? And for almost 50 years!

The diagram below shows how the language has evolved but the principles were already in place even before "sustainability" and "climate change" became common everyday terms. Raquel Billiones, Editor-in-Chief

Reference

 World Medical Association. Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. Published 2013. [cited on 2021 Nov 30]. Available from:

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Upcoming issues of Medical Writing



June 2022:

Medical devices

The implementation date of the EU Medical Device Regulation has arrived, marking a new era of heightened attention to medical device safety and performance. This issue will explore the experiences, challenges, and lessons learned over the last years preparing for the MDR requirements as well as potential opportunities these changes bring. Moreover, we touch base on the implementation of the EU In-Vitro Diagnostic Regulation and on other aspects of writing for medical devices.

Guest Editors: Kelly Goodwin Burri and Beatrix Doerr



September 2022:

A virtual workforce

Working remotely/working from home has become the norm these days. This issue will focus on various aspects of working from home – the good, the bad, the ugly. We will have articles on the challenges of writing from home, managing teams and also, on how some of us overcome these challenges and enjoy this opportunity.

Guest Editor: Archana Nagarajan

The deadline for feature articles is June 1, 2022.



CONTACT US

If you have ideas for themes or would like to discuss any other issues, please write to **mew@emwa.org.**

December 2022:

Open Science and Open Pharma

Open access ensures that the highest quality, peer-reviewed evidence is available to anyone who needs it, anywhere in the world. This issue will focus on how open access and plain language summaries improve transparency, advance medical science and ultimately improve patient care. Focus will also be given to how Open Pharma, a group of pharmaceutical companies and other research funders, alongside healthcare professionals, regulators, patients, publishers and other stakeholders in healthcare, are driving this goal.

Guest Editors: Martin Delahunty, Tanya Stezhka, and Chris Winchester

The deadline for feature articles is September 1, 2022.

