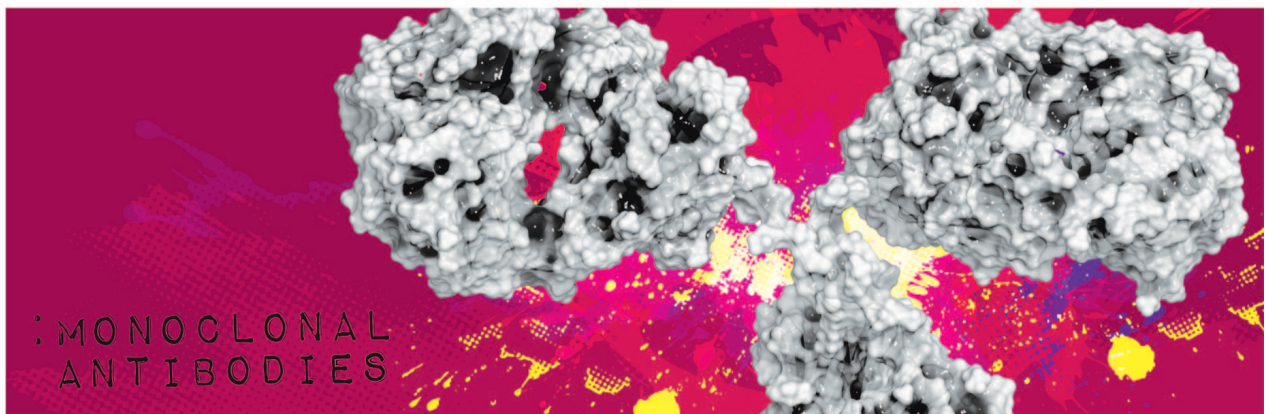
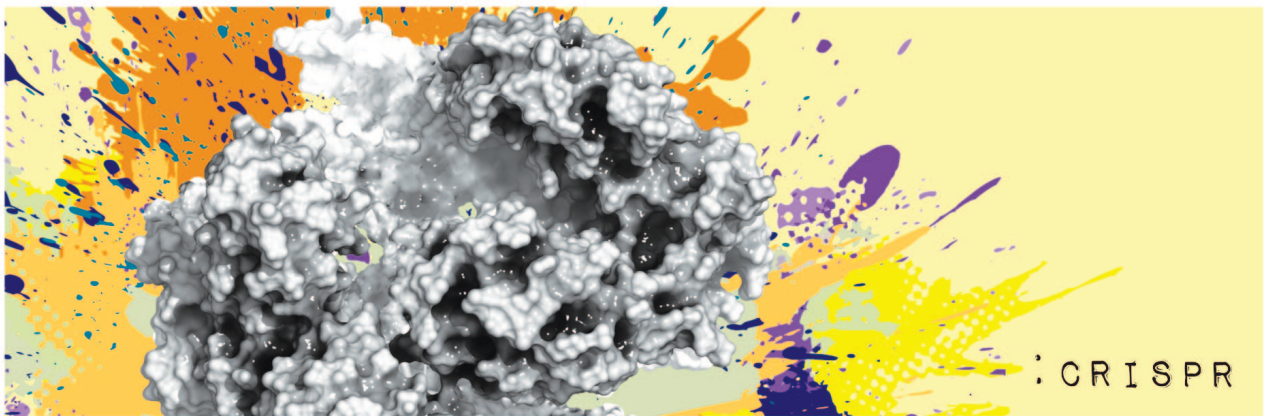


Medical Writing

Biotechnology



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- Harold Swanberg, MD: Why and how EMWA should remember him
- A veterinary surgeon reflects on her cancer journey
- Tools to revolutionise your digital workspace in 2024

Volume 32 Number 4 | December 2023



EUROPEAN MEDICAL WRITERS ASSOCIATION



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.

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Medical Writing



THIS ISSUE December 2023 | Volume 32 Number 4

Biotechnology

“Biotechnology, as diverse as the colours of the rainbow, has touched all our lives in one way or another; some would even say it has ‘encroached’ upon all aspects of daily life – ready or not.”

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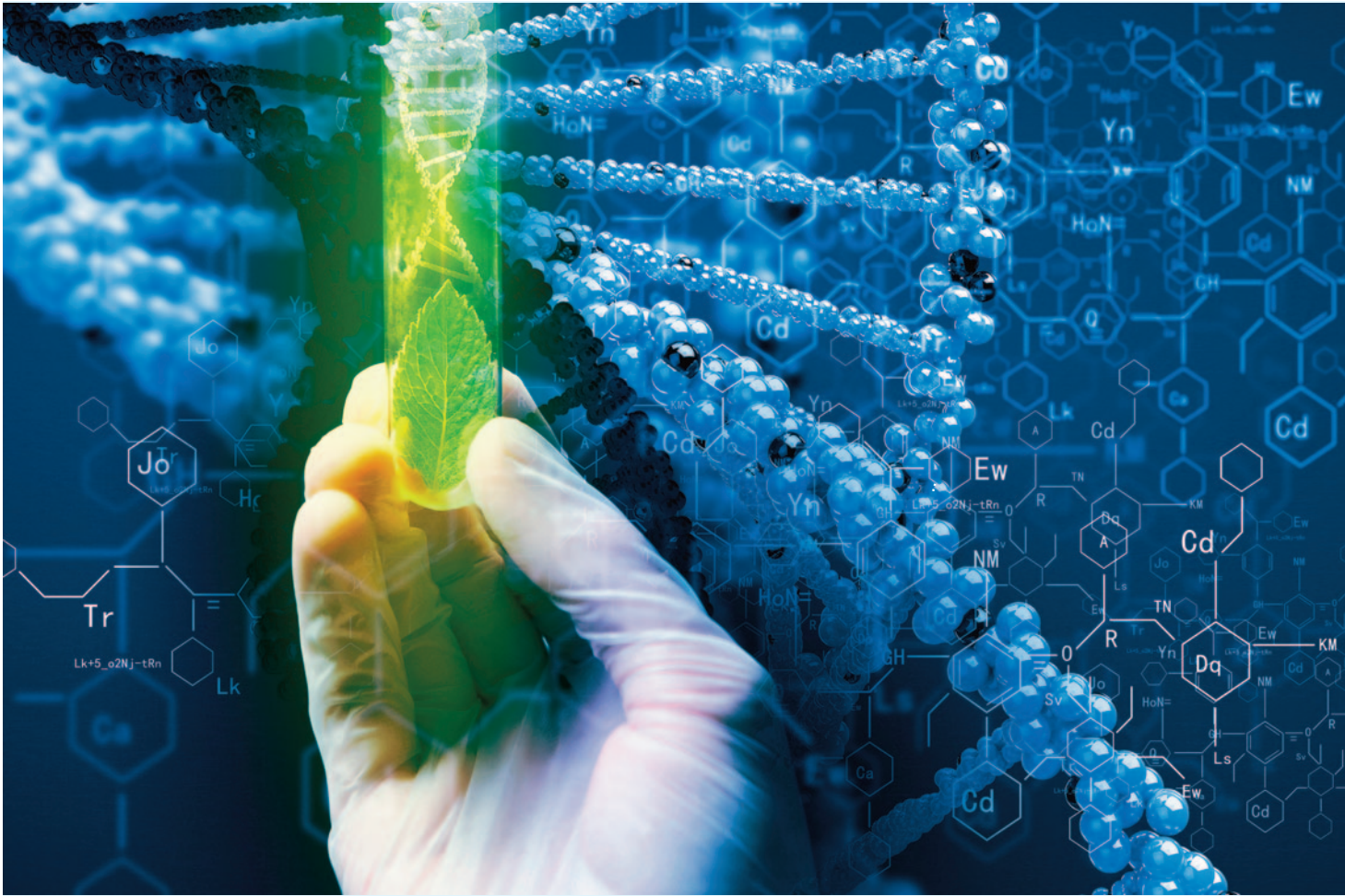
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Medical Writing explores the many faces of biotechnology

This *Medical Writing* issue focuses on the crucial role of medical writing and communications in biotechnology and product development in healthcare. In the pharmaceutical and medical device industries, biotechnology uses biological systems and living organisms in R&D and production processes for product development. Some biotechnologies include biologic and biosimilar pharmaceuticals, vaccines, and advanced therapy medicinal products (ATMPs), including gene and cell therapies and tissue engineered products.

Biotechnology is not a new topic in *Medical Writing*. Contributions to the Biotechnology section, which I edit, have shown how biotechnology is applied in different ways. It supports the pharmaceutical product lifecycle, for instance, in non-clinical

GUEST EDITOR



Jennifer Bell
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doi: 10.56012/zskr5275

work using *in silico*, *in vitro*, and animal testing methods as outlined by **Vanessa Zaitz Bittencourt** and **Sheng-Chih Chang** in our March 2022 issue.¹ Biotechnology and artificial intelligence (AI) interface where AI makes finding healthcare solutions easier and faster, wrote **Ahmad Nazzal** in our June 2022 issue.² And some biotechnology might seem a little ... curious, as written about by **Jana Kubátová** in our December 2022 issue, where she described how one person's healthy

gut microbiota can be transplanted *via* their faeces to help a person with unhealthy gut microbiota.³ Indeed, biotechnology is a platform technology that is applied so broadly that some applications seem unusual.

Medical Writing provides readers with information to help them in their careers, and this issue highlights the broad applications biotechnology has in areas supported by medical writers. It is important to pay attention to how individuals define biotechnology because definitions vary depending on a person's background, for example, academic vs. industrial.

Biotechnology is used in biomanufacturing, also known as bioproduction. "Biomanufacturing" and "bioproduction" are terms that are familiar to the pharmaceutical industry.⁴ They are also familiar to industrial



So, don't drop
biotechnology
product boxes
on a
transportation
cross dock and
leave them
there in 40°C
heat!

biotechnology used outside the pharmaceutical industry. **Jim Philp**'s article "Biomufacturing and One Health" outlines the significance of biomufacturing to One Health. One Health focuses on human-animal-environment interface health threats. Jim's article is particularly interesting to our readers because it is from the perspective of someone who has never worked in the health and medical industry. Jim has extensive biotechnology experience in academia and industry and, since 2011, in government at the **Organisation for Economic Co-operation and Development** as a policy analyst. Considering One Health interfaces, Jim's insights are important from an environmental health and sustainability perspective.

Other feature articles are more familiar in a health and medical industry setting. EMWA's Editor-in-Chief **Raquel Billiones** reports on answers to five questions about non-clinical medical writing put to Astra Zeneca's **Ruggero Galici**. Real Life Sciences' **Elliot Zimmerman** advises on how to overcome confidential information challenges faced by study sponsors today, including biotechnology company sponsors. Freelance medical writer **Archana Nagarajan** educates us on advances in CRISPR systems and gene therapy. CRISPR is considered an ATMP so might be regulated in Europe alongside gene therapies, somatic-cell therapies, and tissue-engineered products. Avi MedComms' **Avi Saha** educates us on the Pharma 4.0 CAR T cell therapy paradigm shift. Regulatory Science Manager and Writer **Ivana Turek** highlights information on cannabinoids and psilocybin derived from plants for medicinal use in cancer patients. Freelance medical writer **Anna Jesionek** discusses how to write for scientific journals about pharmaceuticals developed from plants. And Morula Health's **Lucy Hargreaves** discusses the evolution of biotechnology from ancient civilisation to the modern day and how medical writing developed alongside it.

While perhaps not biotechnology itself, support services personnel like those in biobanks and supply chains require an understanding of biotechnology, particularly from a storage temperature and mechanical vibration perspective. Mechanical vibrations and suboptimal temperatures can cause biotechnology product defects that are risky for patients and bad for company reputations. *So, don't drop biotechnology product boxes on a transportation cross dock and leave them there in 40°C heat!*

Biotechnology is controversial. My view is that biotechnology is more benign than it is given credit for and it has the potential to make a positive difference in people's lives.^{5,6} I hope this sentiment is reflected in this issue. I want to thank feature and regular section article authors for their contributions. I also want to thank Biotechnology section contributors from earlier *Medical Writing* issues.

Jen



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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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About the guest editor

Jen Bell worked in pharmaceutical and medical device manufacturing and distribution quality management roles from 2010 to 2018. She has a life science education and is interested in One Health concerning threats in the animal-human-environment interface. Jen is passionate about the potential for biotechnology to improve lives. Today, she is a freelance biotechnology consultant and medical writer.

Meet EMWA's AI Working Group

The group focuses on providing an overview of the AI landscape for our members – its opportunities, future potential, ethical framework, risks, and limitations and the impact AI will have on the medical writing role.

The AI Working Group will actively discuss how we will address this transition in our profession.



Sarah Tilly (chair)



Slavka Baróniková



Martin Delahunty



Namrata Singh



For receiving and providing information, discussion, ideas, networking and more
Contact: info@emwa.org

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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:

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- Advertising

Finance

Journal

- Submitting articles

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- Web team

Freelance Business Group

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- Leading workshops
- Professional development
- Webinar contributions
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- Pharmacovigilance
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WHY VOLUNTEER?

- Help promote the role of medical writers and strengthen our association
- Help to raise standards in our field
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- Improve your knowledge of medical writing and related topics

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If you are a member of EMWA and eager to support ongoing initiatives, please contact info@emwa.org.

From the Editor

Biotechnology – diverse as the colours of the rainbow



Raquel Billiones

Editor-in-Chief

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doi: 10.56012/jewm8154

Ask 10 people what “biotechnology” means and you will get 10 different answers.

Some would categorise biotechnology by colours (Figure 1):¹

Red biotechnology:

- Medical research

Green biotechnology:

- Plant-based/agriculture

Blue biotechnology:

- Marine/ocean ecosystems

White biotechnology:

- Industrial/commercial production

Yellow biotechnology:

- Food production

Grey biotechnology:

- Bioremediation

Brown biotechnology:

- Desert research

Gold biotechnology:

- Bioinformatics and nanobiotechnology

Violet biotechnology:

- Ethical and legal issues in biotechnology

Dark biotechnology:

- Biological warfare

Or by species: animal, plant, microbial;

Or by platform: in vitro, in vivo, in silico...

But science is too complex and diverse to be colour-coded or pigeonholed. Taking the simple examples of the aspirin (from green to red to white) and the yeast (from green to yellow to white), biotechnology is the veritable chameleon.

Going back to the Greek roots of “bios” (life) and “techne” (craft or skill) is not helpful. The term “life” is no longer binary and artificial intelligence puts a whole new meaning to craft or skill.

What is clear is that biotechnology, as diverse as the colours of the rainbow, has touched our

lives in one way or another; some would even say it has “encroached” into all aspects of daily life – ready or not.

Power and responsibility

“With great power comes great responsibility.”

Thanks to Hollywood, this age-old adage is identified not only with superpowers, but also with biotechnology gone haywire. Cliché aside, this quote is undeniably applicable to biotechnology regardless of definition, colour, species, or platform. Harnessing the power of biotechnology comes with huge benefits as well as dangers. See suggested readings below.

Medical writers and communicators are key in demystifying the complex world of biotechnology. By writing and reporting the science accurately in a comprehensible manner, we help keep biotechnology safe and honest.

Kudos to Jennifer Bell for putting this issue together. And thank you to the authors, contributors, and the MEW editorial board.

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By writing and reporting science accurately in a comprehensible manner, medical writers help keep biotechnology safe and honest.

Suggested readings on biotechnology

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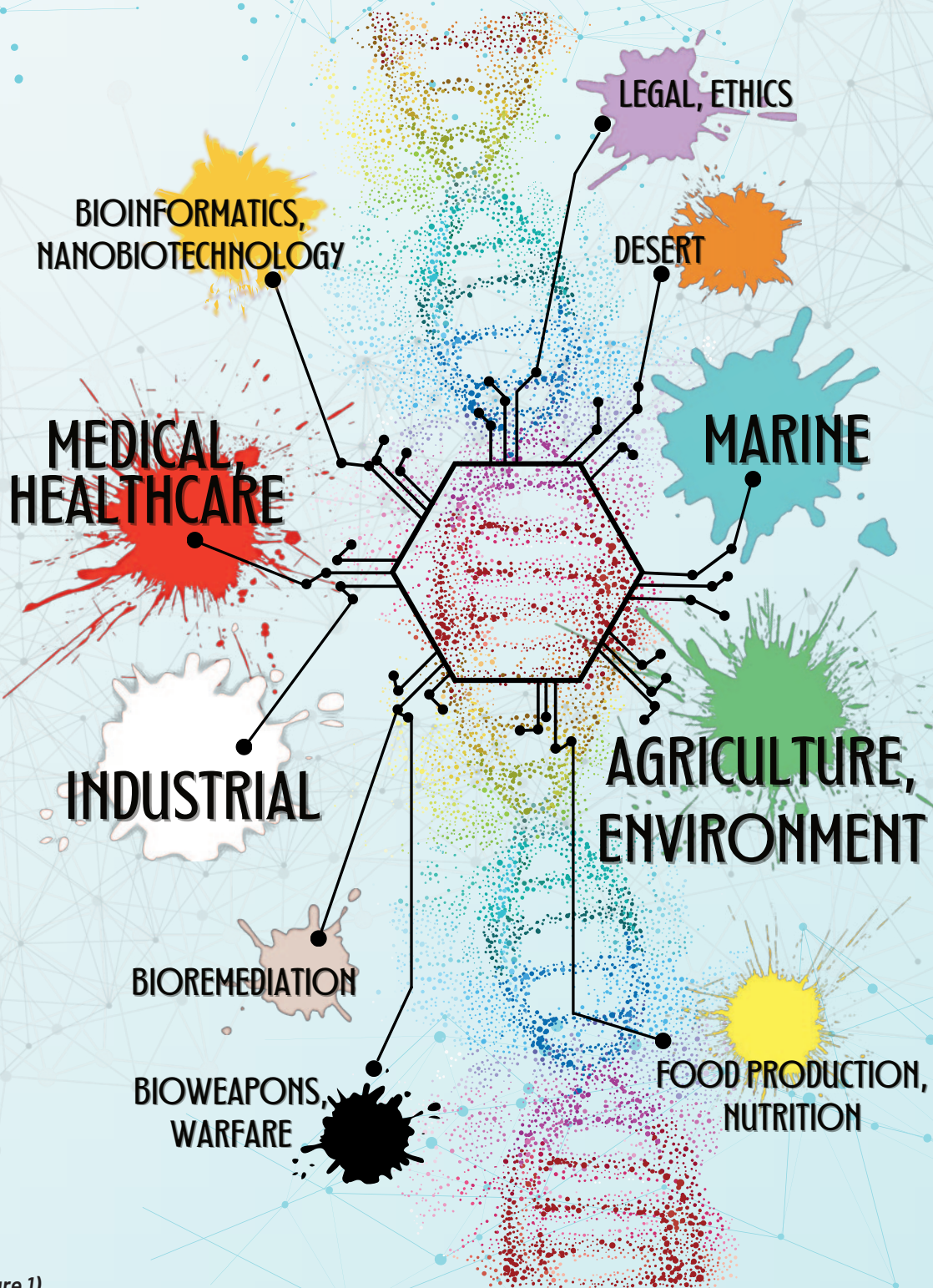
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BIOTECHNOLOGY

The 10 key research areas by color



(Figure 1)

Illustration: Judit Mészáros

President's Message

Moving to the virtual space...



Maria Kołtowska-Hägström

EMWA President 2023-24
president@emwa.org

doi: 10.56012/choi1701

recipient of the 2015 John P. McGovern Medal for excellence in biomedical communication from the American Medical Writers Association, and in 2017 was awarded an honorary doctorate in civil laws from The University of the South (Sewanee). In 2019, the judges for the John Maddox Prize, which promotes those who stand up for science in the face of hostility, gave him a commendation for his work at Retraction Watch.

On Friday Nov. 10, we attended two fantastic mini-symposia: in the morning, on publication writing in plain language, and in the afternoon on artificial intelligence and medical writing. That evening concluded with a very well attended Freelancer Business Forum. The conference continued until late November with a seminar discussing the ways of working efficiently on and in our own business, and 28 online workshops.

A proud tradition

The history of our conference dates back to 1992, with our first meeting in Brussels. In 1995, in Bruges, we hit our next milestone, hosting workshops for the first time. Since then, the conferences have constantly grown in attendance, and the breadth and attractiveness of offerings, including a wide range of workshops and different fora of networking opportunities. For example, in 2012, full-day symposia were introduced; in 2015, the Expert Seminar Series debuted; and in 2017, the Internship Forum, which later became Getting Into Medical Writing (GIMW) initiative, started. Last spring in Prague, we held Expert Discussion Groups for the first time. The number of attendees of spring conferences has increased from 335 in Budapest (2014) to 455 at Prague 2023. Interestingly, the number of participants in the autumn F2F conferences used to range between 200 and 250, and once virtual conferences were introduced, it jumped to over 300 in 2020, reaching almost 450 this November.

My dear EMWA members and friends. We are now approaching Christmas, a festive season that, regardless of personal beliefs, gathers families and friends to celebrate their bonds and relationships. This is also a good time for reflection and recollection of our EMWA family.

I would like to start with the conferences, which are major EMWA activities. This November, we had the 56th EMWA Conference and the first in the series of autumn virtual ones. It is true that during the pandemic, we organised virtual conferences, and building on that experience, the EMWA Executive Committee decided to run autumn conferences virtually; the spring conferences will remain F2F events. However, in an attempt to accommodate all needs and knowing that people want to stay connected, we have opened local hubs during the

virtual conferences. This initiative gives an opportunity for EMWA members from the same country or region to not only attend the opening session and mini-symposia together but also to network in real life. This year, we had hubs in Benelux, France, Germany, Italy, Portugal, Serbia, and Switzerland.

The opening session on Thursday Nov. 9 included a very inspiring talk on publication retractions given by Ivan Oransky, MD, who is co-founder of Retraction Watch, editor-in-chief of *Spectrum*, and distinguished journalist in residence at New York University's Arthur Carter Journalism Institute. Ivan previously was president of the Association of Health Care Journalists and vice president of editorial at Medscape. He has also held editorial leadership positions at *MedPage Today*, Reuters Health, *Scientific American*, and *The Scientist*. He is the

Getting Into Medical Writing Members

Chair: Evguenia Alechine

Co-chair: Clare Chang

| | |
|----------------------|--|
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| Marata Singh | Barbara Bartolini |
| Francesca Capellini | Ivana Turek |
| Raquel Billiones | Zoya Ashabi |
| Sarah Hopwood | Abe Shevack (Ambassador programme liaison) |



A sincere thank-you goes to the conference organisation

- Slavka Baronikova, our Conference Director
- Nadia Grewal, a member of the Conference team
- Claire Whittingham and the EMWA Head Office team
- Laura Collada Ali and Jules Kovacevic, Education Officers, and the EMWA Professional Development Committee (EPDC)
- Workshops leaders and speakers.

When mentioning GIMW, I need to add a few pieces of information. This initiative has grown outside the conferences and F2F meetings, and it now organises very popular online events. The last one, run in September 2023, was attended by hundreds of participants from all over the world. After a welcome given by Evguenia Alechine and Ivana Turek, who moderated the meeting, Sarah Hopwood introduced medical writing and explained the role medical writers play in the biomedical research world. Then, Evguenia gave a talk on practical hints about leveraging LinkedIn in your professional career. Overall, the programme was very interactive, leaving lots of time for discussion and questions.

The main areas covered were:

1. EMWA offerings such as Special Interest Groups (SIGs), Ambassador Programme, *Medical Writing* (journal), Creative Team, and Freelancer Business Forum
2. Regional networking experience with the latest EMWA initiative, namely, opening the door for Local EMWA Groups (LEGs). We'll talk more about LEGs in the March 2024 issue
3. Overview of the November conference. By the way, the presentation of the November conference most likely encouraged people to attend it and resulted in such unprecedented number of delegates.

All of these activities would not be possible without Evguenia and Ivana who chair the group and the whole dedicated team – Thank you!

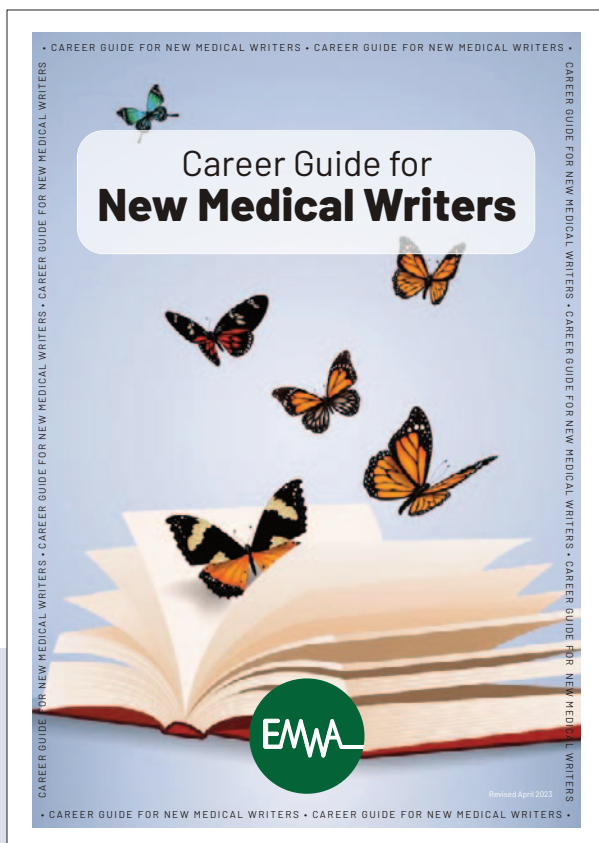
I also planned to write about another of EMWA's babies – the

new Regulatory SIG led by Jules Kovacevic, but I am afraid it needs to wait for the next issue as this is already quite long! The President's Message is not meant to take up all the space in the journal ☺.

With this I am leaving you, and wish you the most wonderful, relaxing, and full-of-love Festive Season or Christmas for those who celebrate Christmas, and a Happy and Peaceful New Year. It's hard to believe it is already 2024!

Maria

The GIMW team produced the *Career Guide for New Medical Writers*, a resource highly appreciated by newcomers – and anyone who wants to get more insights about medical writing as a career path. You can find it on the EMWA website.





EMWA Ambassador Programme news

On Sept. 20, 2023, **Gökye Ayan**, a new member of EMWA, gave a talk to 15 postdocs at the Max Planck Institute for Evolutionary Biology Postdoc Retreat in Plön, Germany. The meeting aimed to help postdocs in navigating their career paths. Goyke spoke about her transition into medical writing, the EMWA education programme, conferences, and resources on the EMWA website.

On Sept. 22, 2023, **Abe Shevack** introduced the Ambassador Programme briefly and led a breakout session for participants during the Getting Into Medical Writing online event. This event drew 200 participants and featured speakers from the Executive Committee, panels on EMWA offerings, and the experiences of networking groups in the UK, Netherlands, France, Germany, Switzerland, Portugal, Italy, and Spain, as well as breakout sessions on different topics.

On Sept. 25, 2023, **Arunon Sivananthan** and **Martina Colluci** represented EMWA as exhibitors at the NetworkPharma Medcomms Careers Event organised by Peter Llewellyn at the Heathrow Conference Centre. This event was again very well attended, with over 500 participants. Arunon and Martina were very busy answering questions about EMWA and the conferences, demonstrating the resources of the EMWA website, and discussing careers in medical writing. The conference was a great success, and seasoned and aspiring participants expressed keen interest in how EMWA can bolster their journeys as medical writers.

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).



DID YOU KNOW?

Existing EMWA members can receive a 10% discount off their next year's EMWA subscription for referring a new member to EMWA. For more information, please contact Head Office at info@emwa.org

CORE Reference

CORE Reference (<https://www.core-reference.org/>) is a resource designed by members of EMWA and AMWA to help medical writers navigate relevant guidelines as they create clinical study report (CSR) content.

Check out CORE Reference's updated lists of ICH, EMA (including CTR and CTIS),

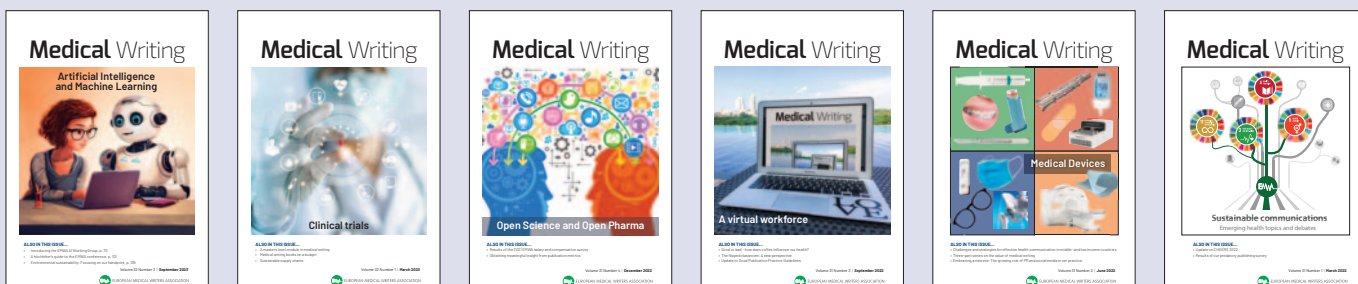


FDA, and other regional guidances; best practice documents; and other tools and resources supporting clinical trial reporting;

transparency and disclosure of clinical documents; real-world data and artificial intelligence/machine learning in the regulation of medicines.

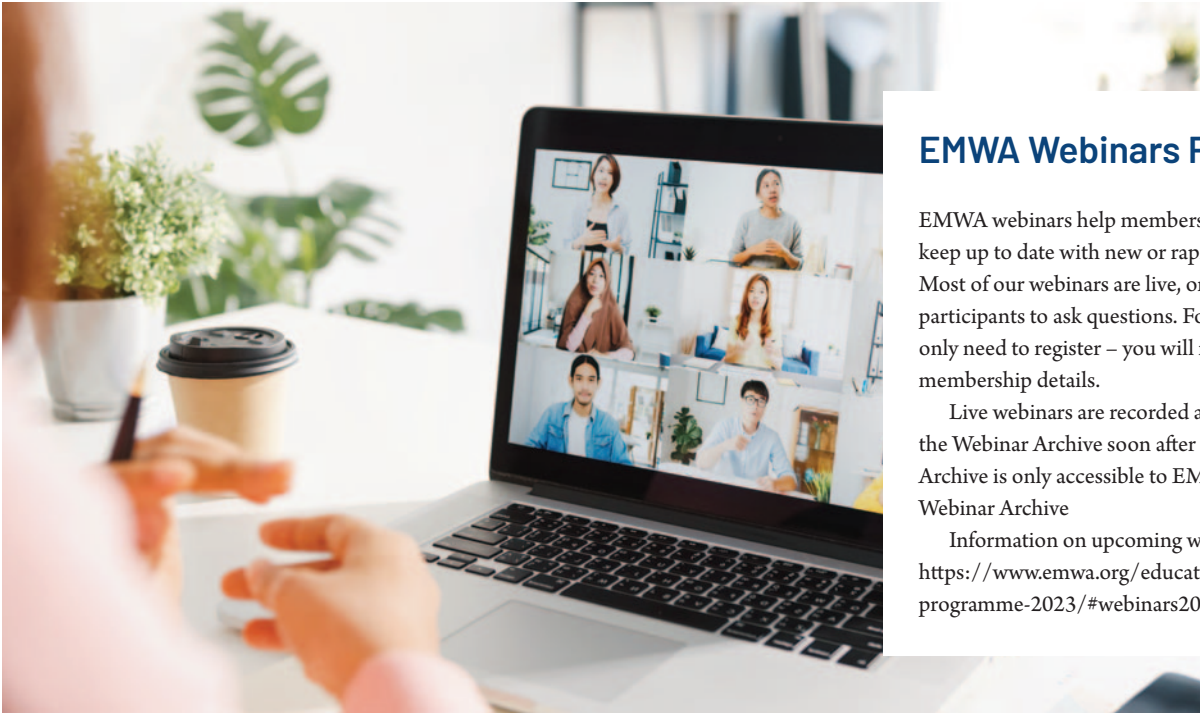
The CORE Reference NewsSummary encompasses medicines, vaccines and devices; information is archived at: <https://www.core-reference.org/news-summaries/>

Sign up for the bi-monthly email service at <https://www.core-reference.org/subscribe>



Check out the back issues of EMWA's journal *Medical Writing*

at <https://journal.emwa.org/>



EMWA Webinars Programme

EMWA webinars help members develop skills and keep up to date with new or rapidly developing areas. Most of our webinars are live, online seminars allowing participants to ask questions. For live webinars, you only need to register – you will need your EMWA membership details.

Live webinars are recorded and uploaded to the Webinar Archive soon after the event. The Webinar Archive is only accessible to EMWA members: Webinar Archive

Information on upcoming webinars can be found at <https://www.emwa.org/education/emwa-webinars-programme-2023/#webinars2023>



Freelance Business Group news

The Freelance Business Group (FBG), has responded to popular demand by creating an EMWA members LinkedIn group especially for freelancers. The concept is to use this closed group for members to post their questions about freelancing issues, share interesting information about being a freelance medical writer, advertise events, and even share jobs/opportunities that could interest other freelancers.

If you are in, or are considering stepping into, the freelance world, join our group today and help us strengthen our network between EMWA conferences:

<https://www.linkedin.com/groups/12769131/>



Scam EMWA e-mail – Please be vigilant

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.

Biomanufacturing and One Health

Jim Philp

Directorate for Science, Technology, and Innovation
Organization for Economic Cooperation and Development (OECD), Paris, France

doi: 10.56012/mrpm2606

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Abstract

At a time when the scope of One Health is expanding, the term “biomanufacturing” has taken on new significance as a new route to more sustainable manufacturing in the face of the current overwhelming reliance on fossil resources for fuel, energy, and materials. This article looks at how One Health and biomanufacturing interact from policy, technical, and societal viewpoints. The biofoundry is explored as a missing link in the design phase of biomanufacturing and examples are given where the potential of biofoundries can be enhanced in selected environmental and human health applications.

The medical writer role

A clear role for medical writers will be to delineate change to regulatory systems necessitated by technologies that allow for the faster generation of candidate molecules and their filtering through technologies such as quantitative structure-activity relationships (QSARs). The medical writer role will become clearer while reading this article.

The OECD single definition for biotechnology

The Organization for Economic Cooperation and Development (OECD) leads policy discussions among its member countries, which span the globe from North and South America to Europe and Asia-Pacific. The OECD’s single definition of biotechnology is:

*The application of science and technology to living organisms, as well as parts, products, and models thereof, to alter living or non-living materials for the production of knowledge, goods, and services.*¹

The global policy landscape

To date, 195 member states of the United Nations Framework Convention on Climate Change (UNFCCC) are party to the Paris Agreement, the global agreement to slow climate change caused by carbon emissions that was signed in Paris in 2015. The plan is to achieve well below a 2°C rise in global temperature, a goal that requires net-zero carbon emissions by mid-century. The proximity to 2050 calls for very fast action, and many of the needed technologies to store and recycle carbon, and truly new, low-emissions industrial production systems, are not ready for deployment. After a long period of policy focus on fuels and energy, it has been realised that the effort will require all sectors in all countries.² While climate action is top priority in sustainability policy, it is part of the wider concept of sustainability, which has environmental as well as economic and social pillars. The concept is enshrined in One Health, where human, animal, and environmental health all intersect (Figure 1).

“Through Executive Order 14081, the Federal Government will deliver reports to the President on how biotechnology and biomanufacturing can further societal goals related to health, climate change and energy, food and agricultural innovation, resilient supply chains, and cross-cutting scientific advances.”⁴

EXECUTIVE ORDER OF U.S. PRESIDENT
JOSEPH R BIDEN, SEPT. 12, 2022

Sustainability ...
is enshrined in
One Health [and]
biomanufacturing
is a more recent
entrant in serious
policy debates.

Biotechnology is used in biomanufacturing, also known as bioproduction. Biomanufacturing and bioproduction are terms that are familiar to the pharmaceutical industry. Biomanufacturing is a more recent entrant in serious policy debates. It was thrust upon centre stage with the Biden Administration Executive Order (see above) on biomanufacturing issued on September 12, 2022. Since then, the Ministry of Science and Information and Communication Technology–ICT (MSIT) of Korea announced the National Synthetic Biology Initiative to enhance the country’s capabilities in biomanufacturing.⁵ One of four goals set is to

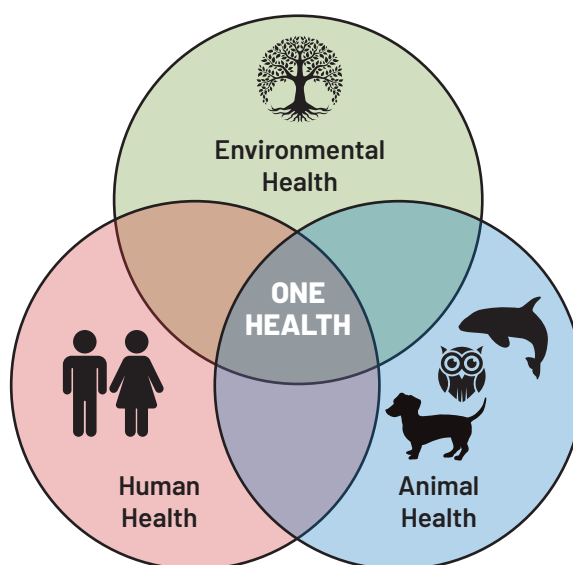


Figure 1. The intersection of human, animal, and environmental health is One Health

(after Ratnadass and Deguine, 2021)³

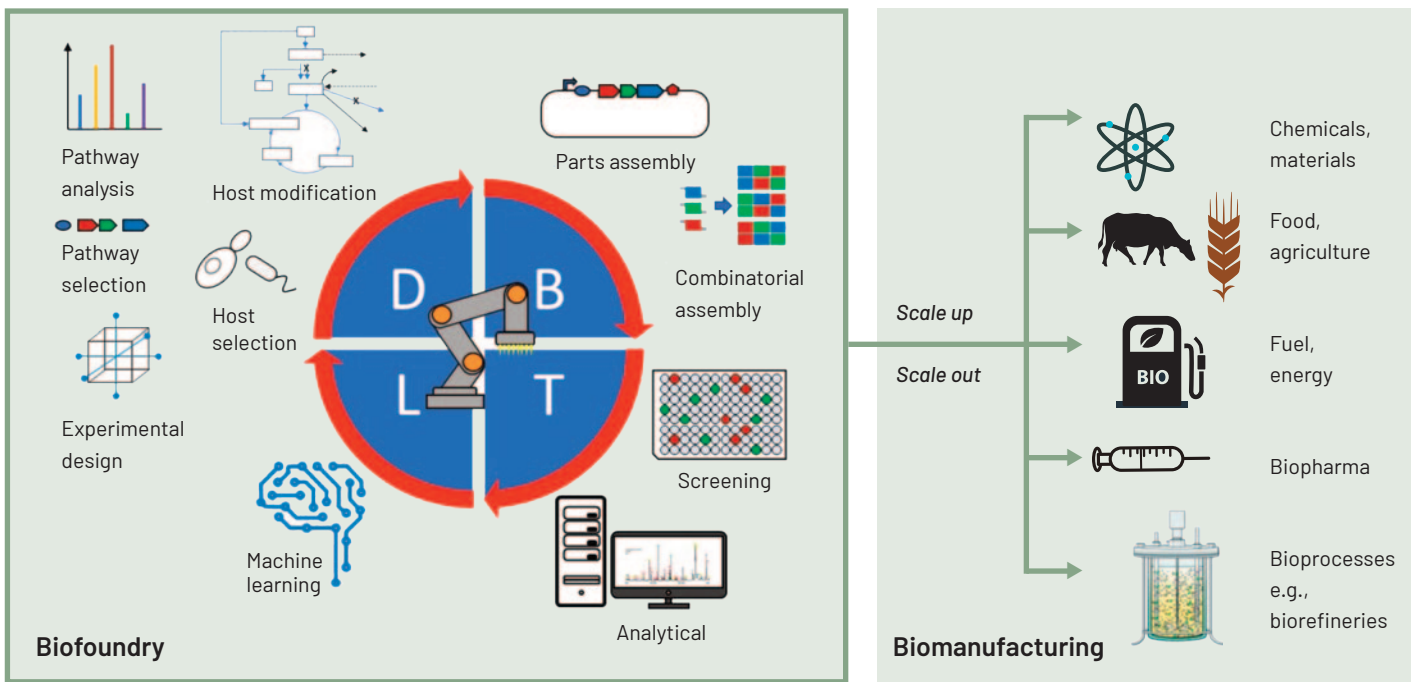


Figure 2. The biofoundry as the missing link in biomanufacturing: Automating the Design-Build-Test-Learn (DBTL) iteration cycle

Standards, automation, and machine learning are key to the success of this approach. As in modern manufacturing, the site of the design (the biofoundry) can be totally separated from the site of manufacturing (typically the biorefinery), using data transfer to dematerialise the process.

transition 30% of the manufacturing industry to a bio-based industry within the next 10 years.

And on November 14, 2022, EuropaBio, Europe’s largest biotechnology industry group, announced a new cross-sectoral Biomanufacturing Platform to strengthen the link between biotechnology and competitiveness, health, and sustainability across Europe. The platform has the mission to “represent biomanufacturing at the highest policy levels in Europe, to ensure that it is visible and recognised within the industrial strategy and Europe’s green and digital transitions.”⁶

Application across human, animal, and environmental health

Gurdo et al. (2022) “... argue that some of the solutions [...] could help consolidate a bioeconomy in times when alternatives to oil-based production (subjected to all sorts of political and economic sways) are urgently needed.”⁷

This article is themed on biomanufacturing as a future industrial production system. In human health, this is not so new, but for industrial production of fuels, chemicals, and materials, the goal is the gradual replacement of reliance on fossil resources like oil and gas. One of the major challenges of bio-based production systems like

fermentation is that the microorganisms used are not optimised for use in large-scale systems, which inhibits the fulfilment of industrial biotechnology as an engineering and manufacturing discipline. The most promising design tool to overcome this challenge is the biofoundry. Biofoundries are highly automated facilities that use laboratory robots (Figure 2) programmed for specific tasks defined in a workflow. It can be seen that the biofoundry is a platform technology applicable across many of the key sectors of relevance to One Health.

In theory the use of renewable carbon to make molecules identical to the products of the petrochemicals industry (so-called “drop-ins”) should lead to reductions in emissions. Much evidence seems to bear this out.^{8,9,10} From a human, animal and environmental health perspective, there are no more pertinent examples than the fossil-based thermoplastics, which are non-biodegradable over hundreds of years, but are subject to fragmentation into microplastics and nanoplastics in the oceans, the destination of many millions of tonnes per annum.

Point Nemo is the most remote area on Earth, more than 2,500 km from nearest land in all

directions. Water samples taken during the most recent yachting Ocean Race revealed 320 microplastic samples per cubic metre of water, up from 9 to 41 per cubic metre of water, depending on the source, in the previous race.¹¹ If accumulated in marine animals for human consumption, then there is the prospect of amplification to humans with the potential to cause health problems as yet unexplored. A more graphic illustration, however, is the consumption of “macroplastics” by seabirds, unable to distinguish plastics from food, which then die a wretched death filled with plastics (Figure 3).

Are microplastics an existential threat?

It has been estimated that there are 170 trillion pieces of plastic in the oceans.¹³ Does this pose some existential threat to all health (animal, plant, human, ecosystem)? There are at least two reasons why knowledge gaps need to be filled. First, nanoplastics have the potential to affect marine biota by ingestion. Second is the transfer of highly toxic chemicals, such as persistent organic pollutants (POPs) and endocrine disruptor chemicals (EDCs) along with the plastics. As hydrophobic materials, in the oceans they



Figure 3. A seabird killed by the consumption of plastics floating in the oceans

(Courtesy of Chris Jordan Photographic Arts, "Midway: Message from the Gyre")¹²

accumulate hydrophobic pollutants from ocean water, thus concentrating them on the plastics.¹⁴ The extent to which this causes harm to marine species is uncertain. And the threat is not restricted to the marine environment; microplastics have been found in raindrops and breathable air.¹⁵ The discovery of plastic particles in human blood¹⁶ surely warrants research on their fate and effects.

Why the biofoundry?

The demands of the DBTL cycle are not to be underestimated in terms of workload, time, and costs involved. Even today, much of the DBTL cycle in synthetic biology is semi-artisanal. The overarching function of the biofoundry is to accelerate and automate the cycle with increasing consistency and throughput while reducing labour (lumpen pipetting) and thus cost. Biofoundries mostly aim at streamlining the engineering of microbial chassis for chemical production. The key is throughput.

Microplastics have been found in raindrops and breathable air. The discovery of plastic particles in human blood surely warrants research on their fate and effects.

The huge advances in genome sequencing, resulting in a current cost for a human genome of around USD600, have facilitated high-throughput design and build. It is now possible to automate the "test" phase as well though advances in technologies such as microfluidics.

Now the bottleneck lies in the "learn" phase of the DBTL cycle¹⁷ and machine learning holds out the hope of being able to further accelerate the cycle. Integrating machine learning into the DBTL cycle could, for example, aid in the development of accurate models for clinical studies and precision therapies, even leading to "diagnostic and therapeutic" microbes that can identify diseases *in situ* and produce drugs *in vivo* based on the diagnoses.¹⁸ In the chemical and environmental fields, similarly bacteria could be developed to break down cellulosic biomass, transport the produced sugars into the cell and then ferment those to a desired product, e.g., biofuels¹⁹ and bioplastics.²⁰ This consolidated bioprocessing has been a long time coming and

it looks like automation is the way to bring it to reality.

QSARs, machine learning, and the biofoundry

A goal of several decades has been the production at a competitive scale of biodegradable plastics that would be able to tackle the scourge of plastics in the oceans. There are several candidate molecules but little market penetration. Perhaps the biofoundry could be the design platform to increase the number of candidates. There would still be the bottleneck at testing and learning,



however. Here there may be a role for machine learning and AI to identify the most effectively degraded candidates under different conditions. Back in 1976, Klaus Kieslich published a 1,262 page volume on the microbial transformation of non-steroid cyclic compounds. Since then, electronic databases have replaced paper.²¹

The real power of electronics should be predictive capabilities. The most useful tools may be quantitative structure-activity relationships (QSARs), and their integration into biofoundry operations might provide this predictive power. AI/machine learning/deep learning models for

prediction, often using databases of QSARs, can now be used to predict the biodegradability of organic chemicals and bio-based plastics.²² It is speculated, then, that it may be possible to integrate these electronic models into the highly automated biofoundry to predict the biodegradability of new candidate molecules for biodegradable plastics.

The utility of QSARs in the biofoundry has potential way beyond biodegradable plastics. In human and environmental health a few examples are:

- *In vitro* and *in silico* toxicology testing before

clinical trials of a putative drug molecule.²³

- Predicting oxidative stress in humans caused by organic chemicals.²⁴
- Predicting the environmental toxicity of pollutant chemicals.²⁵

In drug design, virtual screening emerged as a powerful computational approach to screen large libraries of small molecules for new hits with desired properties that can then be tested experimentally. The underlying principle is that variations in structural properties cause different biological activities.²⁶ The ideal is to reduce the



number of candidates to be tested experimentally, and to rationalise their choice, in a similar manner to the rationalisation of choices of candidate bioplastics above. Among the virtual screening approaches, QSAR analysis is the most powerful method due to its high and fast throughput and good hit rate.²⁷ Yet there are still many constraints in drug design. Ensemble-based machine learning approaches have been used to overcome constraints and obtain reliable predictions.²⁸

Further downstream: scale-up and scale-out

While this article concentrates on upstream issues in design, it is worth mentioning some of the challenges on the right-hand side of Figure 2 relating to scaled-up manufacturing. The challenges are different for (bio)pharmaceuticals and chemicals/materials. For pharmaceuticals, the production volume is comparatively much smaller than, say, scaling up a bioplastic production to the point where it can compete in the marketplace. Pharmaceuticals have much higher added value than commodity chemicals, thus making small-scale production more easily profitable. While pharmaceuticals have a rigorous regulatory system, that is not to say regulation of chemicals and materials is trivial.

The sheer volume of production of a bio-based commodity chemical or a bioplastic creates major roadblocks to scaled production. Fermentation processes for such products generally have low titres, which necessitates expensive downstream processing to concentrate a dilute product from a bulk aqueous phase. And fermentation processes are generally much slower than petrochemical processes. This microbe-based manufacturing of commodity chemicals is thwarted by the fact that they are highly reduced and non-natural compounds relative to the carbohydrate feedstocks. Yim et al. (2011)²⁹ reported a successful metabolic engineering exercise to make 1,4-butanediol (BDO), a commodity chemical used in the annual manufacture of over 2.5 million tonnes of valuable polymers. That process has been successfully commercialised,³⁰ but there are

many more targets that need to be addressed: the chemicals industry manufactures at least 70,000 different products, the most important and highest volume being from petrochemistry.

Concluding remarks

It is possible, then, to make a link between the goals of the DBTL cycle, especially in the bottlenecked “learn” phase and the goals of QSARs. To date, this link is missing in the literature. As QSARs are mathematical models, in theory their integration into the complex software operations of biofoundries should not be impossible. They would represent a contribution to the learn phase of the DBTL cycle.

Finally, this short article points to much larger social, human health and environmental implications associated with the term One Health.

This short article points to much larger social, human health, and environmental implications associated with the term One Health.

There is a coincidence in history of several Grand Challenges that make the immediate future of humans perhaps the most challenging of all time. Environmental health, human health, and animal health collide in myriad ways, making solutions difficult. As these Grand Challenges interact in complex ways rather like an ecosystem,³¹ the eventual solutions must also be interactive: a solution that acts on only one part of the interactive

ecosystem is likely to initiate other impacts elsewhere in the ecosystem.

A clear role for medical writers will be to delineate change to regulatory systems necessitated by technologies that allow for the faster generation of candidate molecules and their filtering through technologies such as QSARs.

Disclaimers

The views expressed are those of the author and are not necessarily those of the OECD or the governments of OECD member countries.

Disclosures and conflicts of interest

The author declares no conflicts of interest.

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Five questions for Ruggero Galici on nonclinical medical writing



Ruggero Galici is Senior Director of Nonclinical and Clinical Pharmacology Medical Writing at Alexion Pharmaceuticals Inc, AstraZeneca Rare Disease Unit and heads up global early phase regulatory medical writing activities. In this role, he facilitates the transition of early phase programmes from first-in-human research to clinical trial applications and investigational new drug submissions.

Ruggero has a background in drug discovery, nonclinical and clinical development, a PhD in

pharmacology, and post-doctoral training. He has led pharmacology teams to advance small molecules and biologics to the clinic and has served as subject matter expert to compound development teams. Ruggero has more than 20 years of experience in scientific and regulatory writing. He can be found on LinkedIn at <https://www.linkedin.com/in/rgalici>.

Medical Writing Editor-in-Chief Raquel Billiones asked him five questions about his career and expertise.

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Raquel Billiones (RB): How did you get into this profession?

Ruggero Galici (RG): I got involved with scientific writing early on in my career. As I go back in time with you, I realise that it has been a natural transition for me to switch from leading translational pharmacology laboratories to writing scientific documents. For example, when I was a post-doctoral fellow in the US at the University of Texas Health Science Center and at Vanderbilt University, I wrote several grants sponsored by the US National Institutes of Health, submitted abstracts to scientific meetings, and published several articles in peer-reviewed journals. Eventually, I ended up working in large pharmaceutical companies within R&D where I progressively shifted my role from scientific writing (e.g., research technical reports [RTR], pharmacokinetics/pharmacodynamics [PK/PD] reports,) to regulatory writing (e.g., briefing documents, investigator's brochures, protocols, clinical study reports [CSRs], clinical development plans, and non-clinical and clinical modules in preparation of investigational new drug [IND] and new drug application [NDA] submissions).

RB: What are the documents that nonclinical medical writers develop?

RG: Within the pharmaceutical industry, there is a variety of documents requiring nonclinical writing support. They typically fall into 5 major areas of expertise (chemistry, manufacturing, and control [CMC], bioanalytical, pharmacology [PK], and toxicology), and in 3 general categories (RTRs, publications, and regulatory documents). RTRs and publications are typically written with a scientific mindset and approach. Regulatory documents summarise the RTRs (e.g., the source documents), and are written for regulatory agencies using strategic and lean writing approaches (e.g., briefing documents, summary of nonclinical pharmacology). These kinds of documents provide the regulatory agencies with an overview of the nonclinical package supporting clinical development.

RB: From your perspective, is there a difference between clinical and nonclinical medical writing?

RG: It depends on the purpose and content of the documents, so I am tempted to avoid generalisations. For example, Phase 1 clinical study reports, summaries of clinical pharmacology studies, and summaries of pharmaceutical studies and associated analytical

methods are highly technical documents with great similarity to nonclinical summaries and RTRs. These nonclinical and clinical regulatory documents require knowledge and understanding of pharmacology, PK/PD relationships, toxicology, and safety. On the other hand, writing a nonclinical pharmacology summary is fundamentally different from writing a summary of clinical safety.

Within the regulatory space, there are several important similarities between nonclinical and clinical writing that should be highlighted. For example, regardless of the type of document, the typical operational steps medical writers undertake are the same from planning to submission readiness. Also, nonclinical and clinical regulatory documents are typically written with the same strategic and lean authoring approaches.

Another similarity is that, regardless of the type of document, significant investigative work from medical writers is needed. For example, we analyse and synthesise the content of source documents, whether we review an RTR to support the development of an investigator's brochure, or we review a CSR to support the development of a summary of clinical pharmacology.

Regardless of the type of document, the typical operational steps medical writers undertake are the same from planning to submission readiness.

RB: Do you have any pearls of wisdom you want to share with students and young scientists who may be interested in the medical writing profession?

RG: There is no magic bullet to break into the profession of medical writing. Medical writers have diverse education and training, but they typically have a common passion for science. Broadly speaking, the ability to understand and talk science is an advantage in medical writing, particularly when authoring nonclinical documents and actively engaging with subject matter experts (e.g., pharmacologists). For example, this is when we add value to teams by cross-checking the scientific accuracy of content, by asking questions to clarify the meaning of sentences, and by making suggestions on experimental design and statistical analysis. By quickly absorbing complex scientific and medical concepts and data, we can effectively and efficiently summarise the content in regulatory documents and/or scientific publications.

Medical writers add value to teams in other ways as well. We typically own the document,

and we provide subject matter experts with templates and guidance on content and, to some extent, regulatory requirements. We also keep abreast of novel platforms aimed at assisting with the development of documents (i.e., automation technologies). Medical writers wear multiple hats. Soft skills are essential, particularly the ability to effectively communicate complex scientific and medical content and distill it into key messages, storyboards, nonclinical and clinical summaries, and plain language summaries. We act as psychologists when we manage different opinions and people with different backgrounds during a document conflict resolution meeting. We are project managers when we take care of all operational aspects of document development from planning to approval.

RB: In keeping with the theme of this issue, can you tell us why nonclinical writing is very important in biotechnology?

RG: Nonclinical writing is essential in determining the success of programmes throughout

the clinical development lifecycle from Phase 1 to registration. Nonclinical writing is particularly important in early phase programmes from small biotechnology companies with a single asset at pre-IND stage, to large pharmaceutical companies with multiple assets at different phases of clinical development. For example, as early phase programmes make the transitions from research to first-in-humans, regulators around the world review for the first time the nonclinical data and provide their feedback based on the quality and completeness of these data.

RB: Thanks so much for sharing your expertise with our readers!

Disclosure and Disclaimer:

The interviewee and interviewer work for the same company. The views and opinions expressed in this article are the authors' own and are not necessarily shared by their employer or by EMWA.



Overcoming confidential information challenges faced by study sponsors today

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Abstract

As health authorities aim to increase clinical trial transparency and visibility to the public, pharmaceutical manufacturers are facing new pressure points. New regulations require the disclosure of clinical trial application data, many of which contain sensitive and confidential information about company intellectual property including, but not limited to, its manufacturing methods, drug composition, names of suppliers, and future development plans. Many manufacturers are examining their processes to minimise references to this confidential data during the document authoring process and how they track and identify confidential information throughout the study lifecycle. This has created a catalyst for medical writing, transparency, legal, and regulatory teams to collaborate and enhance their processes to minimise disruption to the trial approval process while embracing the opportunities to share more with the public.

Introduction

Policies and regulations such as Health Canada Public Release of Clinical Information (PRCI), EMA's European Union Clinical Trial Regulation (EU CTR) and EMA Policy 0070 are exposing operational challenges for pharmaceutical and biotechnology manufacturers in the identification, tracking, disclosure, and management of confidential information (CI); specifically known as confidential business information (CBI) by Health Canada¹ and commercially confidential information (CCI) by the EMA² throughout the clinical lifecycle. Note that throughout this article the

term CI will be used.

While these policies and regulations require a significant amount of information pertaining to the trial itself be disclosed, including the trial results, there is a line drawn regarding information that remains proprietary to the manufacturer.

Health Authority expectations

Health Canada's PRCI

The PRCI initiative is designed to increase transparency in the drug and medical device approval process while protecting CI. By making clinical information publicly available, Health Canada aims to promote research and innovation.

Health Canada states the following regarding its definition of CI:

- "CBI", in respect of a person to whose business or affairs the information relates, means – subject to the regulations – business information:
 - That is not publicly available
 - In respect of which the person has taken measures that are reasonable in the circumstances to ensure that it remains not publicly available
 - That has actual or potential economic value to the person or their competitors because it is not publicly available, and its disclosure would result in a material financial loss to the person or a material financial gain to their competitors.

Sponsors can request, with justification, certain information be redacted if they believe it meets the criteria for confidentiality. The justification of certain redactions may require the manufacturer to draw on information within their internal corporate plans (e.g., future development of new indications based on secondary outcome data). Consequently, Health Canada requests that the manufacturer submit an annotated version of all clinical information in scope of publication with any and all proposed redactions highlighted for

Confidential information is information contained in the clinical trial which is not in the public domain, or publicly available, and where disclosure may undermine the legitimate economic interest or competitive position of the owner of the information.

regulator review. Any text the manufacturer proposes to redact must remain readable, and all proposed redactions should be accompanied by specific and detailed justification recorded using the "Proposed Redaction Control Sheet" in .CSV format.¹

EMA

The EMA considers CCI as any information contained in a clinical trial application or provided during the trial life cycle that is not in the public domain or publicly available, and where disclosure may undermine the legitimate economic interest or competitive position of the clinical trial sponsors or marketing authorisation applicants/holders.³



The EU CTR expects the following regarding CI:

- Sponsors may indicate CCI in non-public version documents for the health authority and member state reviewer's awareness.
- The EMA may request additional information to support the justification for confidentiality.
- The sponsor may redact CCI from public version (known as "for publication") documents posted to the Clinical Trials Information System (CTIS).

Implemented in 2015, EMA's Policy 0070 was suspended, with certain exceptions, in December 2018, due to Brexit and eventually COVID-19. EMA has since relaunched Policy 0070 with a gradual rollout from September 2023 applicable for new active substance approvals, negative and withdrawn applications.⁴ The re-launch includes certain changes to the policy including the use of a revised anonymisation report template and proactive notification of expected CI prior to the draft submission. The second phase of the re-launch is likely to take place in 2024 with details pending announcement from EMA.



EU CTR operational challenges observed by pharma manufacturers

1. Regulatory rejections

Proposed CI by study sponsors has historically been tracked by Health Canada and EMA at a 65%⁵ and 60%⁶ rejection rate respectively due to:

- Information marked as CI by the sponsor that is already in the public domain
- Information marked as CI by the sponsor that is not innovative
- Information marked as CI by the sponsor that is in the public interest

2. Ownership and authority

Consensus decision regarding CI references in a trial document for a given asset, programme and/or study is a common challenge within global pharmaceutical teams today. Typically, the identification of CI is a collaborative effort led by intellectual property (IP) legal, medical writing, regulatory, safety, clinical and non-clinical teams, and transparency and disclosure teams. With no single owner, decision making in some organisations has proven difficult while balancing protection of the information with the potential risk of delays due to regulatory push back.

3. Tracking CI throughout the clinical lifecycle

Accurate tracking of CI pertaining to any given asset, programme, or study can be challenging due to:

- Changes in classification of CI over time
 - Awareness of publications in the public domain that may refer to specific references once deemed confidential
 - Consistency across global trial registries; specifically what information is being disclosed on each

Easing the CI burden

The following operational considerations may assist medical writers and cross-functional colleagues in setting a repeatable and scalable business process for identifying, managing, and tracking CI consistently across studies. These recommendations are especially applicable for those pharmaceutical manufacturers submitting studies via CTIS, the EMA system used to facilitate trial applications and disclosures in Europe.

1. CCI procedures defined specifically for your organisation and team structure can play a significant role in streamlining CI related decisions, process, and outcomes

- Implement an authoring minimisation initiative; include references to CI that is required and minimise repetition of those references within the document
 - Define a consistent deferral strategy and decision process
 - Document the hand-offs between teams, CRO, redaction service provider
 - Set expected turnaround times for document redaction including review and approval cycles and final version updates
 - Clearly define roles and responsibilities regarding review and approval of CI across functional team members
 - Document resource mobilisation and action plans for Requests for Information (RFIs) e.g.; RFI response PI
2. Tracking all CI in a centralised "library"
 - Create a centralised listing of CCI per asset, programme, and/or study
 - Include cross-functional team leads from safety, manufacturing, IP legal, corporate librarian, and transparency in reviews and approvals
 - Set maintenance procedures for tracking changes over time. What is CI today may not be tomorrow
 - Refer to the library during the document authoring process to support minimisation techniques
 3. Finalise internal standards and authoring procedures
 - Revise document authoring templates to include minimisation expectations, excluding unnecessary references to CI wherever possible when authoring clinical documents
 - Maintain awareness of current CI at all times during the authoring process
 - Categorise documents into groupings for prioritisation, review, and approval:
 - **Group 1** – "Dense" documents that typically contain the most references to CI such as the protocol and investigator brochure
 - **Group 2** – Other documents with fewer references to CI, e.g.; PI CV, proof of insurance, proof of payment
 - Define common use scenarios for regulatory document management system(s) which may support your review and approval processes

4. To prevent unnecessary or excessive redactions which may expose inadvertent errors or missed redactions, the following minimisation techniques are recommended:
 - **DO** include **ONLY** the content that is required to meet the document's objective and nothing additional
 - **DO** highlight or designate CI in the document at the time of authoring for review by the transparency and/or redaction team member
 - **DO NOT** reference CCI in the document's Table of Contents, body, header/footer, and table titles
 - **DO NOT** duplicate content; instead include cross-references such as, "refer to Section A", thereby decreasing the number of instances of CI within a document(s).

5. Cross-functional team members in regulatory, safety, manufacturing, IP legal, and transparency, must share a common understanding of what CI is (and is not):
 - Demonstrate practical examples using previous public version documents
 - Explain/illustrate the justification and decision process for those examples
 - Include positive (is CI) and negative (is not CI) examples and explain why
 - Review the most current library with cross-functional team leads

Overcoming challenges with redacting documents

The task of redacting CI from regulatory documents may be laborious and error prone if the proper tools and technology solutions are not utilised. Study teams may run into challenges meeting tight turnaround times especially when faced with processing multiple documents in a short period of time to meet the document submission deadlines and trial approval schedule. Use of a purpose-built redaction solution for your organisation can help with expediting and streamlining the redaction, review, and approval process. Examples of capabilities that can accelerate your redaction processes are as follows:

- Apply study-specific saved searches to identify and redact specific terms and references within a document.
- Apply saved searches to one or more documents simultaneously.
- Enable collaboration with team members directly in the document to avoid non-secure



messaging and emailing of sensitive files and file version control issues.

- Generate a systemic audit trail to view all redaction marks and justifications for one or more documents.
- Use integrated project management tracking to report progress, anticipated redaction completion dates, and management visibility.

Disclosures and conflicts of interest

The author is employed by Real Life Sciences, which provides anonymisation software and services discussed in this article. The author declares no conflicts of interest.

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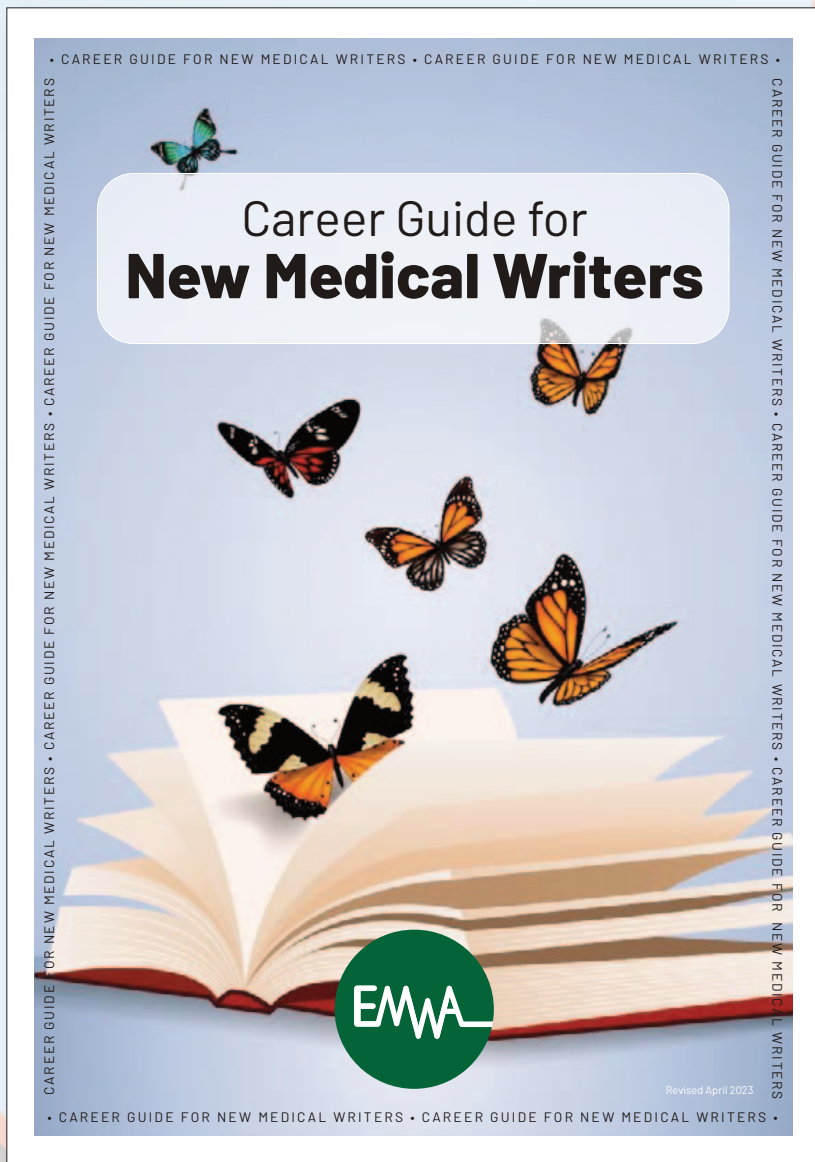
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Living medicine: The story of CAR T cell therapy

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Abstract

The advent of chimeric antigen receptor (CAR) T cell therapies follows a decades-long quest to personalise the treatment of disease. This article highlights the early research that paved the way for the field today, touching on early pioneers in the field and the biotechnological methods used to engineer CARs. With six CAR T cell therapies approved by US and EU regulatory bodies, and many more to come over the next decade, the field is challenged by slow manufacturing times and limited accessibility. Future CAR-based treatments will include additional cell types and indications, as well as automated and continuous manufacturing protocols that will help reduce the cost of goods.

Introduction

Cure is a strong word, used hesitantly and infrequently when describing any kind of cancer treatment. Cancer of any kind is a devastating diagnosis, and overpromising yet underdelivering is all too common.

In the same vein, hope is exactly what cancer patients need, to comfort them during one of the most challenging parts of their lives. And hope is what a new type of cancer immunotherapy called chimeric antigen receptor (CAR) T cell therapy, a type of cell and gene therapy (CGT), promises to patients who have gone through multiple lines of treatment to no avail.

But cure too, is a real possibility. In contrast to complete remission, which is defined as a lack of any signs or symptoms of cancer at any given time point, the term “cure” suggests the cancer will never return. For Doug Olson and Bill

Ludwig, some of the first patients to receive CAR T cell therapies, cure is a daily part of life. Both have been cancer-free for over a decade, and the infused CAR T cells they were administered continue to live on with them, a positive sign that they may continue to protect against relapses.¹

What is CAR T cell therapy?

CAR T cells are genetically engineered T cells that kill cancer cells directly by targeting specific surface antigens.² They harness the intrinsic “seek and destroy” capabilities of T cells but can be customized by using viral vectors and non-viral methods to insert genes that redirect the T cell for a more targeted effect.^{3,4}

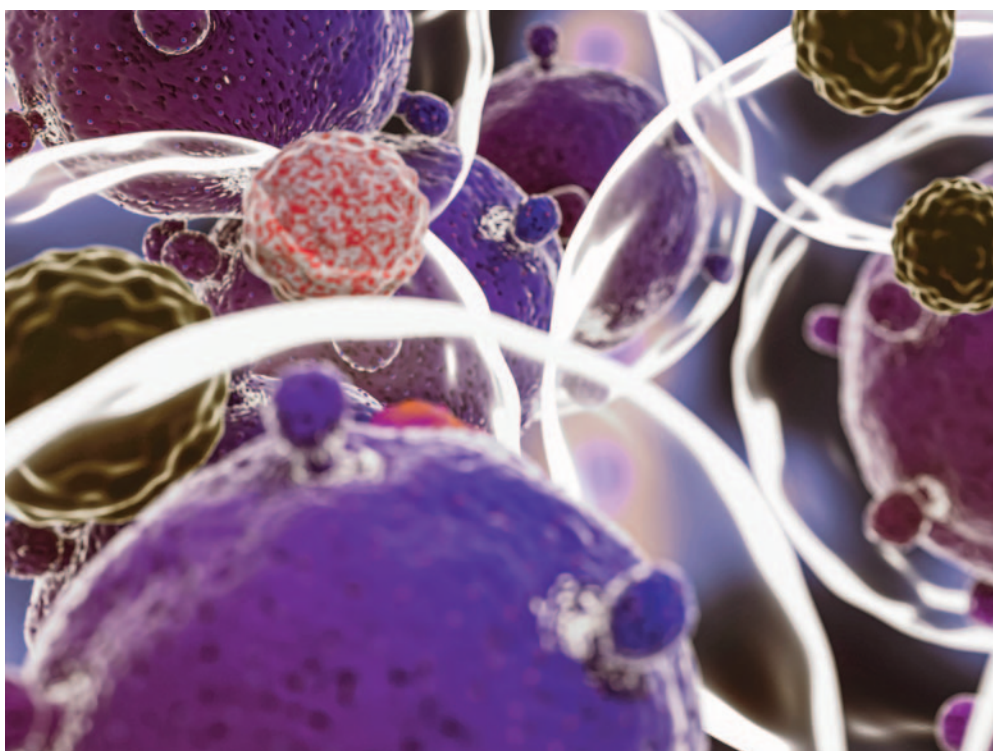
As of today, there are six CAR T therapies available for treatment, approved by both US and EU authorities (Table 1). Each of them requires only one dose to work, after which the cells continue to proliferate in the patient’s body after treatment, conferring, in theory, long-term protection against the disease. Clinical trials showed high rates of response to treatment, with

many patients seeing their cancer disappear completely.⁵ However, some patients still relapse and the majority of patients experience side effects. Understanding why some patients achieve remission and others don’t is a daunting task, and factors such as prior medication use, the timing of treatment, how the CAR T cells were grown, and the cellular structure of the CAR T cell are some factors explaining varied treatment effects.⁶

Due to the immunosuppressive tumour microenvironment and the varied nature of solid tumour cells, current generation CAR T cells have a harder time selectively targeting solid cancers. Currently approved therapies are indicated exclusively for blood cancers, which tend to express antigens more uniformly.⁷

The role of biotechnology in CAR T cell therapy

Biotechnology may be defined as the innovative and creative application of biological substances and processes to develop industrial-scale solutions to complex problems. Biotechnological



advancements drive the pharmaceutical industry forward through its constant striving for safer and more effective therapies. They also benefit the food, energy, and healthcare industries.

Biopharmaceutical companies are often developed around specific biotechnological methods. One prominent example is CRISPR Therapeutics, a company co-founded by Nobel laureate Emmanuelle Charpentier, one of the two researchers who discovered CRISPR-Cas9 technology for gene editing. This tool has been adopted widely due to the ease by which genome editing can be customized. Many major players in the CAR T cell therapy space use it to improve the potency and safety of CAR T cell therapies.⁸

This process often begins in research laboratories, where manufacturing processes are developed through trial and error and subsequently refined. Once a consistent approach is discovered, a therapy can make its way to the clinic. Here, a multidisciplinary effort is required to make the process more reproducible, so that a consistent product can be produced in preparation for later-stage clinical trials and commercial manufacture, where adherence to current Good Manufacturing Practice (cGMP) guidelines is required.

Since the first regulatory approvals of CAR T

cell therapies in 2017, there has been an explosion of interest in this field. Every aspect of this treatment is evolving at a rapid pace, including regulatory, manufacturing, supply chain and logistics, pricing and access, and the possible indications. Despite their popularity today, CAR T cell therapy was no overnight success story.

How CAR T cell therapy came to be

The first chimeric T cell receptors were engineered in the late 1980s and demonstrated for the first time that T cells can be supercharged with chimeric genes, allowing them to target specific cells.^{9–10} The possibilities were now endless. In 1993, one of these researchers, Zelig Eshhar, from the Weizmann Institute of Science in Israel, proposed a method to use CAR T cells to target tumours, creating the first generation of CARs.¹¹

Chimeric T cell receptors do not only target specific antigens, they can activate other CAR T cells to help fight cancer.¹² When CAR-T cells encounter cancer cells displaying the target antigen, the CAR's extracellular domain binds to the antigen. This binding triggers a signalling cascade within the CAR T cell, leading to T cell activation and proliferation. The activated CAR T cells proliferate and lead to a robust immune response, consisting of cytokine release, helping

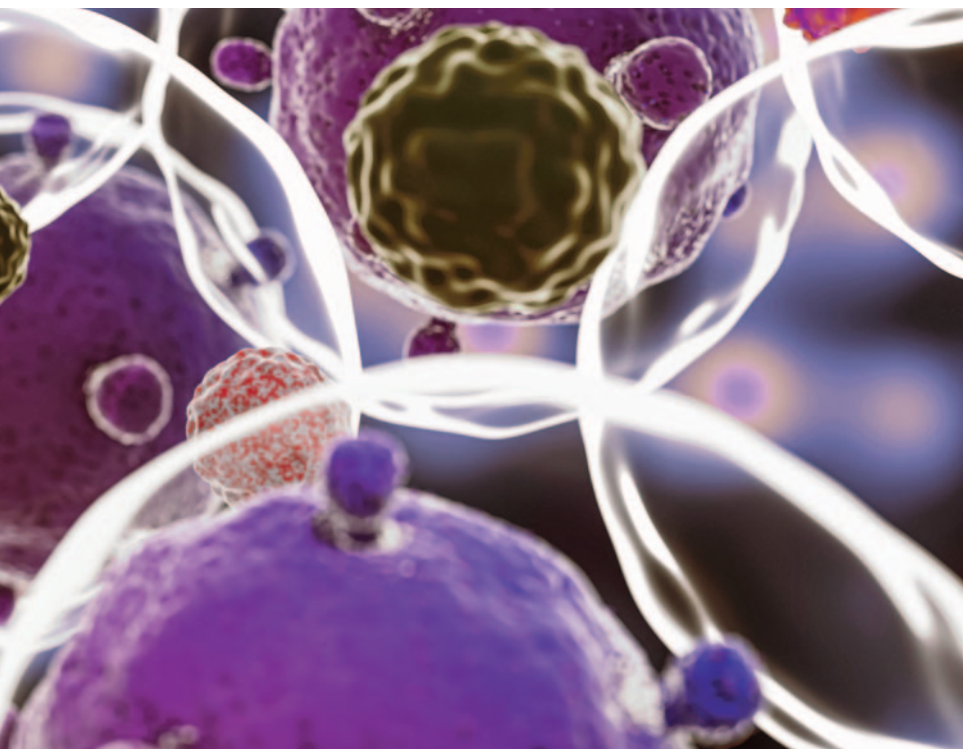
to eliminate the target tumour cells.

One of the pioneers in CAR T cell therapy, Carl June at Penn Medicine, did not expect the treatment to apply to cancer when he first began researching it. In the mid-1990s, June was working to treat human immunodeficiency virus patients with genetically engineered T cells. Although this treatment was not effective against the virus, June and his colleagues made one important discovery: the activated T cells were found in the blood circulation of almost all the patients months after treatment, indicating the potential for long-term protection.¹³ This phenomenon is called persistence and is an important element of how CAR-based therapies work.

CAR T cell therapies entered their first clinical trials in the early 2000s, to target kidney and ovarian cancers, two types of solid tumors.^{14–15} Not only were the cells ineffective, they had “on target, off cancer” effects, destroying healthy tissue. These findings spoke to the importance of target specificity, and the need to engineer T cells that were more precise.

A breakthrough occurred only a few years later, when preclinical research conducted by three independent research teams and led by Michel Sadelain, Carl June, and Steven Rosenberg, demonstrated that CAR T cells targeting the cluster of differentiation 19 (CD19) antigen, a common marker found on B cells, had significant anti-leukemic activity.^{16–18} Clinical trials on anti-CD19 CAR T cells were underway in the early 2010s, for acute lymphoblastic leukaemia and chronic lymphocytic leukaemia, two malignancies that mostly involve B cells. For the first time, patients achieved partial or complete remission with this treatment.^{19–20} Emily Whitehead was one of those patients. When she was enrolled in the clinical trial when she was just a child, she was given only a few weeks to live and no other treatment had worked previously. Today, she has been cancer-free for ten years.

Now, other patients like her, such as Doug Olsen and Bill Ludwig, who were refractory to previous lines of treatment and had relapsed, have another lifeline. Unfortunately, most of the patients who hope to receive this treatment face unacceptable wait times. Bringing cell and gene therapies to patients at scale is not yet possible with current methods, but that is a major factor driving the industry forward.





Bringing CAR T cell treatments to more patients

One of the greatest challenges facing CAR T cell therapy, as well as cell therapy more broadly, is the complicated manufacturing process. The six approved therapies are manufactured using autologous T cells, which means that they are collected from and delivered to the same patient. This vein-to-vein workflow typically takes two to three weeks. The patient’s T cells are isolated from peripheral blood mononuclear cells, enriched, grown to the desired dosage, and preserved until administration in the autologous CAR T cell therapy.²¹

In contrast, allogeneic CAR T cells would come from any healthy donor and would be processed otherwise in the same way. The race is on to develop effective allogeneic, or “off the shelf”, CAR T cell therapy treatments because they would make this therapy more accessible to

patients. Autologous therapies, on the other hand, are often transported across continents multiple times before they are given to the patient. The major disadvantage of allogeneic CAR T cell therapy is a higher risk of graft versus host disease and that the innate immune system will attack the CAR T cells.

Instead of a one-size-fits-all approach to cancer treatment, cell and gene therapies are individualised therapies. Each treatment is manufactured one at a time, resulting in long wait times. According to one physician survey, about 25% of patients eligible for CAR T cell therapy died in the process of waiting for treatment.²² About a third of patients receive the treatments too late, which lowers their effectiveness and increases mortality risk.²³⁻²⁴ Bringing more

CAR T therapies to patients will involve further testing of their effects as first- and second-line treatments and building a faster manufacturing process.

The process is the product

One unique aspect of the manufacturing of CAR T cell therapies is that “the process is the product.” This adage is a subject of debate; however, it continues to guide the industry. Because of the variable nature of cellular products, not as much is known about the therapy itself and its mechanisms of action compared to small molecules and biologics.

Because of this, regulatory authorities require that manufacturers of CGT products use the same manufacturing process every time they release a new

Bringing cell and gene therapies to patients at scale is not yet possible with current methods.

Table 1. Approved CAR T cell therapies available in the United States and the European Union

BCMA denotes B-cell maturation antigen. CD19 is a protein expressed on the surface of B cells. Both are common targets for CAR-T cell therapies.

| Brand Name | Scientific name | Manufacturer | Disease treated | Target antigen |
|------------|---------------------------|--------------------------------------|---------------------------|----------------|
| Abecma | idecabtagene vicleucel | Bristol-Myers Squibb | Multiple myeloma | BCMA |
| Carvykti | ciltacabtagene autoleucel | Janssen Biotech, Inc. | Multiple myeloma | BCMA |
| Breyanzi | lisocabtagene maraleucel | Kite Pharma, Inc. | DLBCL, HGBCL, PMBCL, FL3B | CD19 |
| Kymriah | tisagenlecleucel | Novartis Pharmaceuticals Corporation | ALL, DLBCL, FL | CD19 |
| Tecartus | brexucabtagene autoleucel | Kite Pharma, Inc. | ALL, MCL | CD19 |
| Yescarta | axicabtagene ciloleucel | Kite Pharma, Inc. | HCBL, DLBCL, FL | CD19 |

The indications for each CAR T cell therapy listed in this table include marketing authorisations from both the EU and the US, but differ based on the region. ALL: acute lymphoblastic leukaemia. BCMA: B-cell maturation antigen. DLBCL: diffuse large B-cell lymphoma. FL: follicular lymphoma. FL3B: follicular lymphoma grade 3B. HGBCL: high-grade B-cell lymphoma. MCL: mantle cell lymphoma. PMBCL: primary mediastinal large B-cell lymphoma.

batch of product. This even applies to the choice of equipment used to process the cells. Any changes to the manufacturing process require submitting evidence that the product has not changed in any meaningful capacity, as evidenced by comparability studies.²⁵

Manufacturing changes are inevitable as more knowledge of the product and process develop together. But ideally, it is recommended to start with the best process and have all the expertise built in the company from the beginning, a difficult feat for any organisation. In contrast to running a marathon where you know where the finish line is and can always see the road in front of you, successfully commercialising a cell and gene therapy product is akin to a marathon on a road under construction.

The role of quality writing in this field

Medical communications play a vital role in keeping professionals informed of the latest developments in the CGT space. Writers should stay abreast of regulatory and manufacturing news, as well as be aware of macroeconomic forces. With cell and gene therapies set to be the fastest-growing type of pharmaceutical product over the coming decade, as measured by the number of clinical trials,²⁶ the US FDA is preparing to approve therapies faster. This has led to, for example, changing the name of the Office of Tissues and Advanced Therapies to the Office of Therapeutic Products, a “super office” as they describe it.²⁷

Anticipating the future needs of biotech companies is important in understanding how to position a new innovation or product in the best way possible for success. Communicating strategically cannot occur alone here; collaboration within company departments as well as external partners is essential for acquiring key insights that might benefit a company’s stakeholders.

This type of writing could be exciting for those who enjoy working in a dynamic environment, and intimidating for those more accustomed to working alone, and less so in a journalistic fashion. What excites me is knowing that what I create depends on data and ideas that are unique, context-dependent, and do not exist yet in the public domain. Effective scientific communication is the bridge between innovation and transformation in this field and provides the opportunity to be both creative and acutely aware of the scientific issues at hand.

What the future holds

Bringing down the costs of CAR T cell therapies is a top priority.²⁸ The treatments that are on the market today cost £450,000 for the treatment alone, but the total cost of care in the US healthcare system has been found to exceed \$1M for some patients.²⁸⁻²⁹ Discussions of lowering the cost of goods cite Pharma 4.0 as a necessary step in this endeavour and involves digitisation, automation, and the continuous manufacturing of biomedical products.³⁰ Another way to reduce costs is to enable allogeneic CAR T cell therapies and manufacturing them more centrally to the patient, eliminating overseas shipping and vastly improving patient reach.³¹

Autoimmune and cardiometabolic diseases may also be one day treated through CAR-based therapies, and a variety of cell types could be used as starting material.³² Clinical trials are underway for CAR natural killer cell therapy, CAR macrophage therapy, tumour infiltrating lymphocyte therapies, T-cell receptor-based therapy, and extracellular vesicle therapy. Central to all of this innovation are people, and industry is working rapidly to train scientists to expand manufacturing capacities in the rush to get products to the clinic.

What we know today about cell and gene therapies will undoubtedly change in five to ten years. However, considering the scientific hurdles CAR T cell therapy has overcome in order to be as effective as it is today, and the hope that this treatment could ward off cancer, forever, and after just one dose, guarantees that study of CAR T cells will continue.

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

Disclosures and conflicts of interest

Avi Saha is employed by ChemoMetec A/S (Allerød, Denmark), a leading manufacturer of cell counting and analysis equipment used by the life science industry, including manufacturers of cell and gene therapies.

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The March 2024 edition



Translation

Medical translation is a complex and demanding field requiring specialised knowledge, skills, and expertise. In this issue, we explore a range of topics, including the role of medical translation in clinical trials and regulatory affairs, the importance of terminology management, the use of technology and machine translation, ethical and legal considerations, the impact of cultural differences, quality assurance and risk management, and the emerging trends and challenges in the field. This issue provides valuable insights into medical translation and its contribution to enabling communication with different audiences from different backgrounds.

Guest editors: Ana Sofia Correia and Claire Harmer

The deadline for feature articles has now passed.

Psychotropics:

A scientific, regulatory, and public view on the medicinal use of cannabinoids and psilocybin

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Abstract

Research on psychotropics is gaining more popularity worldwide and support from drug regulatory agencies, which recognise the unmet medical needs of certain patient communities, such as patients with mental disorders and patients with cancer who experience depression. Cannabinoids and psilocybin have shown promising results in preclinical studies and clinical trials, but the current clinical evidence is scarce, and the regulatory requirements are strict due to high potential for drug abuse. The US FDA has recently released a draft, non-binding guidance on clinical trials with psychedelics. Europe is currently falling behind the US and Canada in terms of regulating psychotropic substances. The article provides a general introduction on conducting clinical trials with psychotropics and the regulatory requirements (as of October 2023) when submitting marketing authorisation application. In the near future, as more data becomes available, research on psychotropics will definitely shape the European regulatory landscape.

Psychotropics are popular again

Drug development is a risky but rewarding endeavour.¹ About 90 percent of clinical drug development fails in the Phase I stage. But when a drug is approved, patients benefit: it can

improve their quality of life or can turn a terminal prognosis into a chronic disease. This is especially true for cancer treatment. The projections calculated using current real-world data on cancer show that by 2040, 28 million people will be affected by the disease worldwide, and the investment in cancer research has been growing steadily every year with a slight plateau during the coronavirus disease 2019 (COVID-19) pandemic.^{2,3} Effective cancer treatment can cure the disease or at least improve a patient's overall survival and quality of life.⁴ But often, patients develop depression and are at a higher risk of suicide, and therefore are prescribed strong antidepressants to help them cope with their symptoms.⁵ Patients are often given strong opioids to manage pain, but long-term usage leads to increased tolerance or resistance making opioids ineffective.⁶

A similar scenario is seen in patients with mental disorders. It can take time for the medicine to take effect and to find the correct dosage, and some side effects can have a major impact on a patient's quality of life (such as

weight gain, sexual dysfunction, dizziness, or suicidal thoughts).^{7,8} Especially severe forms of mental disorders, such as post-traumatic stress disorder and major depressive disorder, are challenging to treat.⁹

Consequently, new research on psychotropics has created a fresh field of opportunities: the development of new biotechnological methodology (cell culture) to meet the research objectives of the pharma industry and clinical research laboratories. If effective, psychotropics can be used to treat neurological diseases, especially in patients with breakthrough depression (recurring depression) or patients with terminal cancer.¹⁰

This article explores the scientific, regulatory, and public positions on potential medicinal use of cannabinoids (cannabidiol and tetrahydrocannabinol) in pain and depression, and psilocybin's potential to improve patients' wellbeing. It also provides an update on the status of the biotechnological methodologies (cell culture) that could be used to produce the mentioned substances, and latest recommenda-

Abbreviations

| | |
|-------------|---|
| CBC | Cannabichromine |
| CBD | Cannabidiol |
| CBDA | Cannabidiolic acid |
| CBG | Cannabigerol |
| CBGA | Cannabigerolic acid |
| CBN | Cannabinol |
| CMC | Chemistry, Manufacturing, and Controls |
| CRISPR-Cas9 | CRISPR-Associated protein 9 |
| EFPIA | European Federation of Pharmaceutical Industries and Associations |
| MDMA | 3,4-methylenedioxy-methamphetamine (also known as ecstasy or molly) |
| NHS | National Health Service |
| THC | Tetrahydrocannabinol |
| THCB | Tetrahydrocannabutol |
| THCA | Tetrahydrocannabinolic acid |
| THCAS | Tetrahydrocannabinolic acid synthase |
| THCV | Tetrahydrocannabivarin |

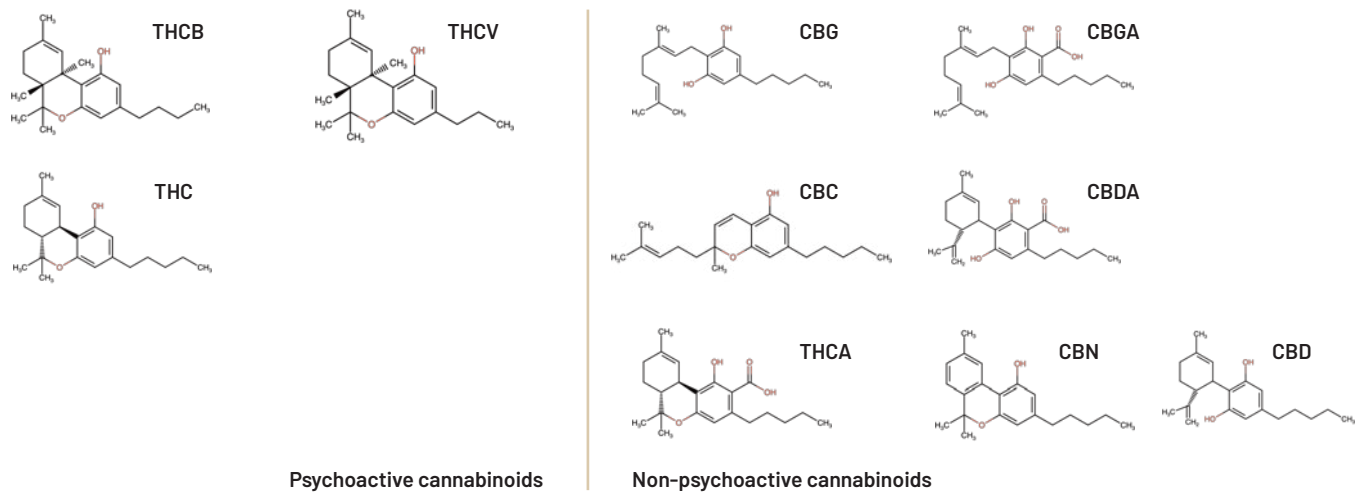


Figure 1. Chemical formulas of various cannabinoid molecules

Abbreviations: CBC, cannabichromine; CBD, cannabidiol; CBDA, cannabidiolic acid; CBG, cannabigerol; CBGA, cannabigerolic acid; CBN, cannabinol; THC, tetrahydrocannabinol; THCA, tetrahydrocannabinolic acid; THCB, tetrahydrocannabutol; THCv, tetrahydrocannabivarin;

tions (as of October 2023) published by the regulatory agencies on preparing documentation when conducting clinical trials and submitting marketing authorisation application.

**Biotechnological production:
The best way to ensure high-quality
medicine for patients, or just
innovation start-up hype?
A scientific perspective**

Biotechnology is defined as “the technique of

using microorganisms, such as bacteria, to perform chemical processing, such as waste recycling, or to produce other materials, such as beer and wine, cheese, antibiotics, and (using genetic engineering) hormones, vaccines, etc”.¹¹ Increased interest and investment into psychotropics means a higher demand on the market. While traditional manufacturing using chemical synthesis and extraction work well, albeit with minor downsides (impurities, racemate mixture, highly expensive purification),

biotechnologists are still looking for innovative and efficient ways to maximise the production of psychotropics using the cellular metabolism pathways of various hosts.

Cannabis – a natural producer of psychotropic and non-psychotropic substances

Cannabis sativa L. is the sixth most important crop in the US.¹² Besides recreational and medicinal uses, the plant can be used for production of clothing and nutrition products



Photo: Indorgo Canada

Figure 2. Cannabis buds that produce CBD



Photo: Thomas Elliott

Figure 3. Glandular trichomes in Cannabis sativa L.

Table 1. List of cannabis-derived medicinal products

| Brand name | Active compound(s) | Authorised in countries | Indication | Route of administration |
|-----------------------|--|--|---|-------------------------|
| Epidyolex® | CBD | EU (not available in every country), US (named Epidiolex®) | Lennox-Gastaut syndrome, Dravet syndrome, adjunctive therapy of seizures associated with tuberous sclerosis complex | Oral |
| Marinol® (dronabinol) | (-)-trans-delta-9-tetrahydrocannabinol isolated from the plant | EU (not available in every country), US, Australia | Cancer treatment, AIDS, multiple sclerosis | Oral |
| Cesamet® (nabilone) | synthetic (-)-trans-delta-9-tetrahydrocannabinol | EU (not available in every country), US, Australia | Cancer treatment | Oral |
| Sativex® (Nabiximols) | Cannabis herbal preparation (extract of cannabis)(oil) THC and CBD | EU (not available in every country) | Multiple sclerosis | Oral |

(seed oil, protein powders, etc.). Cannabinoids, the major group of compounds present in the plant, show various health benefits (anti-cancer, painkilling, muscle and nerve relaxing) and some of them exhibit psychoactive characteristics.^{13,14} The well-known cannabinoids are the psychotropic Δ^9 -tetrahydrocannabinol (Δ^9 -THC, isolated in 1964) and the non-psychotropic cannabidiol (CBD, isolated in 1940).¹⁵ Other cannabinoids are cannabidiolic acid (CBDA), cannabigerol (CBG), cannabinol (CBN), cannabichromene (CBC), and the derivatives of tetrahydrocannabinolic acid (Δ^9 -THCB, Δ^9 -THCV, Δ^8 -THC). Current research confirms that only THC, THCV, and THCB have psychotropic characteristics.¹⁶ (Figure 1) THC and CBD have the same “relative” (precursor substance), cannabigerolic acid (CGBA), which is produced in the glandular trichomes. Glandular trichomes are hair-like growths that secrete various secondary metabolites; they are found on the leaves, stems, and flowers of the plant.^{17,18} The highest CBD concentration is found in the glandular trichomes of the cannabis flowers, which are used for CBD isolation at the industrial scale (Figures 2 and 3).

Latest in vitro and animal studies have shown that CBD has anti-anxiety, anti-nausea, anti-arthritis, anti-inflammatory, and immunomodulatory properties. Interestingly, preclinical studies have shown that CBD can work synergistically with anti-cancer agents and improve their efficacy.¹⁹ Toxicity studies on CBD

have shown that it is generally well tolerated, except in very high doses.²⁰ On the contrary, the THC interferes with the regulation of cancer development, promoting cancer and inflammation. There is a high risk of abuse in chronic therapy, and animal studies have shown high mortality and reproductive atrophy and hyperplasia.^{21–24}

A recent systematic review on worldwide clinical trials with cannabis for therapeutic purposes reported that most of the clinical trials were performed in the US, Brazil, Australia, Netherlands, Israel, Switzerland, and the UK.²⁵ The EU clinical trials register lists 73 clinical trials involving cannabis (as of October 2023) and 17 of them test the efficacy of CBD against pain (as of October 2023).^{26,27} The most common indications are: cannabis use disorder, effects of THC and its toxicity, cancer, multiple sclerosis, pain, and fibromyalgia. Clinical Trial Information System (CTIS) lists six clinical trials with cannabis.²⁸

ClinicalTrials.gov lists many interventional clinical trials using cannabis; the most common indications are depression, marijuana abuse, pain, cannabis dependence, and multiple sclerosis.²⁹ Currently, there are four medicinal products authorised for the European market (Table 1). One of the products is Sativex, developed by Jazz pharmaceuticals (GW pharmaceuticals). Sativex® is an herbal preparation in the form of an oral mucosal spray containing a standardised cannabis extract, nabiximols. The

extract contains 27 mg/mL THC and 25 mg/mL CBD.³⁰ Several safety studies with Sativex® have been conducted, especially for pain management in patients with cancer.³⁰ Latest studies did not show that Sativex® is superior to placebo.^{31–33}

Cannabinoids can be produced by direct extraction from plants, by chemical synthesis, or using microbial cells (fermentation). The most common way to produce CBD in the industrial setting is to grow *Cannabis sativa* either in greenhouses or outdoors and to chemically extract CBD and THC from the plants.³⁴ In recent years, the CRISPR-Cas9 gene editing technique has enabled the industry to produce plants that are more resistant to climatic hazards and diseases, that yield more cannabinoids, and that produce more or less of specific metabolites.³⁵

The industry claims that the main benefit of the traditional isolation is the co-isolation of other compounds (terpenes, flavonoids) in very low concentration, which could be responsible for improving the therapeutic effect (also called “entourage effect”).^{36,37} The entourage effect is defined as a synergistic cooperation of compounds in *Cannabis sativa* that increases its efficacy. However, the regulatory and public data available on the entourage effect are scarce.

Chemical synthesis of cannabinoids is less efficient than the traditional method.³⁸ So, a novel approach for cannabinoids synthesis was developed in 2019: microbial fermentation.³⁹ Microbial fermentation enables production of a

single compound in a single-cell organism such as yeast, bacteria, or algae.³⁴ Luo et al. introduced cannabis genes into yeast (*Saccharomyces cerevisiae*), giving it the ability to metabolise sugars into CBGA (the precursor of THC and CBD). The CBGA yield, however, was low (milligram and microgram scale).⁴⁰ Lange et al. were able to produce the enzyme Δ^9 -tetrahydrocannabinolic acid synthase (THCAS) using yeast (*Pichia pastoris*).⁴¹ THCAS catalyses the production of THCA from CBGA, THCA is the precursor substance of THC.⁴¹ THC production has also been tested in other organisms, such as *E.coli*, *S. cerevisiae*, and *K. phaffii*.^{34,42} The attempts to biosynthesise cannabinoids in algae chloroplasts are still in the early start-up business stage as the method has proven to be very expensive; algae has thick cell walls which require complex and expensive techniques to break them.³⁴

Favero et al. published a list of patents (filed as of 2014) for cannabinoid biosynthesis using microbial fermentation.³⁴ The latest patents (from 2020 to October 2023) use

Cannabinoids can be produced by direct extraction from plant, by chemical synthesis, or using microbial cells (fermentation).

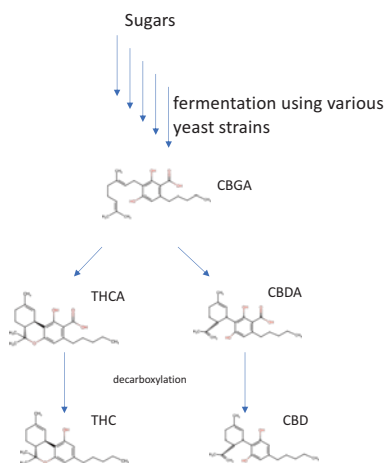


Figure 4. Favero et al., demonstrated a biochemical method to synthesise THC and CBD from sugars.

Sugars are fermented using various yeast strains to produce CBGA and subsequently using various chemical techniques to yield pure THC and CBD. The method is still in its infancy.

Abbreviations: CBD, cannabidiol; CBDA, cannabidiolic acid; CBGA, cannabigerolic acid; THC, tetrahydrocannabinol; THCA, tetrahydrocannabinolic acid.

yeast or bacteria to produce cannabinoids via the geranyl pyrophosphate pathway by introducing various *Cannabis sativa* genes or enzymes.³⁴ Two companies in the USA patented cannabinoid synthesis in microalgae.³⁴ Available information shows that production of cannabinoids using biotechnological methodology is still in its infancy (Figure 4).

Psilocybin – the magic in magic mushrooms

Psilocybin is a natural psychoactive tryptamine isolated from magic mushrooms (most common genus is *Psilocybe*).^{43–45} First industrial isolation of psilocybin was done by A. Hofmann from the Mexican mushroom *Psilocybe mexicana* Heim (Figures 5 and 6).⁴⁶

Synthetic psilocybin was first marketed in the 1960s by Sandoz under the brand name Indocybin®.⁴⁴ Initially marketed for clinical research, it was abused as a recreational drug, which led to research being put on hold for 30 years.⁴⁷ Clinical trials have shown that psilocybin in small doses can help people achieve mystical experience (altered state of consciousness).⁴⁸ Only high doses of psilocybin showed a potential to treat depressive state and negative attitude in patients with advanced cancer, which was confirmed by the patients and their observers. The treatment increased the overall wellbeing of the patients.⁴⁹ However, a clinical study performed by Griffiths et al. confirmed that higher dosage led to increased recurrence of adverse effects (headaches, nausea, dizziness, anxiety).⁴⁹ The reporting of higher anxiety, albeit by a small number of patients, is common in almost every clinical trial on psilocybin.^{48,50} There have been two *Nature* articles on patients with post-traumatic stress disorder treated with psychotropics

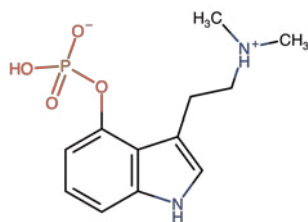


Figure 5. Chemical structure of psilocybin

that reported overall life quality improvement since their treatment.^{51,52} Currently there are no authorised psilocybin products on the market, but 11 clinical trials are ongoing (according to EMA Executive Director Emer Cooke).⁵³ Australia has approved psilocybin for medicinal use in psychiatric patients in 2023.¹⁰

Psilocybin can be isolated from magic mushrooms, produced via microbial fermentation (using procaryotic or eucaryotic hosts), or chemically synthesised from hydroxyindole.^{45,54} Flower et al. were able to synthesise psilocybin (approximately 30 mg/L) and 13 derivatives of psilocybin using genetically modified *E. coli* in a small-scale using tryptamine.⁴⁵ This de novo synthesis is a novel approach that was only tested at a microscale and should be analysed for suitability for industry-scale production.⁴⁵ Current limitations for microbial fermentation are the optimisation of the methods for higher yield production, purification, and up-scaling.

Current regulatory guidance: a friend or a foe?

Cannabis

With the US and Canada pioneering cannabis legalisation⁵⁵ and the rising therapeutic demand for cannabis products and derivatives in Europe, the pressure to regulate cannabis products in Europe is on the rise. The EMA has published a guidance document on cannabis-derived medicinal products.⁵⁶ According to the guidance, there shall be no difference in marketing cannabis-derived medicinal products, as the Marketing Authorisation Holders (MAHs) should comply with the definition of a medicinal product (Article 1(2) of Directive 2001/83/EC).



Figure 6. Magic mushrooms close-up

Medicinal products are submitted in the form of a dossier (Common Technical Document, CTD) and the applicant must include the results of pre-clinical research and clinical trials. If the active substance falls under well-established use (known use for more than 10 years in the EU), the applicant can submit scientific literature, which should demonstrate safety and efficacy of the new medicinal product (Article 10a of Directive 2001/83/EC).⁵⁷ There are also exceptions for herbal medicinal products. If they have been used for more than 30 years (at least 15 years in the EU) and are intended for use without medical surveillance and aren't administered by injection, then the Traditional Herbal Medicinal Products Directive (Directive 2004/24/EC and Directive 2001/83/EC (Article 16a)) applies.⁵⁷ On the contrary, if the requirements for herbal medicinal products are not fulfilled (not well-established use under Article 10a or traditional use under Article 16a(1)), then the application must comply with the general requirements of the Marketing Authorisation Application (they fall under the definition of medicinal products).⁵⁷ Furthermore, in October 2022, the European pharmacopoeia (Ph. Eur.) published monographs on *Cannabis flos* (flowers) and extracts from cannabis, which will be published in January 2024 in the Ph. Eur. Supplement 11.5 and will take effect as of July 2024.^{58,59}

At the moment, the European Federation of Pharmaceutical Industries and Associations (EFPIA) does not have a position statement on cannabis-derived products and psilocybin, but they acknowledge the importance of the psychotropics, which was published in the EFPIA pipeline innovation review (dated August 2022).^{60,61} The US FDA has not approved any medicine containing cannabis, but has authorised cannabis-derived substance (CBD in Epidiolex®/Epidyolex®) and synthetic cannabis substances (dronabinol in Marinol and Syndros and naboline in Cesamet®).⁶² The US FDA is supporting cannabis-derived medicine only if the benefits greatly outweigh the risks.⁶²

Psychotropic substances

Psychotropic substances are regulated globally and at the EU level. To prevent drug abuse, the

UN has classified these substances into four schedules, which can be found in the Annex of the 1971 UN Convention on Psychotropic Substances.⁶³ The EU system regulated the drug precursors following specifications listed in the Regulation (EC) No. 111/205 and 273/2004.^{63,64}

Cannabis-derived medicinal products have the same conditions as every marketing authorisation application; the therapeutic benefits must outweigh the potential risks.

Furthermore, plant extracts can be used in a clinical trial but have to comply with the general requirements defined in the Ph. Eur., national pharmacopoeias, and the EMA guidance documents.⁶⁵ However, every country can further tighten the requirements.⁶⁵

As for the development of psychotropic substances, the EMA has not published any guidelines regarding clinical trial development and marketing authorisation. Cannabis-derived medicinal products have the same conditions as every Marketing Authorisation Application; the therapeutic benefits must outweigh the potential risks.⁶⁶ However, the EMA and the US FDA published various general guideline documents on conducting clinical trials with psychotropic substances.⁶⁶ In August 2023, the US FDA published a draft guideline on developing psychedelics. It is focused on conducting clinical trials, data collection, and patient safety. In general, the applicant must provide sufficient CMC data (which are an important part of the CTD), and the application varies depending on the substance origin (i.e. from plant material, algae, etc.).^{67,68} EMA indirectly followed the US FDA steps and published a draft guidance on conducting clinical trials for major depressive disorder in September 2023.⁶⁹ The draft guideline also concentrates on psychotropics – psilocybin, LSD, DMT and mescaline – and acknowledges major challenges in clinical trials (placebo, comparator, expectancy and unblinding, dosing, maintenance of effect, safety and psychotherapy).⁶⁹ It is recommended to seek scientific advice prior to conducting clinical trials, due to complexity and safety of psychotropics (concerning side effects).⁶⁹

In March 2023, EMA Executive Director Emer Cooke wrote a letter in which she confirmed that the EMA wants to focus on promoting the development of psychedelics for unmet medical needs, especially for mental health conditions, as the risk profile seems to be low.⁷⁰ In Europe, the research on psychotropics

is still very restricted, in comparison to Canada, the US, and Australia. As of July 2023, Australia allows the prescription of psilocybin and MDMA (ecstasy) as medicine.¹⁰

The public view on psychotropics

According to Wikipedia, some countries in Europe have legalised medicinal and scientific cannabis use while recreational use is only tolerated.⁷¹ For example, in Germany, according to a draft document published in September, possession of 25 grams of cannabis and cultivating up to three plants for individual purposes are allowed.^{72,73}

Recreational use is very restricted in Netherlands; it is tolerated only in licensed coffeeshops.⁷⁴ They can only sell small quantity of cannabis (less than five grams and no more than five plants) to residents of Netherlands.⁷⁵ Legalised medicinal use of cannabis is a very different story: it is allowed in most of the EU countries (with slight differences in regulatory requirements), UK, and other countries.⁷¹

Travelling with psychotropics may be challenging but still possible, depending on the country's requirements. Most of the restrictions are published on the International Narcotics Control Board website⁷⁶ with a disclaimer that it is advised to contact the embassy or consulate of the corresponding country before travelling.⁷⁷ Magic mushrooms are generally considered illegal for cultivation, sale, transport, and possession, except in a few countries (such as Netherlands and Austria).

Many health associations have published their position statements on cannabis, and they vary. The American Psychiatric Association doesn't see any benefit in treating psychiatric disorders with cannabis, and it opposes the use of cannabis in children, adolescents, and young adults up to the age of 25.⁷⁸ The American Nurses Society regards cannabis beneficial only for patients who really need it and if the treatment has been proved to be effective.⁷⁹ The UK's National Health Service published a guidance for prescribing cannabis-derived products; it does not recommend medicinal use for chronic pain unless for clinical trial purposes.⁸⁰ Globally, traditional medicine is getting more recognition; the WHO is striving to incorporate traditional medicine into conventional healthcare and deliver more evidence-based data. The topic was discussed in August 2023, in India, at the First WHO Traditional Medicine Global Summit.⁸¹

What does the future hold for psychotropics?

Psychotropic drugs have shown promising results in treating symptoms of mental health disorders and pain management, and their potential to improve patients' wellbeing should not be neglected. However, as Spiderman said, "with great power comes great responsibility". The main challenges in using psychotropics as therapy are managing their side effects,⁸² carefully considering the patient population, and regulating the environment in which they are used (hospital, doctor's office, etc.). Patient safety is the highest priority and can be ensured by establishing regulatory guidances, risk mitigations, and worldwide regulations to prevent drug abuse that occurred during the 1960s. The US Centers for Disease Control and Prevention reported that cannabis-induced disorder is most common in people who use cannabis during youth or adolescence and use it frequently.^{83,84} With so much contradictory scientific data, regulatory agencies (especially in Europe) are delaying in publishing mandatory guidances on conducting research with psychoactive substances and their marketing authorisation. According to the US FDA Director of Psychiatry Tiffany Farchione, psilocybin is still an investigational product.¹⁰ Nevertheless, the regulatory agencies acknowledge the unmet medical needs and are working towards finding solutions for it.

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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 declares no conflicts of interest.

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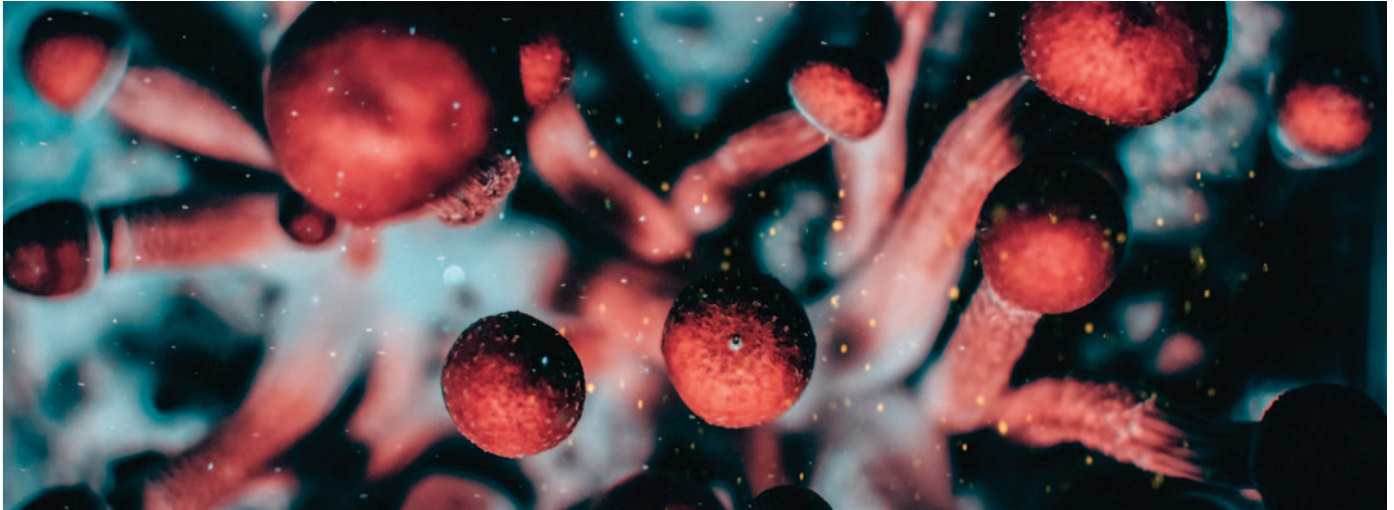


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Don't miss!

The June 2024 edition



Soft Skills for Medical Writers

Medical writing is a highly specialised field that requires a unique combination of technical knowledge, writing skills, and soft skills to produce high-quality work. While technical knowledge and writing skills are undoubtedly important, it is how one interacts with people that can truly set medical writers apart and enable them to succeed in their careers. This issue will focus on how soft skills are used within the different areas of the medical writing industry, and we hope it will provide valuable insights and inspiration for medical writers at all stages of their careers.

Guest Editors: Clare Chang and Nicole Bezuidenhout
The deadline for feature articles is March 1, 2024.

The evolution of biotechnology: From ancient civilisations to modern day

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Abstract

This article takes you on an intriguing exploration of the intertwined histories of biotechnology and medical writing. From ancestral plant cultivation to revolutionary advancements in genomics, proteomics, and bioinformatics, we delve into the profound evolution and influence of biotechnology on humanity. We also shine a spotlight on the critical role of medical writers, who meticulously document, interpret, and communicate these scientific breakthroughs to wider audiences. This article offers a key to understanding the convergence of science and communication, highlighting the incredible journey of biotechnology and medical writing.

Introduction

Exploring the history of Biotechnology and Medical Writing (Figure 1) reveals its evolution from ancient times when people harnessed living organisms for their benefit, to today's transformative advancements.

In the year 1919, the world of science was introduced to a term that would shape the future of numerous industries and finally give a 1000-year-old idea a name. Károly Ereky, a Hungarian agricultural engineer, conceived the term *biotechnology*.¹ His vision encapsulated the potential power of living organisms leveraged for industrial purposes. Broadly, biotechnology refers to the use of living systems and organisms, or

Interestingly, this early form of biotechnology not only preserved the bodies but also inadvertently led to the preservation of ancient pathogens.

their derivatives, to modify or produce products for humanity's benefit. This definition encompasses the recent growth in genomics, proteomics, and bioinformatics but also the advancements made by ancient civilisations.

Biotechnology in ancient civilisations

In roughly 6000 BC, the Sumerians and Babylonians harnessed biotechnology and mastered the art of fermenting yeast to brew beer.² It was a practice rooted in observation and tradition, rather than scientific understanding. They harnessed the natural process of fermentation, which is now commonly used by many pharmaceutical companies, where yeast found in the environment interacts with the sugars in grains or fruits.³ This interaction leads to the breakdown of complex molecules into simpler ones, producing alcohol as a byproduct. Beer and other alcoholic products became an integral part of their societal and religious practices.³ Even without the knowledge of the biological intricacies, these ancient civilisations successfully used biotechnology in their everyday lives.

In 4000 BC, the Egyptians began using a form of biotechnology in their intricate process of mummification.⁴ It was a religious and cultural practice aimed at preserving the body for the afterlife but showed a basic understanding of biotechnology. The Egyptians applied natural preservatives, such as natron, oils, and resins, which helped dehydrate the body and prevent decomposition.⁴ The natron created an environment hostile to microorganisms, most commonly bacteria, thereby preserving the bodies for centuries. Interestingly, this early form of biotechnology not only preserved the bodies but also inadvertently

led to the preservation of ancient pathogens. These pathogens, encapsulated within the mummified remains for millennia, present a unique opportunity for scientists today to examine and understand the diseases of the past with modern biotechnological tools.⁵ These mummification practices, as with 6000 BC fermentation, were deeply rooted in observation, tradition, and empirical understanding, rather than scientific understanding. However, they still formed a vital component of life and culture in these times.

By 1000 BC, the Chinese were building on the fermentation discoveries of 6000 BC and using biotechnology to brew alcohol.⁶ It not only served as a staple in social gatherings and religious rituals, but also as a symbol of hospitality and camaraderie. The consumption of alcohol became deeply woven into the fabric of their society, as it was customarily offered to guests as a gesture of goodwill and celebration.⁶ The Chinese also recognised the therapeutic potential of alcohol, incorporating it into their traditional medicine practices – e.g., as an anaesthetic during surgery.⁷

The Romans made use of biotechnology in many aspects of their lives.⁸ Their innovative use of concrete was formed from a biotechnological process involving the microbial mediation of minerals, resulting in the hardening of the concrete.⁸ This process, like the natural formation of minerals, was leveraged by the Romans to create concrete structures that have stood the test of time. The Pantheon and the Colosseum are examples of Roman concrete's resilience, hinting at the success of the biotechnology process involved.

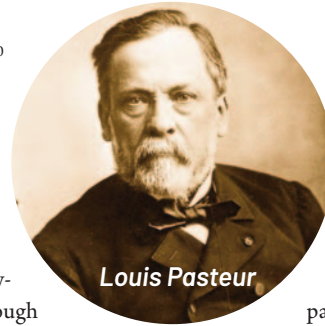


Biotechnology in the common era and the development of medical writing

The Renaissance period saw significant advancements in medical writing. A renewed interest in studying the human body and the natural world led to notable developments in medical knowledge. The invention of the printing press in the 15th century played a crucial role in disseminating this knowledge through the widespread publication of medical journals and texts.⁹ These journals served as platforms for physicians and scientists to share observations, discoveries, and theories, promoting the exchange of ideas and collaboration within the medical community.

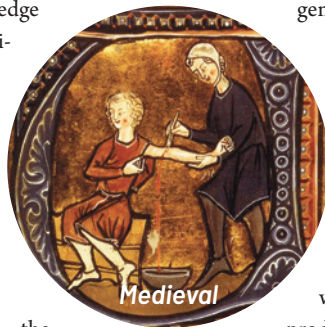
During the Middle Ages, the practice of traditional medicine witnessed significant advancements with an increased reli-

ance on biological substances.¹⁰ Herbal remedies became prevalent, with healers and apothecaries cultivating medicinal gardens to source a variety of plants.¹⁰ These plants were used in concoctions, balms, and tinctures, prepared using knowledge passed down through generations, often incorporating elements of fermentation and distillation.¹⁰ Another groundbreaking discovery was also made: certain types of mould could effectively treat infections² – e.g., probably penicillin. Initially, applying mouldy bread or decaying plant matter to wounds may have seemed counter-productive. However, it was later observed that such treatments significantly improved wounds. Unknown to them, medieval



Louis Pasteur

practitioners were harnessing the bacteria-inhibiting properties of the mould, effectively using a form of biological warfare to combat infections. This innovative use of natural resources laid the foundation for the earliest forms of antibiotics and paved the way for many modern antibiotics to be derived.



Medieval

Scientific revolution and medical writing

Fast forward to the 1800s: the scientific revolution took off. A more formalised study of biotechnology led Louis Pasteur to make groundbreaking discoveries in the field of germ theory that revolutionised microbial biotechnology.² His research focused on the causes of various diseases through the identification and understanding of microorganisms. The experiments and observations he conducted led to the development of

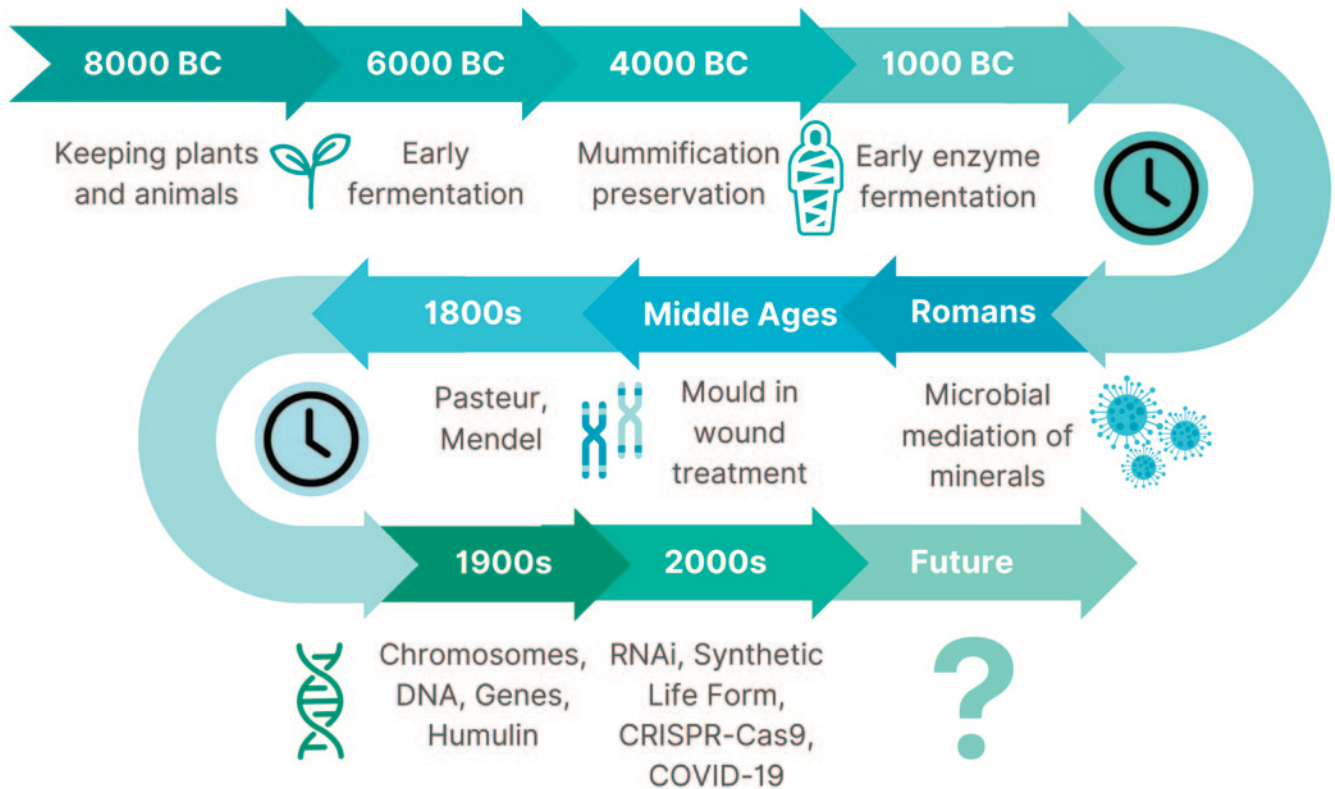


Figure 1. An overview of the history of biotechnology from 8000 BC to recent advancements made in the 2000s

techniques like pasteurisation, which played a significant role in food safety and disease prevention.

In 1865, Gregor Mendel, an Austrian priest and scientist, began studying his pea plant and decided to do some experimentation in biotechnology.² He crossed plants that had different forms of the same trait, such as purple or white flowers, and recorded the traits of the saplings. He noticed some traits only appeared when both parents had them, different traits were inherited independently of each other, and the ratios of the sapling traits could be predicted by mathematical law.

These observations led him to make the ground-breaking discovery of dominant and recessive traits and discover the fundamental principles of genetics, now known as Mendel's laws of inheritance.²

It was during this period that medical writers began to form vital roles in the scientific community. They played a large part in documenting Pasteur's work and communicating his findings to the medical community and public in a more comprehensible and accessible way. Early medical writers mostly consisted of physicians, surgeons, or professors who wrote about their own observations, experiments, or discoveries in medicine. They wrote textbooks, manuals, or treatises for teaching or reference purposes. Building on the Renaissance period advancements and as the scientific revolution took off, journalists, editors, and publishers began to write pieces on medical topics for newspapers, magazines, and journals. *The Lancet*, a popular journal that is still highly influential today, was founded during this time in 1823 by Thomas Wakley.¹¹ The American Medical Association (AMA) was founded in

1847 and started publishing its own journal.¹² A turning point for medical writing came in 1896 when Henry Smith Williams published *The History of Science from the Ancient Greeks to the Scientific Revolution*, which was one of the first comprehensive histories of science and medicine.¹³ As more medical discoveries were made, the roles of these medical writers became more imperative to keep the public and students updated.

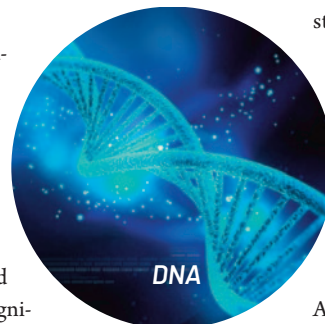
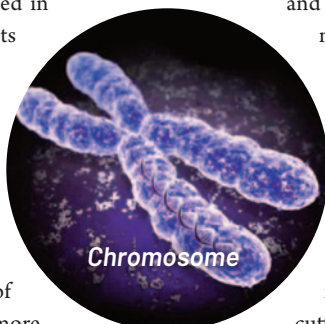


Biotechnology and medical writing in the twentieth century

In the early 20th century, biotechnology reached new heights. A pivotal moment in genetic research occurred when Walter Sutton and Theodor Boveri proposed the chromosome theory of inheritance.² This ground-breaking theory established a connection between the laws of inheritance formulated by Gregor Mendel and the observable behaviour of chromosomes during cell division. Their work provided a crucial foundation, forging a deeper understanding of how genetic traits are passed from one generation to the next. In 1928, Alexander Fleming discovered penicillin, the world's first antibiotic, when he noticed the inhibition of bacterial growth by a mould.² Fleming's discovery underscored the power of biotechnology, drawing on the knowledge of ancient civilisations and projecting it into the realm of modern medicine.

The 20th century was a landmark moment in the history of biotechnology, with ground-breaking scientific discoveries acting as catalysts for the modern biotech era. In 1944, a trio of scientists – Oswald Avery, Colin MacLeod, and Maclyn McCarty – made a significant contribution to our understanding of heredity, demonstrating that DNA is the genetic material that carries hereditary information.¹⁴ Their discovery set the stage for another monumental discovery in 1953 when James Watson and Francis Crick, leveraging the X-ray diffraction data of Rosalind Franklin and Maurice Wilkins, proposed the now universally recognised double helix structure of DNA that would later serve as the blueprint for life, influencing all aspects of biology.²

A new era dawned in 1970 when Hamilton Smith and Kent W. Wilcox discovered restriction enzymes, capable of cutting DNA at specific sequences; this later won him a Nobel Prize.¹⁵ This discovery paved the way for a turning point in biotechnology in 1973. Herbert Boyer and



Stanley Cohen successfully performed the first recombinant DNA experiment, demonstrating the transfer of a gene from one bacterium to another using a plasmid vector.² This trailblazing experiment laid the groundwork for genetic engineering, a fundamental technique in modern biotechnology.

In 1982, the world's first biotechnology drug was approved by the FDA. Developed by Genentech, Humulin is a human insulin drug produced by genetically-engineered bacteria. This marked a milestone in the field, displaying the extraordinary potential biotechnology held for transforming healthcare and improving human lives.² The approval of Humulin signposted the emerging power of genetic engineering as a tool for drug development, setting a new precedent for the start of the millennium. This era of genetic breakthroughs also saw the contributions of scientists like Kary Mullis, who invented the polymerase chain reaction (PCR) technique, revolutionising the way we study and manipulate DNA.²

During the 1900s, medical writing started to look familiar to its role today. New fields and disciplines such as genetics and biochemistry, among others, pushed medical writers to new limits; they had to constantly learn to keep on top of new discoveries and innovations. The European Medical Writers Association (EMWA)¹⁶ and the American Medical Writers Association (AMWA)¹⁷ were established and provided support for medical writers through training, networking, and opportunities to extend their work. The standards and guidelines they published became deeply rooted in ethical and quality medical writing and are still used worldwide today. Medical writing became a dynamic and demanding profession as governments and the public became more involved in medicine and health. It required a combination of critical thinking, scientific knowledge, and communication skills to inform and educate the public about the latest news, trends, and controversies in medicine. The diversification of the role continued into the 2000s and morphed into the significant role medical writers play today.

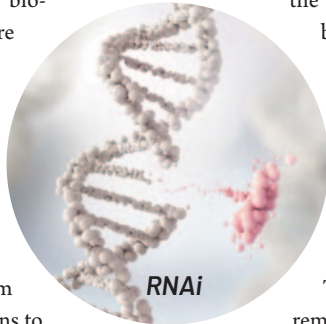
Modern-day biotechnology and medical writing

The dawn of the 21st century brought forth another transformative era in biotechnology. In 2006, Andrew Fire and Craig Mello were awarded the prestigious Nobel Prize in Physiology or Medicine.¹⁸ The distinguished recognition was for their ground-breaking discovery of RNA interference (RNAi). This mechanism had profound implications in the realm of genetics, as it provided a means to silence gene expression using small RNA molecules.¹⁸ Their discovery of RNAi added a new dimension to the understanding and manipulation of genetic material and the development of personalised medicine, further propelling biotechnology into previously uncharted territories. In a revolutionary stride in 2008, J. Craig Venter and his team accomplished a feat that was once thought to be science fiction – they synthesised an artificial bacterial genome and transplanted it into a recipient cell.² This remarkable achievement created the first synthetic life form, an event that not only marked a significant milestone in the field of biotechnology, but also sparked discussions about the possibilities and ethical implications of synthetic biology.

In 2010, Jennifer Doudna and Emmanuelle Charpentier made a breakthrough discovery with the CRISPR-Cas9 system – a formidable tool that revolutionised genome editing by enabling precise alterations in DNA sequences.²

This ground-breaking technology was leveraged in 2013 when Feng Zhang and his team reported the first successful application of CRISPR-Cas9 for genome editing in mammalian cells.¹⁹

The rapid development and potential applications of this technology, however, soon stirred a global dialogue around the ethical and societal implications of genetic modification, especially in humans. There was even talk of bringing back the woolly mammoth by cloning preserved thigh bones.²⁰ Reflecting this, the International Summit on Human Gene Editing²¹ was convened in 2015 to deliberate on the ethical and social dimensions of using CRISPR-Cas9 for modifying human embryos. However, in 2018, He Jiankui sent



shockwaves through the scientific community and the world with a startling announcement.

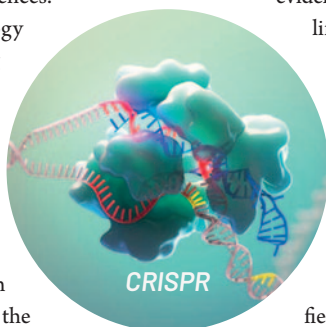
He stated that he had successfully created the world's first gene-edited human babies using the ground-breaking CRISPR-Cas9 technology.²²

This significant achievement sparked a firestorm of global controversy and widespread condemnation, challenging the ethical boundaries of biotechnology like never before. The incident served as a stark reminder of the immense responsibility that accompanies the power of genome editing, and the urgent need for regulation in this rapidly evolving field.

Only a few years later, there was an industry-defining moment in 2020. An unprecedented achievement allowed the FDA to approve the first COVID-19 vaccines developed using the innovative messenger RNA (mRNA) technology.²³ This technology instructs cells to produce a viral protein that triggers an immune response, a significant leap in vaccine development. It reflected the culmination of over 10,000 years of biotechnological advancement, highlighting the power of biotechnology in confronting global health crises. It marked a beacon of hope amid a global pandemic and highlighted the potential of biotechnology, not only as a tool for progress, but as a weapon in safeguarding humanity's future.

Conclusion

In reflecting on biotechnology's history, it is evident that the human desire to harness life's tools to solve complex problems has been both a blessing and a curse. This journey has given rise to phenomenal advancements; anyone now working with monoclonal antibodies and other therapeutic biotechnology products are now working with genetically-modified organisms! However, this journey has recently showed some darker sides. Such moments serve as stark reminders of the perils of unrestricted scientific exploration and the future of biotechnology. However, it is equally important to remember that every stumble is a step forward on the path of learning. Medical writers have played a crucial role in this journey by critically articulating data about biotechnology. They have helped to further



advance the field and get drugs developed. Their ability to communicate complex scientific information in an accessible and comprehensible manner has been vital in bridging the gap between the scientific community and the public and fostering a deeper understanding of biotechnology and its impact on humanity.

My definition of biotechnology is with all its potential and challenges: Biotechnology is an intrinsic part of our existence – woven into the fabric of our lives, our society, and indeed, our very world. The ongoing journey of biotechnology is not merely about mastering life's mechanisms, but also about evolving our understanding of ethical practices.

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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 standardised 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

Don't miss!

The September 2024 edition



Clinical trial transparency and disclosure

The clinical trial transparency and disclosure space continues to grow at pace. With the EU Clinical Trial Regulation being applicable since the 2022 launch of the Clinical Trials Information System comes increased requirements for public-facing documents. Provision of a summary of clinical trial results in lay language is also now mandatory in the EU. Challenges continue in balancing protection of personal data of trial participants with transparency, especially in the wake of the COVID-19 pandemic. All of these bring opportunities for medical writers to drive best practice in authoring clinical trial documents with disclosure in mind.

Guest Editors: Holly Hanson and Alison McIntosh

The deadline for feature articles is June 1, 2024.

Advances in the CRISPR-Cas9 system and gene therapy

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Abstract

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-Cas9 is a genome editing tool that helps scientists modify the DNA of living organisms selectively and precisely. The discovery of this system has led to changes in the approaches to gene therapy. In this article, I delve into the role of CRISPR-Cas9 in the development of treatment using gene therapy and the drawbacks of this system. Also, I discuss the role of medical writers in the dissemination of information and research on CRISPR-Cas9 and gene therapy.

Gene therapy involves the manipulation of genes or their expression inside cells to treat a disease or to stop its progress. Various mechanisms by which gene therapy can work include: replacing a mutated gene with a healthy copy of a gene; turning off a mutated gene or turning on a healthy gene; or correcting a mutated gene to treat a disease.¹

Genome editing over the years

The eukaryotic genome is made of millions of base pairs (bps) of DNA. Breakthrough research in the 1980s showed that mammalian cells can incorporate exogenous DNA in their genomes through homologous recombination (the process of exchange of genetic material between two strands of DNA with very similar base sequences). However, the rate of integration is quite low. This rate is enhanced by the introduction of double-stranded breaks (DSBs) using endonucleases called meganucleases

(enzymes that recognise a 14-40 bp DNA stretch). However, the specificity of meganucleases is a drawback. Furthermore, the DSBs are repaired through a non-homologous end joining (NHEJ) mechanism, which is error-prone and can delete or insert DNA sequences. The discovery of zinc-finger nucleases (ZFNs) furthered the field of genome editing. Each zinc finger module can identify 3 bps of DNA; thus, multiple zinc finger modules can be assembled to achieve higher binding specificity and increase the efficiency of homology-directed repair (HDR). Similarly, transcription activator-like effector nucleases (TALENs) can recognise single bp DNA and multiple TALENs can be put together for greater specificity. These discoveries have furthered our research in genome editing (Figure 1).²

The story of CRISPR-Cas system

Even though, ZFNs and TALENs increased editing efficiency, the targeting of various parts of the genome required cloning and expression of new sets of proteins, which proved to be a challenge. The third kind of genetic scissor used in genome editing is Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) – Cas (CRISPR-associated) system, an RNA-protein complex, made of a single guide RNA (sgRNA) and Cas effector protein. CRISPR-Cas is an adaptive immune system found in prokaryotes that protects the bacteria from phage/viral infections. As the CRISPR name suggests, the short repeats of DNA are interspaced by spacer sequences which were found to belong to phages and viruses.³ CRISPR-Cas systems are split into 2 classes (Class 1 has multi-unit effector molecule and Class 2 has a single effector molecule) and 6 types – types I to VI based on the Cas genes and the respective loci, and individual molecular mechanisms that lead to nucleic acid cleavage.^{4,5} The most widely used CRISPR system is the type

II CRISPR-Cas9 that belongs to *Streptococcus pyogenes*.²

CRISPR-Cas9 was first identified in 1987 in *Escherichia coli* and, since then, various research groups have contributed to elucidating the mechanism, functions, and applications of the CRISPR-Cas9 system, culminating in Jennifer Doudna and Emmanuelle Charpentier being awarded the Nobel Prize in Chemistry in 2020 for their breakthrough work on CRISPR-Cas9.⁶ Lander presents a great review of the scientific ecosystem that brought about these discoveries.⁷

Advantages and challenges of using the CRISPR-Cas9 system

The CRISPR-Cas9 system has revolutionised the field of biology. These genetic scissors allow biochemists, cell biologists, geneticists, and molecular biologists to study the functions of various genes and their role in different diseases, gene expression regulation, and epigenetic modification. Apart from its function to study human and animal diseases, the CRISPR-Cas9 system has been used in plant biotechnology and agriculture to produce crops resistant to stress and diseases, with higher yields, etc. To target a specific DNA sequence using CRISPR-Cas9, only the sgRNA needs to be modified and no complex cloning and protein engineering is required as is the case with ZFNs and TALENs. There were still challenges with the CRISPR system as it produced DSBs that could be repaired either through NHEJ (which introduces unwanted genetic changes) or HDR. Thus, research has also focused on improving HDR rates by introducing changes in the Cas9 genes or by inhibiting the NHEJ pathway. Cas9 variants found in nature are large proteins

making them difficult to package in various vectors for delivery. Therefore, scientists have also been working on finding smaller Cas9 variants in other bacterial species. Furthermore, there can be challenges such as lower on-target

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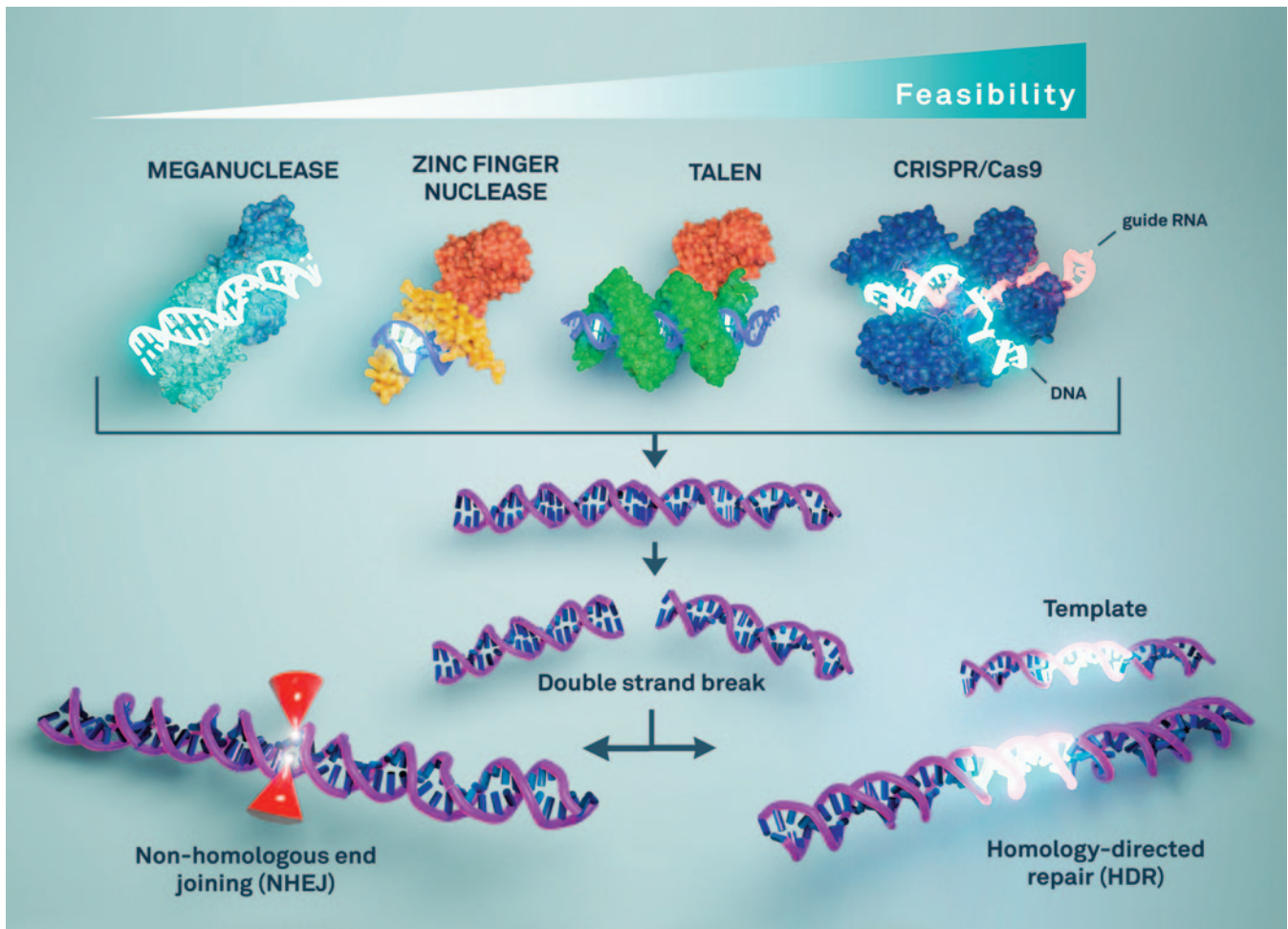


Figure 1. Major genome editing technologies

Feasibility here refers to the increased efficacy of targeted genome editing. Redrawn from Adli M. Nat Commun. 2018;9(1):1911.²

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editing efficiency (on-target editing refers to genetic modifications at the sites intended), off-target editing (genetic modification at unintended sites) and mosaicism (two or more different genetic lines in a single organism).

More details on different CRISPR systems, and the engineered changes to these systems to make them more efficient for introduction into human cells, have been reviewed elsewhere and are beyond the scope of this article.^{2-4,8}

Delivery of CRISPR-Cas9

In vitro, plasmids or RNAs carrying CRISPR-Cas9 are delivered into cells with the use of transfection reagents.⁹ However, this method cannot be used *in vivo*. Methods for *in vivo* delivery are discussed in the next section on gene therapy.

Gene therapy

Integrating and non-integrating vectors

Gene therapy can be *in vivo* (vector directly administered into patients) or *ex vivo* (vector delivered into cultured cells that are taken from patients and later administered back)¹⁰. Furthermore, the vector can be integrating (integrates into the genome) or non-integrating. This is a crucial factor when the therapy targets stem cells or mature post-mitotic cells. For stem cells, it is good to use integrating vectors, so that the corrected DNA passes on to the daughter cells. In cells that are no longer dividing, non-integrating vectors should do the job.¹⁰

The most used vectors in gene therapy and for CRISPR-Cas9 are adeno-associated viral (AAV) vectors (*in vivo*) and lentiviral vectors (*ex vivo*). Gene therapy does come with some risks, such

as insertional mutagenesis with integrating vectors, immune responses to vectors that can be life-threatening, and excessive T-cell activation.^{9,10} AAV is the most common choice, as it has low immunogenicity, thus reducing the likelihood of inflammatory response. For CRISPR-Cas9, special AAVs are constructed as the gene editing system exceeds the carrying capacity of AAVs. Lentiviral vectors have a larger carrying capacity, but can integrate randomly into the genome and, therefore, are not frequently used. In recent times, there has been research into new vectors. For example, baculovirus has a large carrying capacity and does not integrate into the genome and, thus, may be a safer alternative. Lipid-based nanocarriers and polymer-based nanoparticles are also considered promising tools for CRISPR-Cas9 delivery.⁹

Table 1. EMA-approved gene therapies

| Trade name | Year of approval | Indications |
|------------|------------------|--|
| Abecma | 2021 | Relapsed or refractory myeloma |
| Breyanzi | 2022 | Large B-cell lymphoma |
| Carvykti | 2023 | Relapsed or refractory myeloma |
| Hemgenix | 2023 | Haemophilia B (congenital factor IX deficiency) |
| Imlygic | 2015 | Local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma |
| Kymriah | 2018 | Relapsed or refractory follicular lymphoma |
| Libmeldy | 2020 | Metachromatic leukodystrophy |
| Luxturna | 2018 | Biallelic RPE65 mutation-associated retinal dystrophy |
| Roctavian | 2022 | Severe haemophilia A (congenital factor VIII deficiency with factor VIII activity <1 IU/dL) |
| Strimvelis | 2016 | Severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID) |
| Tecartus | 2020 | Relapsed or refractory mantle cell lymphoma |
| Upstaza | 2022 | Severe aromatic L-amino acid decarboxylase (AADC) |
| Yescarta | 2018 | Relapsed or refractory large B-cell lymphoma |
| Zolgensma | 2020 | Spinal muscular atrophy (type I) |

Gene therapy trials

Gene therapy clinical trials began in the 1990s and since then more than 3800 trials have either been performed or are currently ongoing.¹¹ The first gene therapy to be approved by the EMA, in 2012, was Glybera®, a treatment for hereditary lipoprotein lipase deficiency.¹⁰ Since then, several gene therapies have been approved by both the EMA and the US FDA. As of September 2023, there are currently 14 EMA-approved gene therapies (Table 1).¹² The indications of gene therapies have ranged from ultra-rare and rare genetic diseases to various cancers.

The use of CRISPR-Cas9 as a tool for gene therapy has also gained momentum in the last 5 years, with 42 trials in progress using CRISPR-Cas9 for gene therapy.¹¹ There are trials in progress (mostly Phase 1 but a few Phase 2/3) for: monogenic diseases, such as sickle-cell disease, β -thalassaemia, and hereditary amyloidosis; various types of cancers; and infectious diseases (like COVID-19). This year, 2023, is particularly significant for CRISPR-Cas9-based gene therapies as Vertex and CRISPR Therapeutics have submitted their *ex vivo* therapy (exacel) for sickle cell disease and β -thalassaemia,

developed using CRISPR-Cas9, for approval in the US and EU. And in November, 2023, the Medicines and Healthcare products Regulatory Agency (MHRA) approved this therapy in the UK.¹³

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interacts with various other genes and proteins in an organism and the environment to produce a phenotype. This phenomenon is not yet fully understood. Therefore, to modify a gene without clear knowledge of all the

variables presents a moral and ethical conundrum.^{14,15}

While the benefits and risks are understood, the efficacy and safety of this technology is still not clear. Thus, the FDA, EMA, and other regulatory authorities have strict criteria for approval of these therapies and post-market surveillance requirements.

Role of medical writers

Advanced therapy medicinal products (ATMPs), including cell, gene, and RNA therapies, have been gaining momentum; six novel therapies were approved in 2022 and a higher number is expected to be approved in 2023. The field is still new and the challenges of submitting regulatory documents for these therapies are also unique. Medical writers with advanced degrees in genetics, cell biology, RNA biology, and similar fields will have an increasing role to play in the correct interpretation and dissemination of information on ATMPs in a simple and lucid manner.

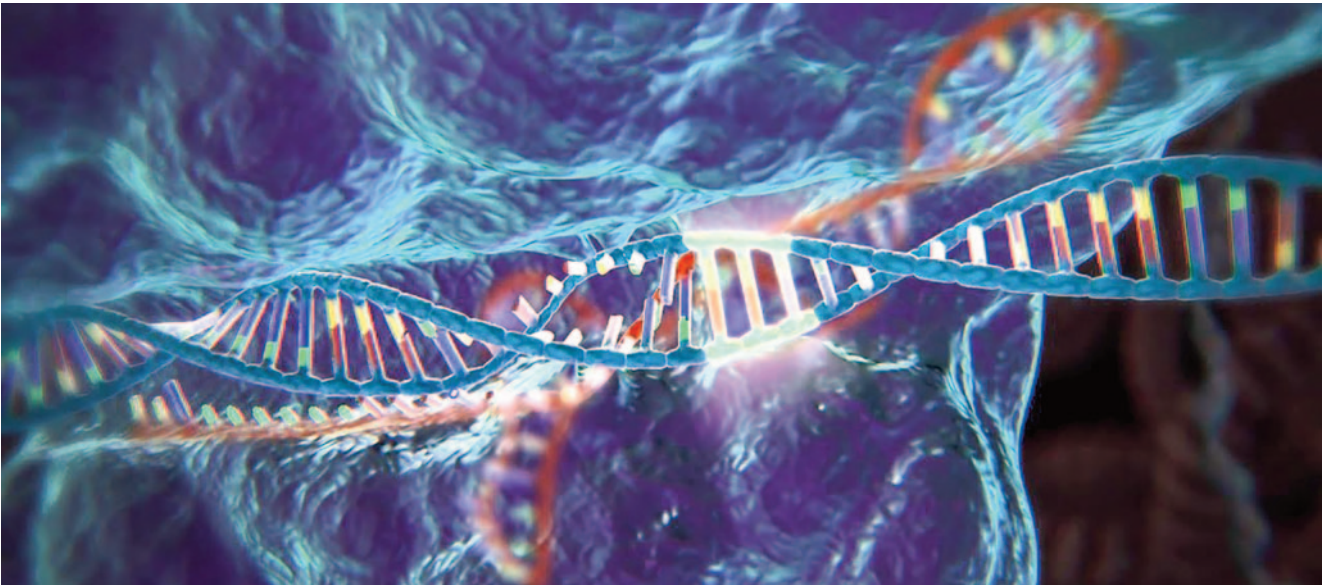
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Harold Swanberg, MD:

Why and how EMWA should remember him

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Abstract

Before the European Medical Writers Association (EMWA) and the American Medical Writers Association (AMWA), there was the Mississippi Valley Medical Editors Association (MVMEA). Most medical writers are unaware of the history of MVMEA and of how it turned into AMWA and EMWA. Here, I chronicle the life of Harold Swanberg, MD, who founded the MVMEA and, when it faltered, reinvented it as AMWA. The story begins shortly after the American Civil War, when medical journals were becoming more respected as sources of information and when editors began to be employed as paid, part- or full-time editors. It continues with the rise and fall of the MVMEA and its rebirth as AMWA. Swanberg's death coincided with the end of his vision for AMWA. However, the new vision for the association – and an international tragedy – allowed AMWA and EMWA to become key forces in developing modern medical writing as a profession.

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Introduction

Many EMWA and AMWA members have heard of Dr Harold Swanberg, whose work led to the development of these associations, but the details of his life are not commonly known. In fact, his life is notable for several reasons.¹ He contributed to the fields of radiology, scientific publishing, medical writing, and chiropractic. He also established three educational foundations, started three journals, and founded five organizations, one only for physician editors of medical journals and one including non-physicians working in the field of scientific publication. And although he did not envision what AMWA and EMWA would become, he created the framework and enthusiasm that made both possible.²

Personal life

William Harold Swanberg, BSc, MD, FACP, was born in Philadelphia in 1891 (Figure 1).³ Details on his early and personal life are scant (*see box below*), but we do know that he was married twice. In 1919, he married Zoe Johnson, his office assistant at the time,³ with whom he had a son, William H. Swanberg, Jr. With his second wife, Mildred W. Chapman, he raised her two daughters, as well as their own daughter, Nancy G. Swanberg. Nancy attended Francis Shimer junior college – at age 15 – and, after studying at the Sorbonne, received a degree in English from the University of Missouri in 1955, at age 20.⁴ In the 1960s, she taught medical writing at Baylor College of Medicine and became an AMWA Fellow in 1963.⁴

Early years

At age 19, Harold was working his way through medical school as an assistant in a histological laboratory when he became interested in “the claims of some of the cults of that period.”⁵ The laboratory appears to have been that of Oakley G. Smith.⁶ (Other sources describe Harold as being a student of Smith, which may be more self-serving than accurate.)^{7,8} Smith himself was a protégé of Daniel David Palmer, the founder of



Figure 1. William Harold Swanberg BSc, MD, FACP (1891–1970), founder of the Mississippi Valley Medical Editors Association and the American Medical Writers Association

chiropractic. For whatever chiropractic has become, it originated from Palmer's pseudo-scientific beliefs about healing. Smith eventually split from Palmer in 1907 and founded naprapathy, which focuses on diet and on manipulating connective tissue rather than the spine.⁸ Oakley Smith had been dissecting spines since 1905, in the interest of chiropractic theory, so Harold's work was undoubtedly related to Smith's investigations.⁸

In 1914, after 4 years of work and at age 23, Harold published *The Intervertebral Foramen: An Atlas and Histological Description of an Intervertebral Foramen and its Adjacent Parts* (Chicago Scientific Publishing; 1914). This book presented the first photomicrographs and scientific descriptions of the intervertebral foramen in cats.⁸ The following year, he published *The Intervertebral Foramina in Man* (Chicago Scientific Publishing; 1915). These books definitively disproved the “stepping-on-the-hose”

theory of chiropractic, which was the metaphor for vertebral pressure impinging on nerve cells as the cause of disease.^{8,9} Several legitimate medical journals gave the book good reviews. It was a standard work in chiropractic for decades¹⁰ and it is still sold on alternative medicine websites.⁷

A year later, at age 25, Harold graduated from the Chicago College of Medicine and Surgery.¹¹

Professional years

In 1917, Harold enlisted in the Army Medical Corps, was commissioned as a First Lieutenant, and studied at the School of Military Roentgenology in Chicago. After leaving the military, he moved to Quincy, Illinois, a small city on the Mississippi River. In 1919, he opened the Quincy X-Ray and Radium Laboratories.³

Harold was instrumental in founding the Physicians and Surgeons Radium Association of Quincy in 1921.³ A short 2 years later, he organised and was elected secretary of the Adams County Medical Society and served as the Society's librarian for 30 years. He also suggested that the Society publish a monthly bulletin.³ The first issue of the *Adams County Medical*

Society Bulletin was published in 1923. Eventually, the name was changed to *The Quincy Medical Bulletin*, which was published until 1970 and, at its peak, was sent to hundreds of physicians.³

A year later, in 1924, Harold started another journal, *The Radiologic Review*, which became the *Mississippi Valley Medical Journal* in 1939. It became *Clinical Medicine* in 1960 and was published until 1978.³

Over the next several years, Harold invented and marketed an applicator for treating gynecological cancers with radiotherapy (Figure 2),¹² maintained a private practice, worked as a radiologist at both Quincy hospitals and some smaller area hospitals, took a graduate course at Harvard, and spent 6 months in graduate studies in Vienna.³

In 1932, he published his second book, *Radiologic Maxims*, a collection of sayings and platitudes about radiology.¹³ The book was not well received.^{14,15} He also published several articles on medical topics and several editorials on social policy (e.g., fluoridation of drinking water, Social Security), as well as on issues in medical writing. In 1935, he helped found the

Mississippi Valley Medical Society and was soon elected secretary-treasurer.

In 1940, he founded yet another association, the Mississippi Valley Medical Editors Association (MVMEA), targeted to the physician editors of state and regional medical journals "to raise standards and to improve the quality of medical writing".⁵ To understand the association, how-

ever, and to avoid some historical confusion, we must go back to the end of the Civil War.

The American Medical Editors Association

With some notable exceptions (e.g., *The New England Journal of Medicine*, founded in 1812; *JAMA*, founded in 1883), for most of the 1800s, "medical journalism" consisted of a handful of serious, society-sponsored journals (including those from state and local medical societies who would be served by the MVMEA); many non-society proprietary journals publishing more-or-less legitimate medical articles; and advertising-driven tabloids (today's "throw-aways"). Out of this environment, shortly after the Civil War, a group of journal editors formed the American Medical Editors Association (AMEA) to promote journal editing as a "distinct medical speciality".^{16,17}

By the turn of the century, AMEA had hundreds of members nationwide, many with international reputations.^{18,19} Several leading medical journals routinely published reports on the Association's annual meetings, policy papers, and presidential addresses.¹⁶ During this period, for the first time, some journal editors became part- or full-time, paid professionals.¹⁶ (A note to researchers: Between 1928 and 1932, an organisation similar to the AMEA,¹⁶ or perhaps a continuation of it,¹⁹ appeared: the American Medical Editors and Authors Association.)

The AMEA was formed at the 1869 meeting of the American Medical Association (AMA). One of the founders – and its first president – was Dr Nathan S. Davis, the founder of the AMA.¹⁹ Over the years, however, the values of the AMEA and the AMA diverged. The AMEA criticised the business practices of AMA presidents George Simmons and his successor, Morris Fishbein, who between them directed (read: ruled) the association from 1889 to 1950.²⁰ (Both were

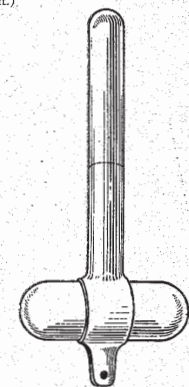
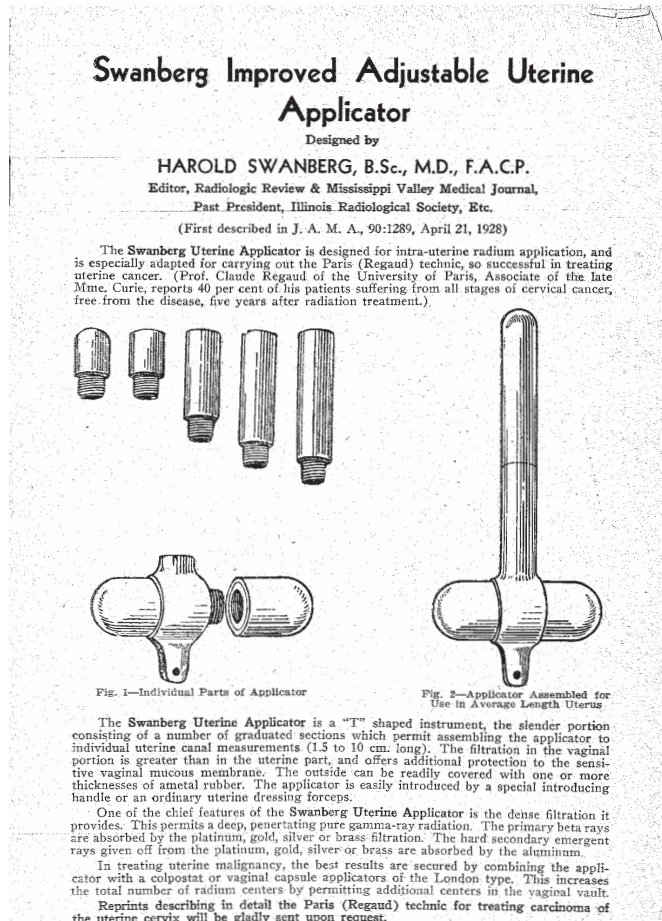


Figure 2. The applicator Harold invented for treating gynecological cancers with radiotherapy

While in Vienna doing graduate studies in radiology, Harold appears to have been introduced to the ideas of Dr Regaud of Paris (an associate of Madame Marie Curie). His applicator is compatible with Dr Regaud's pioneering approach to cancer treatment, which used comparatively small exposures to radium over longer periods.¹²

MEDICAL MANUSCRIPT EDITING SERVICE

One of the principal [sic] objectives of the American Medical Writers' Association is "to help maintain and advance high standards of medical literature." To accomplish this, the English construction and composition of many medical manuscripts should be improved. Many authors of medical subjects would like to have their manuscripts corrected and clarified. This is a service which is available to all members and felows [sic] of the Association. Only manuscripts intended for medical journals or kindred publications from which the authors receive no fees and which do not exceed 5000 words, will be accepted. It is not a commercial service and does not concern itself with the selling of manuscripts, ghost writing or the compiling of bibliographies. There is a nominal charge for this service based on the number of words in the manuscript. (In counting words, count every word in the entire manuscript including title, headings, et.) as follows:

1000 words or less \$500
 Each additional 1000 words or fraction thereof..... \$5.00

Between 1952 until at least 1965, AMWA ran a contract editing service for its members to "help maintain and advance high standards of medical literature".

Harold proposed the service (of course). The first editor was Theodore Peterson, a doctoral student at the University of Illinois, who, after almost 6 years, had edited 600 manuscripts. (Given the spelling and other mistakes in the ad, such a program was, indeed, needed.)

association, Harold decided to create a new national organisation. He persuaded his friend, Morris Fishbein, to offer a 2-hour course on medical writing at the 1948 meeting. On September 29, 1948, the MVMEA was renamed the American Medical Writers Association (AMWA), "America's only association devoted to improvement of the written word of medicine".⁵ Of course, Harold was the secretary/treasurer until 1960.¹ In addition to physician journal editors, the new association accepted as members "laymen connected with the editorial or business staff of medical periodicals, libraries, foundations, and publishing companies."⁵

In founding AMWA, Harold had several goals, most of which were met admirably during his life and some of which continue to drive AMWA's and EMWA's activities today.

- **Publish a bulletin.** When the MVMEA was renamed AMWA in 1948, it adopted the *Mississippi Valley Medical Journal* as its publication.⁵ In 1951, the association also began to publish the *Quarterly Bulletin of the American Medical Writers Association*, which was published until 1985, at which time its name was changed to the *AMWA Journal*.²⁵
- **Start regional chapters.** AMWA began with 42 members. Today, more than 4000 members are included in 16 North American chapters.²⁶ In 1992, the European Chapter became the European Medical Writers Association.
- **Bestow awards.** Early in its existence, AMWA established the Distinguished Service Award for "distinguished contributions to the medical literature or rendered unusual and distinguished service to the medical profession". The first recipient of the award was Harold himself, in 1952. The award is now the Harold Swanberg Distinguished Service Award, AMWA's highest award.²⁶
- **Begin a manuscript editing service.** Between 1952 until at least 1965, AMWA ran a contract editing service for its members, to "help maintain and advance high standards of medical literature". Harold proposed the service (of course), which provided line-by-line critiques but did not do library research, compile bibliographies, or provide ghost-writing.⁵
- **Establish college degree programmes in medical writing.** In 1954, the University of Illinois and the University of Missouri (in conjunction with their respective medical schools) and later, the University of

eventually forced from office for deceptive business practices.)²¹ The AMEA also advocated adding a medical officer to the president's cabinet (which led to the current position of the US Secretary of Health and Human Services),²² an idea vigorously opposed by the AMA, which feared government intervention in healthcare.^{18,23}

Years later, Harold would befriend Fishbein, who became an important AMWA member. But it is no accident that Fishbein disparages the AMEA as a predecessor to AMWA in the very first sentence of the Foreword of the *History of the American Medical Writers Association*: "When I first came into medicine and editing more than 50 years ago, I was confronted with the existence of the American Medical Editor's Association which I found was essentially a trade organisation designed to keep postage rates down, the quantity and costs of

advertising up, and not worrying too much about standards."²⁵ (Harold shared Fishbein's opinion.

However, one critic noted that Fishbein often "makes statements relative to the American Medical Editor's Association, that, to be kind to him, are more critical than correct".)²⁴

That said, Fishbein was an ardent supporter of AMWA from the beginning and used his influence as "the voice of American physicians" to advance the association. He started the Chicago chapter, was president of the Association in 1958, and received the Distinguished Service Award in 1962.²⁵

Back to the MVMEA...

The MVMEA, founded in 1940, was short-lived. The War prevented meetings between 1942 and 1948, at which time the 42 remaining members were losing interest. To save the

When founding the Mississippi Valley Medical Editors Association, Harold Swanberg did not envision its evolution into AMWA and EMWA, but he did create the framework and enthusiasm that made both organisations possible.

Oklahoma, began offering a Bachelor of Science degree in Medical Journalism and Writing. However, the programmes did not do well. In his history of AMWA, Harold mentions only 11 students who enrolled in the programmes and only 2 who graduated.⁵

- **Exhibit at professional meetings.** In Harold's history of AMWA is a 1956 photo of him in front of a large exhibit at an AMWA recruiting booth (created by Harold, of course) at the World Medical Association conference in Havana, Cuba.⁵ In a related project, AMWA published a small book titled *A Group of Papers on Medical Writing*.²⁷ The 11 chapters were written by distinguished AMWA members. An astounding 20,000 copies were published. The book is still relevant and is available for less than \$20.

The end of an era: AMWA changes course

A heart attack ended Harold's medical career in 1959. He died 11 years later but not before publishing Volume I of a planned 2-volume history of the association in 1965.³ (Volume II was never written.) He was also active in AMWA until his death, which coincided with the end of his vision for the association he created.

In the 1960s, the physician members of AMWA were retiring and were not being replaced. To keep the association solvent, the board decided to let non-physicians hold office, a practice Harold vehemently opposed. His last official act appears to have been casting the only vote against the change. The first non-physician president, Eric Martin, PhD, took office in 1970, the year Harold died.²⁸ Although AMWA survived by recruiting non-physicians and members who were not journal editors, by chance, it was also positioned to fill another, and arguably unmet, need of an emerging profession, especially after an international tragedy.

Dr Swanberg was active in AMWA until his death in 1970.

The beginning of an era: The drug that changed everything

Thalidomide was a sedative widely used in Europe to treat morning sickness during pregnancy. In the 1960s, it was linked to fetal deaths and thousands of serious birth defects in newborns.²⁹ In the US at the time, drugs were tested only on rodents and did not have to be tested for teratogenic effects. Clinical trials were



Quincy High School, which Swanberg generously supported throughout his professional life.

He founded the Society for Academic Achievement, which is “dedicated to motivate youth to achieve academic excellence” and that is still active; launched the Quincy Major Learning Programme, to help high school students enter and graduate from college; and was instrumental in establishing the first vocational guidance programme, including a full-time guidance counsellor.

not yet required for FDA approval, and any trials that were conducted were not subject to oversight.³⁰

The thalidomide tragedy led to the 1962 amendments to the Federal Food, Drug, and Cosmetic Act, which required manufacturers to prove both safety and efficacy and greatly increased surveillance and monitoring of the drug-approval process. This tightening of regulations was global.³⁰

The need to meet new and extensive domestic and international licensing requirements created great uncertainty among pharmaceutical companies. To address this uncertainty, 30 pharmaceutical professionals founded the Drug Information Association (DIA) in 1964.³¹ One of the founders (perhaps *the* founder) and its first president was Dr Eric Martin of AMWA.³²

As horrible as thalidomide was, it also probably saved AMWA. Eric became president of AMWA when the need for more complete and standardised regulatory documents greatly increased the demand for regulatory writers. At the same time, the fields of pharmaceutical

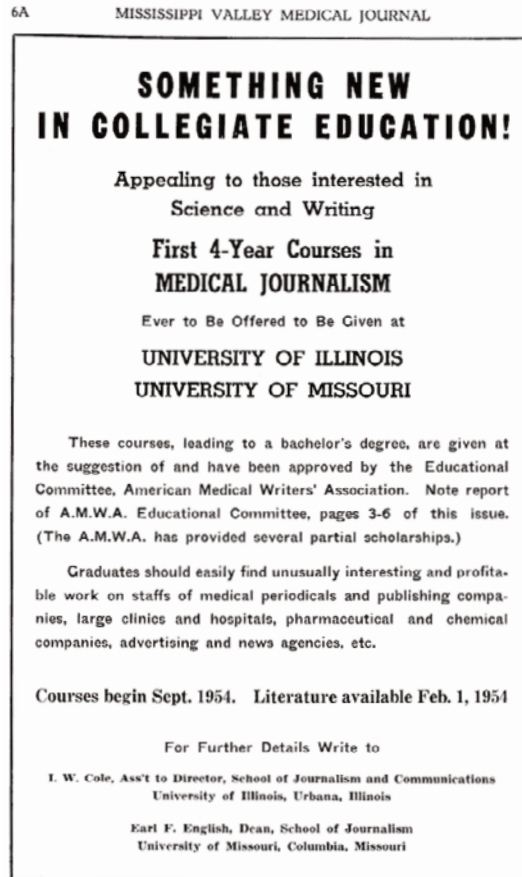
marketing, continuing medical education, and scientific publications also expanded and matured and required skilled medical writers and editors, all of which created a market for more professional training.

Eric and four others created much of AMWA as we know it today: Arnold Melnick, DO, Executive Vice Chancellor of Nova Southeastern University; Red Schiffrin, PhD, Vice President and head of Drug Regulatory Affairs at Hoffman-LaRoche (and widely regarded as an expert in drug approval); Bill Nelligan, the Executive Director of the American College of Cardiology, who (surreptitiously) donated space, clerical support, and the salary for an executive director for 2 years; and Lillian Sablack, AMWA's first executive director, who helped establish the annual meetings and brought order to the administrative functions. (Telephone conversation with Lillian Sablack, July 2020.)

The association began its “core curriculum” to train members as fulltime medical writers, essentially establishing modern medical writing as a profession.

Odds and ends of Harold Swanberg's life

- In 1942, Harold founded the Swanberg Medical Foundation to “sponsor ... things of a charitable, scientific, literary or educational nature... which would bring public and professional honor and respect to the medical profession...”³
- He also founded the Society for Academic Achievement, which is “dedicated to motivate youth to achieve academic excellence”² and that is still active.³
- In 1956, Harold also developed and launched the Quincy Major Learning Program, to help high school students enter and graduate from college.¹
- He was instrumental in establishing the first vocational guidance programme and a guidance counselor position at his local high school in Quincy, Illinois.¹
- He created what might have been the first registry of freelance medical writers and editors, eventually expanded to include “salaried people”⁵
- In the McCarthy era of the 1950s, he was successful in amending the AMWA Constitution to exclude anyone in the Communist or Fascist parties from becoming members. The announcement was titled “Communists and Fascists Beware!”⁵ (The amendment was removed a few years later.)



The beginning of EMWA

In 1990, 14 medical writers from European pharmaceutical companies met to discuss forming a new organisation. In 1992, the European chapter of AMWA was formed, and in 1998, it became an independent association. EMWA now has more than 1000 members from more than 40 countries, 12 of which are outside Europe.³³

These two organisations, AMWA and EMWA, have since become the preeminent associations for training professional medical writers and editors. In addition to their journals and professional development programmes, their members are the faculty at academic programmes in the field; trainers for employees in pharmaceutical companies, journals, and medical communications companies; and authors of hundreds of articles and books in the field.

And all of the above activities were set in motion by a remarkable physician from a small town on the Mississippi River who believed in the importance of good communication.

Advertisement for the first academic programmes for medical writing in the US.

The programmes did not do well. Swanberg's History of AMWA mentions that only 11 students enrolled in the programmes and only 2 graduated. The US still has only 2 certificate programmes, one at University of Chicago (established in 1999) and one at the University of California, San Diego, Extension (established in 2016).

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Conflicts of interest

The author reports no competing interests related to this article.

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How to get your writing found:

Why medical writers and academics need to use search engine optimisation

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doi: 10.56012/fvxn4035

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Abstract

Search engine optimisation (SEO) is the process of optimising your writing so that it can be found easily on the internet. There are five key steps that you can take to increase the discoverability of your work, which will be discussed below. These are:

1. Choose your keywords carefully;
2. Optimise your title;
3. Optimise your abstract;
4. Use your keywords throughout your article; and
5. Build links to your work.

It is important to consider SEO when creating all types of medical writing that will be available on the internet. However, while SEO is important for the discoverability of your work it should never outweigh the importance of good scientific practice and publication.

Introduction

Search engine optimisation (SEO) is a term that few medical writers and academics are familiar with. While it was once the domain of our technology colleagues, it is now something that all medical writers should understand and be actively applying to your work. This is because SEO is a strategy that you undertake to make sure that your work can be easily found online.

Despite many large publishers now providing information on how to optimise your research article prior to publication, SEO is still a relatively new concept for most academics, researchers,

and medical writers.^{1,2} In this article, we summarise the current advice on optimising your work to maximise its discoverability through search engines.

Why is SEO important?

Online information is found by web crawlers, spiders, and bots that trawl the internet. The web pages and files they find are listed in search engines. Notably, Wiley Author Services has disclosed that over 50% of traffic to their online library comes from Google, Google Scholar, and other search engines.¹ Having such a large percentage of traffic coming from online search engines highlights the importance of SEO in the discoverability of research.

Quite simply, research outputs that can be easily found on the World Wide Web will be viewed, downloaded, and cited more frequently than a paper buried on page 10 of your Google search results. It influences the impact of your work and allows you to share your work with the broader community. In a landscape with a rapidly growing body of scholarly literature, SEO helps

people find your work.

How can I improve my SEO?

There are five key steps to optimising your medical writing outputs to help them be found and ranked highly by search engines (Figure 1).

Step 1: Choose your keywords carefully

The easiest place to start is by identifying your keywords. Most of us are guilty of leaving article keyword choice just prior to submitting an article. This is a mistake! Keyword selection and use is fundamental to good SEO and the concept extends beyond the requisite three to five words often required by journals.

Start by considering the target audience for your work; what search terms would they use to look for your paper? It is likely that a healthcare practitioner will use a different search term than a member of the public. This will help you to select your keywords. Once you have some terms in mind you can use Google to help determine other keywords. By simply typing in relevant terms, Google will show you which related

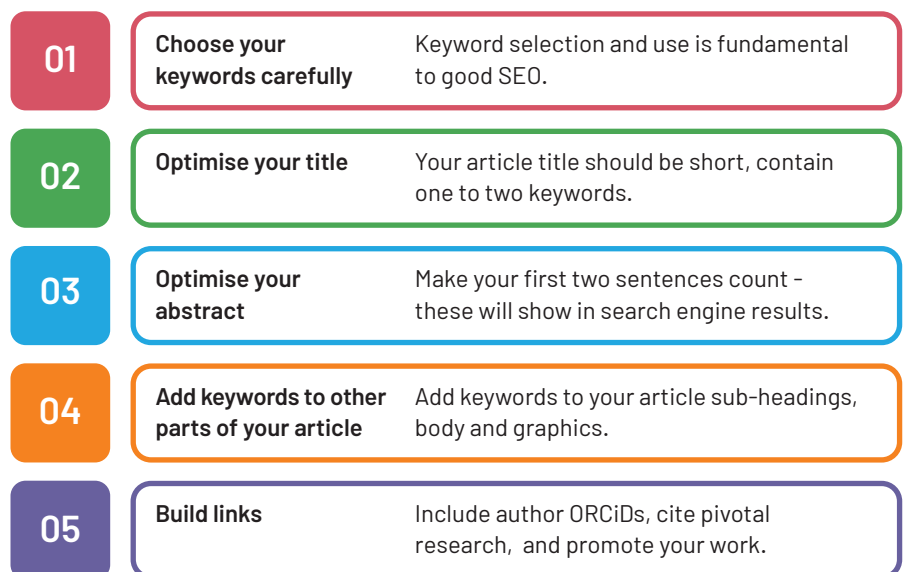


Figure 1: Five steps in search engine optimisation for medical writers

phrases are frequently searched for.

Your keywords should indicate the content of the article (not your results). While some journals still require article keywords to be Medical Subject Headings (MeSH) others will accept any relevant words or phrases. Another tip is to ensure that your keywords are singular and not plural.³ You should also consider spelling. While more people use US English spelling in search engines, your choice of language is often governed by the journal. Once you have decided on your keywords you should try to use them in your title, abstract, and main body of your work.

Step 2: Optimise your title

Ideally your article title should be short and contain one or two of your chosen keywords. It is also recommended that you have a keyword appear in the first 65 characters.^{4,5} This is because most search engines will shorten long titles in their result listings. For this same reason, catchy phrases or puns should only be used in the article sub-title.

It is suggested that you avoid using special characters such as &, *, / and diacritical marks in your title. This is because such papers are often incorrectly cited.³

Step 3: Optimise your abstract

Your next step is to look at optimising your abstract. The first two sentences of your abstract will be displayed in search engine findings, so make them count.^{4,5} Ideally you should try to use your keywords in these sentences and then reuse them between three to six times throughout your abstract.⁴ You may also consider the use of synonyms to increase your chance of your work being found. Again, consider the terms that people in your target audience might use when searching for information. More generally, your abstract should be written succinctly and focus on your essential findings.

Start by considering your target audience; what search terms would they use to look for your paper?

Step 4: Other places to use your keywords

There are other places in your article that can be optimised by judicious use of your keywords. These are:

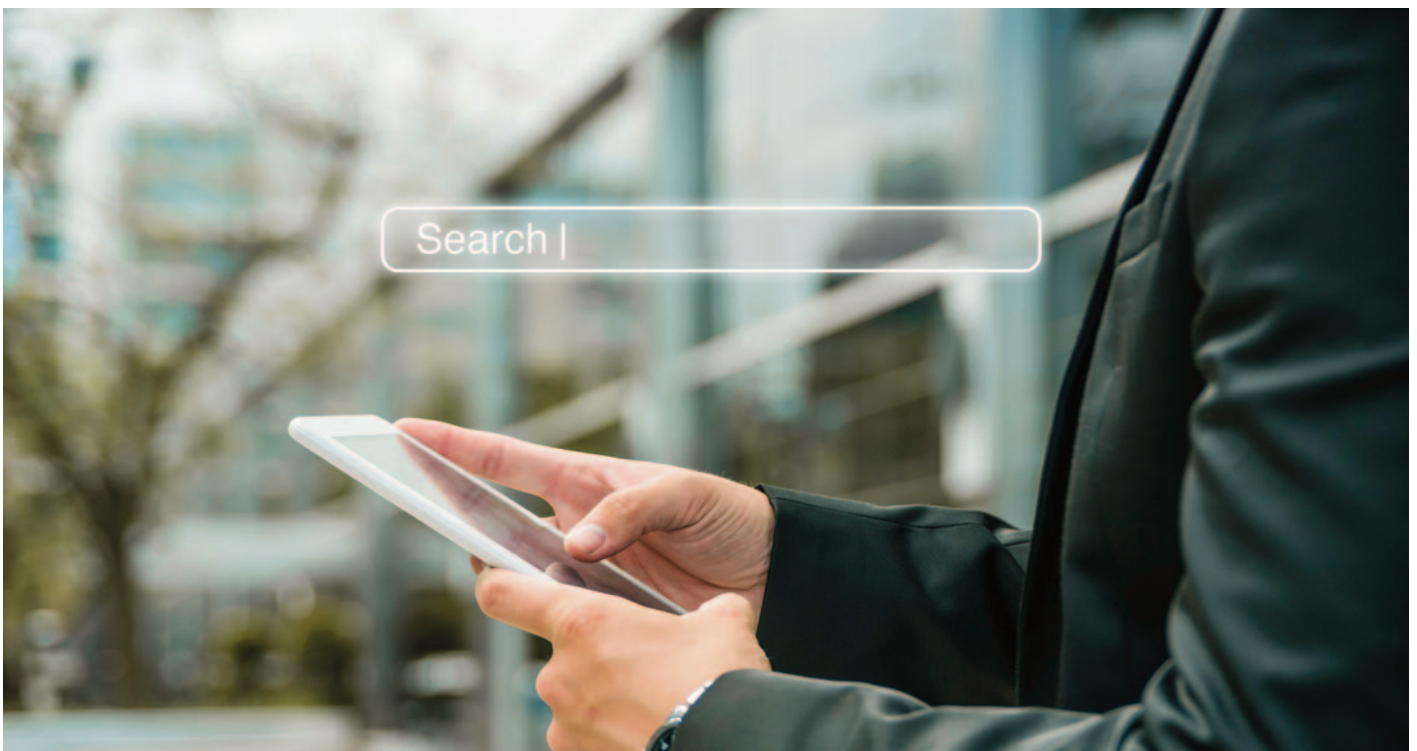
- Sub-headings^{2,4,5}
- Article content^{2,4,5}
- Tables²
- Figures²
- Captions²
- Image Alt text (alternative text)
- Graphics²
- Document file name²

The content of vector graphics (graphics that are made up of paths, as opposed to pixels), such as Encapsulated PostScript file (.eps), Adobe Illustrator (.ai), and Scalable Vector Graphics (.svg) files can be read and indexed by search engines.² Creating vector graphics does not need to involve specialised software and can be achieved in Microsoft PowerPoint. The content of other image types is not indexed but you can save information in the file name.³ As such, if your article has an accompanying graphical abstract, it is important to consider both the file format and the content of the graphic; if you are able to use a vector graphic what keywords will you include?

For other medical writing outputs that are being saved to the web, remember to optimise your file names by including appropriate keywords, e.g. File-Name-SEO.pdf. Further, for files that are saved as portable document files (PDFs), make sure that you add relevant metadata (information saved to the file that is not visible in the document) to the file properties and save it as an archivable PDF/A.

Step 5: Build links to and from your article

SEO can further be improved both by linking to and from your article.



Linking to previous research

By both referencing seminal articles and citing relevant research by the authors, you build links and increase the discoverability of your writing.^{2,4} Similarly, by including all authors' Open Researcher and Contributor ID (ORCID) you help to link your current publication to every author's past work.

Promoting your article after publication

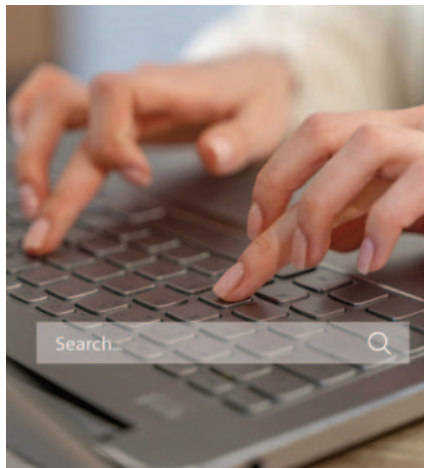
Once your article is written and published, there are still a few strategies you can adopt to ensure that your article is easily found. The volume of inbound links also plays a factor in search engine rankings. One way to increase this is to market your work. Start by telling everyone in your academic and social networks about your new article and sharing its URL. Places to consider sharing include:

- X (formerly called Twitter)
- LinkedIn
- Facebook
- Instagram
- Your website or blog (personal and company)
- Academia (<https://www.academia.edu/>)
- Mendeley (<https://www.mendeley.com/>)
- ResearchGate (<https://www.researchgate.net/>)^{2,6}

Black hat search engine optimisation

Before jumping into the world of SEO you should be aware that there are a set of poor practices, called black hat SEO. These practices have been identified as being used to increase a site's ranking despite breaking the rules and policies specified by search engines. Such practices can result in larger search engines penalising your work by showing it much lower in search results.⁷

The black hat SEO practice that is most relevant to medical writing is keyword stuffing. Keyword stuffing is when the author overuses the



keywords, to the point where they are being used out of context.

Conclusion

It is important to consider SEO for all forms of medical writing including journal articles and reports that will be available on the internet. Good SEO can increase the discoverability and impact of your work. While SEO is important it should never outweigh the importance of good scientific practice and publication.

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The opinions expressed in this article are the authors' own and not necessarily shared by WriteSource Medical Pty Ltd or EMWA.

Disclosures and conflicts of interest

The authors declare no conflicts of interest.

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In vitro plants: How to open a jar containing bioactive phytochemicals

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Abstract

Due to the increasing demand for phytochemicals, plant *in vitro* cultures are a noteworthy, environmentally sustainable method, enabling the biotechnological production of bioactive compounds. Medical writers can find writing scientific articles in this field quite tricky due to the knowledge required at the intersection of botany, chemistry, pharmacy, and biotechnology. This article aims to provide helpful tips for writing about plant biotechnology to minimise the risk of article rejection by scientific journals due to inaccurate description of methods or inadequate data analysis.

Introduction

Plant biotechnology is defined as the use of tissue culture and genetic engineering techniques to produce genetically modified plants that exhibit new or improved desirable characteristics.¹ Plant biotechnology is used to obtain genetically modified crops but also to preserve human health. In human health green (agricultural) and red (pharmaceutical) plant biotechnology cross over each other. Plant biotechnology harnesses modern techniques to use plants as bioreactors to produce bioactive phytochemicals with potential applications in the pharmaceutical industry.

Phytochemicals are divided into primary and secondary metabolites based on



their function in plant metabolism. Primary metabolites are directly involved in plant growth and development (carbohydrates, proteins, and lipids). Secondary metabolites are those that plants biosynthesise in a defense response to threats and stresses in the natural environment (alkaloids, terpenes, flavonoids, and steroids). These compounds are valuable for human use in medicines, flavours, dyes, repellents, and cosmetic ingredients. The market demand for secondary metabolites is still growing, which may endanger some medicinal plants due to over-harvesting.² Yet, chemical synthesis of organic compounds with complex structures is economically unfeasible. Nevertheless, for the last 60 years, plant cell, tissue, and organ cultures have provided assistance, enabling *in vitro* production of bioactive secondary metabolites.

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inner bark of yew trees (*Taxus* sp.) is ecologically

unsustainable as the content of the compound is too low. To treat one patient, six 100-year-old slowly growing trees are required to produce 2 g of pure Taxol[®].^{3,4} *Taxus* spp. cell suspension cultures proved to be an alternative production route.³⁻⁶ The cell suspension culture of *Taxus chinensis* elicited with methyl jasmonate resulted in one of the highest yields of paclitaxel (565 mg L⁻¹, or 29.3 mg g⁻¹ dry weight) so far.⁷ Currently, the production system, developed by Phyton Biotech, which is based on *T. chinensis* cultivation in 75,000-L bioreactors, is the largest commercially viable plant cell culture application.⁵

Among many other medicinally important compounds biosynthesised in plant *in vitro* cultures, it is worth mentioning antitumour indole alkaloids (*Catharanthus roseus*), anticholinergic tropane alkaloids (*Datura stramonium*, *Atropa belladonna*), or immunomodulating ginsenosides (*Panax ginseng*).^{6,7} Although research on *in vitro* cultures has been conducted since the mid-1960s, broad commercialisation of plant *in vitro* systems has not yet occurred.⁷ Efforts are still being made to overcome limitations in scaling up secondary metabolite production, such as insufficient knowledge of biosynthetic pathways and slow *in vitro* cultures growth.⁸

After entering the search term “*in vitro* plant cultures”, PubMed displays over 1000 publications per year for the recent decade, which indicates the potential for medical and scientific writers to show off their skills in this field. Since the world of plants has its own rules (even if they

grow in a jar), it is helpful to know which ones are important when writing a manuscript about plant *in vitro* cultures.

Botanical nomenclature

Scientific plant names, according to the International Code of Nomenclature for algae, fungi, and plants (ICN),⁹ are required when publishing research about plants. Using this nomenclature ensures scientific accuracy and avoids citation errors. Writing “ginseng *in vitro* cultures” is insufficient because various species of *Panax* (ginseng) genus can be used to establish *in vitro* cultures and produce ginsenosides. The most popular species is *Panax ginseng*, but *P. quinquefolius* or *P. sikkimensis* are also used. Importantly, each of these species cultured *in vitro* produces different ginsenoside yield.⁷ Therefore, the precise botanical name of the explant source must be provided in the manuscript (Fig. 1A). To do this, it is preferable to report the genetic identification of the mother plant species and the location where the preserved and archived herbarium specimen of mother plant (representative voucher specimen)

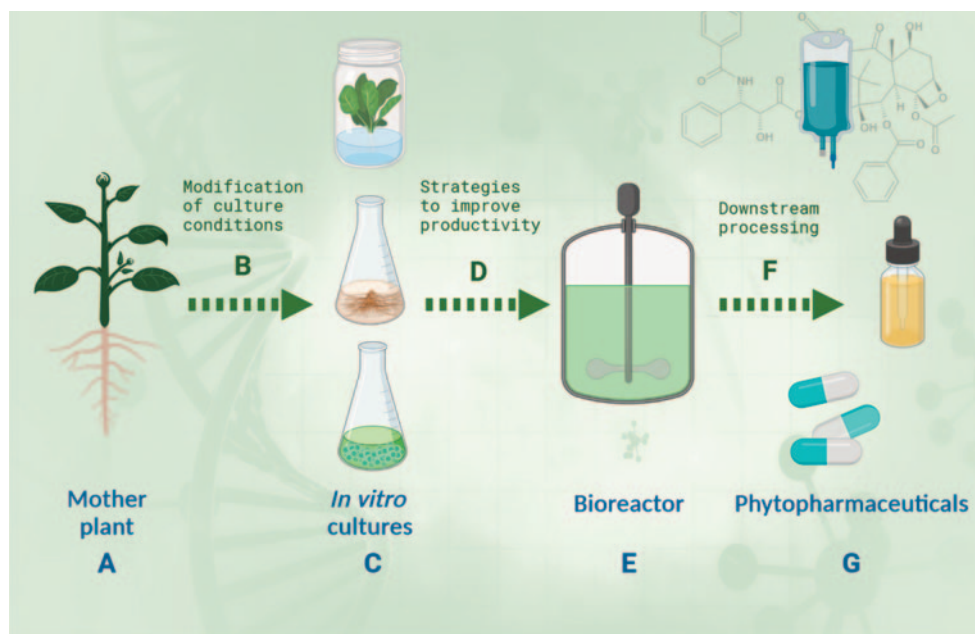
is stored (e.g. university department or horticultural library).¹⁰

The standard Latin binomial nomenclature system, first developed by Carl Linnaeus and still used today, has its own spelling rules. The full plant name is written in italics. The first name identifies the genus and is capitalised, while the second name represents the species and is written in lowercase. The name of the author who named the plant using scientific nomenclature, usually given when the plant is first mentioned in a manuscript, is not italicised (*Mentha piperita* L. – L. is used to indicate Linnaeus). Once the full botanical name has been used in the manuscript, the genus name can be abbreviated to the first initial if there is no possibility of confusion (*M. piperita*), or the common name (mint) can be used, neither italicised nor capitalised. The names of higher taxa, such as family or order, should be written in standard lettering (Lamiaceae, formerly called Labiatae; the common name: the mint family). Placing “sp.” after a genus refers to the genus in general, while “spp.” means “several species of that genus.” Be aware of the synonyms for the same plant resulting from taxonomic

changes (e.g. *Rhododendron tomentosum* Harmaja, previously *Ledum palustre* L.). Using only outdated names may lead to the failure of bibliographic searches to find the article.¹¹ However, the outdated plant name may still be referenced as a synonym (syn.), especially where there is no consensus among taxonomists or the older name is widely known.

Culture conditions

Plant *in vitro* cultures are incubated in controlled aseptic conditions in closed flasks or jars spaced evenly apart in a growth room. Because external factors may affect photosynthesis and other biochemical processes in plants and induce anatomical and physiological changes, data on light (intensity, spectrum, photoperiod), humidity, and temperature should be provided (Fig. 1B). If basic nutrient culture media were applied, indicate references to the original formulations without specifying their exact composition but explain any modifications that were made, e.g. the changes to medium acidity. Abbreviations such as MS (Murashige & Skoog) or SH (Schenk & Hildebrandt) are commonly used to describe



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Figure 1. The production of bioactive secondary metabolites in plant *in vitro* culture

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| <p>A. Initiation of <i>in vitro</i> cultures from the mother plant</p> <p>B. Multiplication of primary cultures and optimisation of culture conditions</p> <p>C. Selection of high-yielding lines</p> <p>D. <i>In vitro</i> strategies to improve productivity</p> | <p>E. The bioreactor system for large scale production of secondary metabolites</p> <p>F. Extraction and phytochemical analysis of bioactive compounds</p> <p>G. Production of phytochemicals as potential drugs</p> |
|--|--|

plant culture media. Similarly, the names of regulators of plant growth and development (plant growth regulators, phytohormones) are usually abbreviated (BAP – 6-Benzylaminopurine, TDZ – Thidiazuron, etc.). The amount of cytokinins, auxins, gibberellins, or other substances added to the medium should be expressed in μM . Precise reporting of the combinations of plant growth regulators used and their accurate concentrations is essential because of their high impact on shoot regeneration, rhizogenesis, or callus formation. Another necessary piece of information is whether the culture medium was liquid (for shaken and stationary cultures), solid (for stationary cultures), or semi-solid (with support for the developing plants, e.g. during micropropagation), which influences the growth of biomass.

Type of *in vitro* culture

Depending on the explant and the culture medium, cell cultures (cell suspensions, protoplasts, or gametic cells), undifferentiated biomass (callus), differentiated tissues (meristems), or organ cultures (shoots, roots, or zygotic embryos) can be established (Fig. 1C).^{6,7} Cell suspensions seem to be a promising source of phytochemicals due to their fast growth, facilitating scale-up to bioreactor systems. However, a certain degree of differentiation is indispensable for producing some secondary metabolites, e.g. essential oils, since several biosynthetic pathways may be fully developed only in specific plant organs.⁷ In the manuscript, explant sources (any meristematic tissues of the mother plant, consisting of continuously dividing cells, that serve as the starting material for *in vitro* cultures) and culture initiation should be described in detail, just as the individual stages of micropropagation (if applicable). If root cultures are to be mentioned in the article, make sure their character is described as adventitious or hairy. Hairy root cultures are formed as a result of an infection with different *Rhizobium rhizogenes* strains (formerly *Agrobacterium rhizogenes*), a soil-borne Gram-negative bacterium, which leads to the integration of the root-inducing plasmid into the plant genome. Transgenic hairy roots, unlike non-transformed adventitious roots developed from stems or leaves, grow rapidly in

culture media without an exogenous application of auxins. They are genetically stable and provide high secondary metabolite production.¹

Strategies for improving productivity

A medical writer may come across specific names of biotechnological approaches employed to improve biomass and secondary metabolite production after high-yielding plant cultures have been selected and culture conditions optimised (Fig. 1D). These approaches should be described in the Materials and Methods section in sufficient detail, with technical specifications, experimental design, and data collection, to enable repetition of the study and verification of the findings.¹² Techniques that typically need to be described are elicitation (the use of biotic or abiotic compounds or factors to trigger the plant's defense response), permeabilisation (the release of product from biomass into culture media), immobilisation (fixing of plant biomass in or on a supporting material or matrix), precursor feeding (the addition of exogenous or endogenous compounds that are converted by plant cultures into secondary metabolites through biosynthetic pathways), and metabolic engineering (introduction of genes encoding specific metabolic enzymes into the plant).⁸

Type of bioreactor

The bioreactor system is a fundamental tool for scaling up the *in vitro* production of secondary metabolites (Fig. 1E). This system allows for the bulk transfer of nutrients and gases and provides constant micro-environmental conditions, promoting rapid growth of biomass. The automated cultivation processes save time and reduce labor costs.¹ The bioreactor design for plant cultures differs from that applied in microbial cultures because not only organs but also plant cells, which are larger than bacterial cells (10-100 μm vs 0.5-5 μm long), may experience mechanical damage in stirred tank bioreactors and foam formation in bubble-aerated bioreactors.¹³ The selection of each bioreactor is unique and

adapted to the type of plant culture, considering efficient oxygen and nutrients supply, low shear stress, proper mixing, and a suitable support system.¹⁴ Because bioreactors show numerous modifications, such as the addition of mist spray, temporary immersion, different shapes of columns, having mesh or basket, using various agitation options, etc., an accurate description is essential, preferably combined with a schematic drawing. Providing references is sufficient if the bioreactor is commercially available, e.g. RITA® systems, and no modifications have been made.

Downstream processing

Downstream processing is often described in manuscripts on secondary metabolite production in plant cultures as an integral part of research. The extraction of bioactive compounds from the plant material¹ and qualitative and quantitative analysis of phytochemicals^{15,16} are essential for screening *in vitro* cultures as well as assessing the effectiveness of the developed large-scale system (Fig. 1F). Without going into details of plant analysis methods, some basic advice can be given to medical writers. The product yield is usually expressed in the following units: mg g^{-1} DW (dry weight), less frequently in mg g^{-1} FW (fresh weight), or mg L^{-1} (in case of cell suspension culture). Bioreactor productivity can also be reported as $\text{g L}^{-1} \text{day}^{-1}$. The spelling of the names of the obtained secondary metabolites should be carefully checked to avoid mistakes, especially when long names based on the chemical structure are concerned. If a compound is not widely known, including its chemical

formula may be considered. To discuss the potential biological activity of the final products (Fig. 1G), assigning them to the appropriate phytochemical group (e.g. essential oils, flavonoids, alkaloids) is helpful.¹

Publishing in the field of plant biotechnology

The instructions for authors and style guide in the target journal will clarify many points not covered in this article. Interestingly, some submission guidelines do not insist on writing common Latin terms such as *in vitro* and *in vivo* in italics. The difficulty in publishing in plant biotechnology is the relatively long time necessary to develop a high-yielding plant *in vitro* system. In this situation, the challenge for the scientist is to meet the expectations for writing a

Precise reporting of the combinations of plant growth regulators used and their accurate concentrations is essential because of their high impact on shoot regeneration, rhizogenesis, or callus formation.

The bioreactor system is a fundamental tool for scaling up the *in vitro* production of secondary metabolites.

scientific article every year, which requires creativity to propose new solutions and innovative strategies.¹² According to a recent study, the main reasons for manuscript rejection by scientific journals in agriculture and plant biology were the lack of novelty, flaws in methods or data interpretation, inadequate data analysis, and poor critical scientific thinking.¹⁷ Therefore, a vital task for a medical writer is to clearly emphasise the novelty in the research and transparently put the complexity of *in vitro* secondary metabolite production on paper.

Conclusions

Although research articles on plant biotechnology do not differ significantly from other papers with an IMRAD (Introduction, Methods, Results, and Discussion) structure, there are a lot of nuances specific to describing plant *in vitro* cultures. Starting from botanical nomenclature, through *in vitro* culture establishment and a bioreactor system development for secondary metabolite production, to the extraction and analysis of bioactive compounds – all these issues may seem complicated to a medical writer outside the field. However, with a good approach to the subject, no jar with plants will be too difficult to open.

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

Disclosures and conflicts of interest

The author declares no conflicts of interest.

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Paving the way towards coordinated clinical trials in public health emergencies in the EU

July 25, 2023

EMA has published a report¹ from a workshop that collected insights and suggestions for possible European Union (EU)-level actions to improve the way clinical trials are set up and conducted in the EU during public health emergencies. The actions presented in the report aim to holistically address the barriers and challenges experienced during the COVID-19 pandemic and the outbreak of mpox disease in setting up adequately sized clinical trials across multiple Member States that enable rapid gathering of sufficient, high-quality evidence to support robust decision-making by health authorities across the EU.

The workshop was organised by EMA's Emergency Task Force (ETF) and the European Commission (EC) on June 9, 2023, with participation from national competent authorities (NCAs), ethics committees' representatives, and academic sponsors.

The workshop discussions emphasised the need for larger studies across several European countries, speedier recruitment, and delivery of conclusive results with accelerated timelines during a public health emergency. Proposed actions focus on two areas:

- The processing and regulatory approval of large, multinational clinical trials in the EU during public health emergencies. This includes e.g., improving coordination between regulators and ethic committees within and across Member States, speeding up assessment and authorisation of clinical trial applications, exploring flexibilities in the implementation of the Clinical Trials Regulation, facilitating the use of the EU Clinical Trials Information System (CTIS);
- The framework for funding and efficient allocation of resources for clinical trials during emergencies in the EU, including the establishment of a Coordinating Committee to support prioritisation of trials, improved mechanisms to identify and rank promising compounds, mobilising EU and Member State funding mechanisms, and measures to help speed up contracting of clinical trial sites.

According to the recommendations, ETF's essential role of providing scientific advice, reviews, and supporting large clinical trials in emergency situations, should be expanded to also include concerned ethics committees on a

voluntary basis to discuss and coordinate clinical trials protocols.

The workshop participants emphasised the need to make Europe a better place for research. The proposed actions will be taken into account by the EC, EMA, and the Member States in establishing a concrete roadmap for improved clinical trials during public health emergencies in the EU. The work on approvals of clinical trials in public health emergencies will be taken forward by the Accelerating Clinical Trials in the EU (ACT EU) initiative, the EU collaboration between the EC, Heads of Medicines Agencies (HMA) and EMA that seeks to transform how clinical trials are initiated, designed, and run. The framework for funding will be specifically discussed with the EC and Member States in the context of current efforts to improve the coordination for funded clinical research in the EU and with international actors.

Reference:

1. Report of the EMA/ETF workshop on Lessons Learned on Clinical Trials in Public Health Emergencies. First published July 25, 2023; EMA/340269/2023.



Towards a permanent collaboration framework for EMA and Health Technology Assessment bodies

September 15, 2023

Over the past three years, EMA and the EUnetHTA 21 (European Network for Health Technology Assessment) consortium have delivered a number of milestones to prepare the EU for the entry into application of the Regulation on Health Technology Assessment. EUnetHTA 21 ceased to operate on September 16, 2023, but preparations will continue for the implementation of the Regulation, under the direction of the Health Technology Assessment (HTA) Coordination Group.

Reviewing achievements over the years at their concluding meeting on September 14, 2023, in Amsterdam, EMA and EUnetHTA 21 highlighted a number of initiatives:

- Completion of seven parallel joint scientific consultations (JSC) for medicines under the EUnetHTA 21 consortium contract. This joint work is intended to improve the generation of robust evidence that meets the needs of regulators and HTA bodies;
- Discussion on evidence needs for advanced therapy medicinal products in oncology, addressing mutual challenges such as indirect comparison and addressing evidence gaps through post-licensing evidence generation;
- Organisation of trainings for patients and healthcare professionals to facilitate their participation as experts in regulatory and HTA processes, alongside collaborative work on methodologies for engagement of patients

and healthcare professionals in assessments;

- Recommendations to optimise the assessment reports of EMA's Committee for Human Medicines (CHMP) for each medicine in order to systematically document key elements of the assessment such as the eligible patient population, choice of comparator and endpoints, as well as relevance of subgroup data.

More information on the achievements is available in a technical report.¹

The Regulation on Health Technology Assessment (EU) 2021/228 which entered into force in January 2022 and applies as of January 2025, will govern the European cooperation between medicine regulators and HTA bodies. Under the new framework, EMA and HTA bodies will collaborate in the context of joint clinical assessments, JSC, and the identification of emerging health technologies.

While aiming to improve the availability of innovative medicines and certain medical devices for patients in the EU, it will also ensure efficient use of resources and enhance the quality of health technology assessment in the EU by ensuring the sustainability of European cooperation. The establishment of the Member State Coordination Group on Health Technology Assessment, as provided by the regulation, and of a stakeholder network, will give a transparent and inclusive

framework to facilitate continued collaboration between partners and reduce duplication of efforts for national HTA authorities and industry.

For the transition period (up to January 2025), EMA and HTA organisations have established a new framework for Parallel EMA/HTA Scientific Advice for the period September 2023 until January 2025, when the HTA Regulation applies. During this transition period, developers can request the involvement of HTA bodies when applying for EMA scientific advice. The outcome of the procedure will be a scientific advice letter from EMA and individual written recommendations from participating HTA bodies. The selection criteria are available in the Guidance on Parallel EMA/HTA body (HTAb) Scientific Advice for the Interim Period.

Preparations are also continuing at EMA to pave the way for the implementation of the regulation. The agency has identified a number of priorities and opportunities for the next 15 months. These include defining a single evidence plan to facilitate development programmes, harmonising views on the strength of the evidence, and involving patients, clinical experts, and other relevant experts in decision-making.

Reference:

1. Report on the implementation of the EMA-EUnetHTA 21 work plan 2021 – 2023. First published September 15, 2023; EMA/290158/2023.

Revised transparency rules for the EU Clinical Trials Information System

October 06, 2023

EMA has adopted revised transparency rules¹ for the publication of information on clinical trials submitted through the CTIS. The simplifications introduced will give access to clinical trial information to stakeholders including patients and healthcare professionals in a faster and more efficient way.

One of the key changes of the revised rules is the removal of the deferral mechanism, which allowed sponsors to delay the publication of

certain data and documents for up to seven years after the end of the trial to protect personal data and commercially confidential information (CCI).

The updated rules strike a balance between transparency of information and protection of CCI. They benefit patients, because key clinical trial information, that patients flagged as being most relevant for them, is published early. They also introduce process simplifications that benefit

clinical trial sponsors who have to protect CCI and personal data. Finally, they benefit healthcare professionals because the resulting system is more user-friendly, facilitating access to information about clinical trials and enrolment in clinical trials, and also increasing awareness of possible treatment options.

The updates were triggered by feedback from stakeholders and experience after the launch of the system. An eight-week public consultation was held between May and June, 2023.

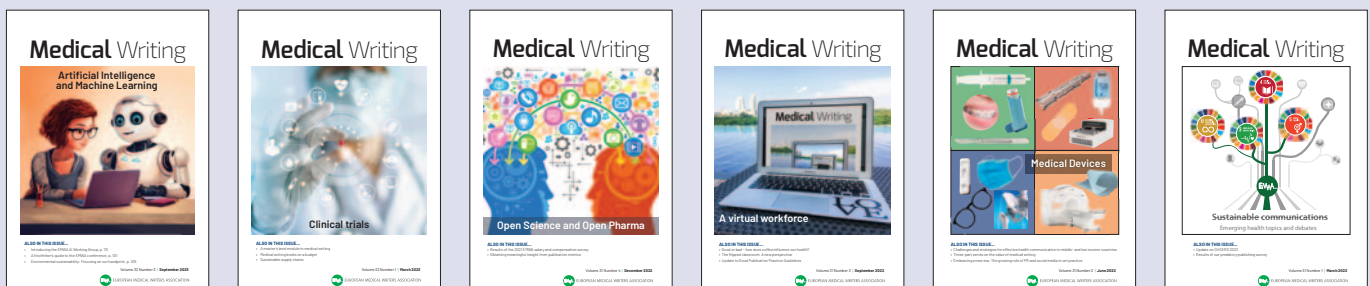
The revised transparency rules will apply after their technical implementation in CTIS, including its public portal, which is expected to be finalised in the second quarter of 2024. The effective date of completion of the process and the entry into application of the new rules will be communicated to the users of the system before they become applicable.

CTIS is the single-entry point in the EU for the submission and assessment of applications for clinical trials for sponsors and regulators. The system includes a public searchable database for healthcare professionals, patients, and the general public to deliver the high level of transparency foreseen by the regulation.

The authorisation and oversight of clinical trials is the responsibility of EU/EEA Member States while EMA is responsible for maintaining the CTIS. The EC oversees the implementation of the Clinical Trials Regulation.

Reference:

1. Revised CTIS Transparency Rules.
First published October 5, 2023;
EMA/263067/2023.



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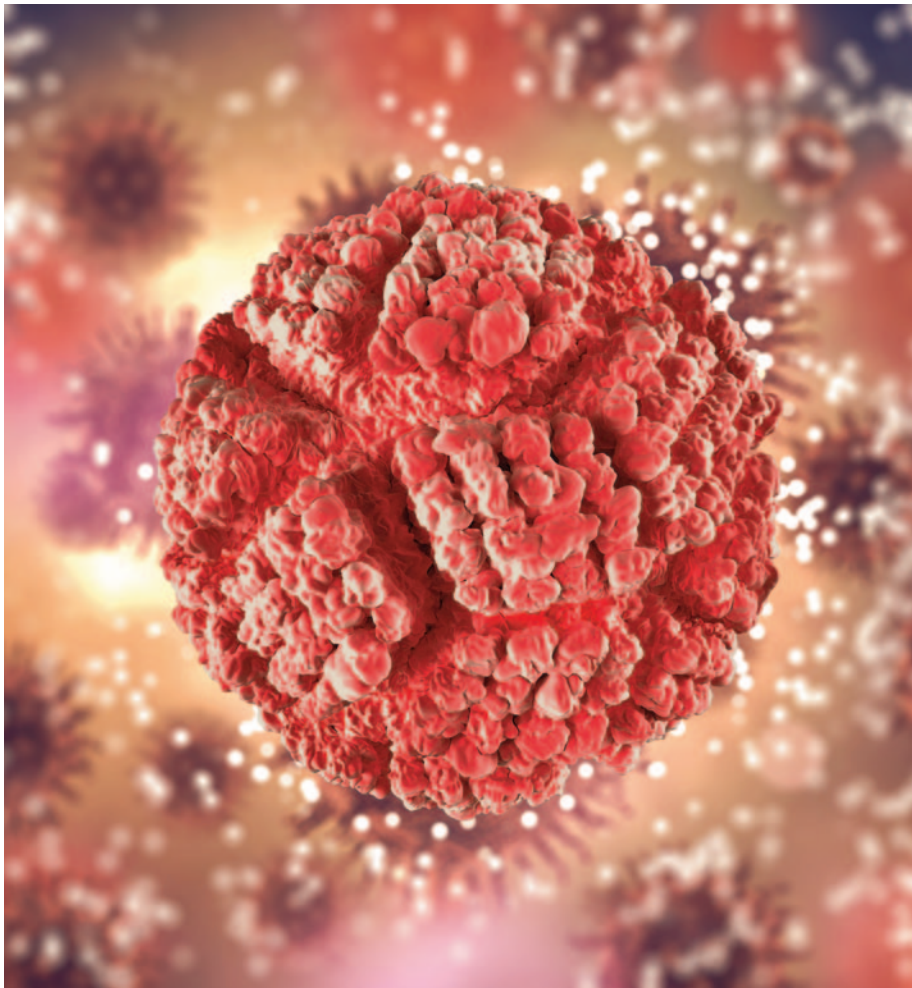
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New treatment option for heavily pre-treated multiple myeloma patients

October 13, 2023



EMA's human medicines committee (CHMP) has recommended a conditional marketing authorisation in the EU for Elrexfio (elranatamab; Pfizer Europe MA EEIG) as a monotherapy (used on its own) for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least three prior therapies and whose cancer has worsened since they received their last treatment.

Multiple myeloma is a rare cancer of the plasma cells, a type of white blood cell that produces antibodies and is found in the bone marrow. In multiple myeloma, the proliferation of plasma cells is out of control, resulting in abnormal, immature plasma cells multiplying and filling up the bone marrow. When plasma cells become cancerous, they no longer protect the body from infections and produce abnormal proteins that can cause problems affecting the kidneys, bones, or blood.

A range of new medicines for the treatment of multiple myeloma have been developed and

approved in recent years, leading to a steady overall improvement in patient survival. However, new medicines are needed for patients who have already been treated with the three main classes of medicines (immunomodulatory agents, proteasome inhibitors, and monoclonal antibodies) and who no longer respond to them.

Elranatamab, the active substance in Elrexfio, is a monoclonal antibody that targets two proteins simultaneously. By attaching at the same time to a protein called B-cell maturation antigen (BCMA), which is present on the surface of the multiple myeloma cells, and to CD3, a protein that is present on the T cells (cells in the immune system), the medicine activates the T cells to kill the multiple myeloma cells.

The CHMP based its recommendation for a conditional marketing authorisation on an open-label, single arm, multicentre, phase 2 clinical trial. The part of trial that was considered as pivotal investigated the efficacy of Elrexfio monotherapy in 123 participants with

refractory multiple myeloma who had received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody, but who had not received prior BCMA-directed therapy. 61% of patients enrolled in the trial responded to the treatment with Elrexfio and more than 70% of the responding patients have a probability to live without their disease getting worse for an average of 15 months.

The overall safety profile of elranatamab was established by analysing data from 265 participants. The most common side effects are a decrease in blood cells, infections, and cytokine release syndrome (CRS) (i.e. a condition causing fever, vomiting, shortness of breath, headache, and low blood pressure). One of the main risks associated with elranatamab use is neurological toxicity including immune effector cell-associated neurotoxicity (ICANS), as these events have the potential to be life-threatening or fatal if not properly managed. Monitoring and mitigation strategies for CRS and ICANS are described in the product information and in the risk management plan that is an integral part of the authorisation.

Elrexfio was supported through EMA's PRIority Medicines (PRIME) scheme, which provides early and enhanced scientific and regulatory support to medicines that have a particular potential to address patients' unmet medical needs. Elrexfio is now recommended for a conditional marketing authorisation, one of the EU regulatory mechanisms to facilitate early access to medicines that fulfil an unmet medical need. This type of approval allows the Agency to recommend a medicine for marketing authorisation with less complete data than normally expected, if the benefit of a medicine's immediate availability to patients outweighs the risk inherent in the fact that not all the data are yet available.

In order to confirm the results obtained from the pivotal trial, the company will have to submit data from a randomised phase 3 trial comparing the efficacy and safety of elranatamab monotherapy and elranatamab used in combination with daratumumab versus the treatment regimen daratumumab, pomalidomide, and dexamethasone in adults with relapsed or refractory multiple myeloma who have received at least one prior line of therapy, but not more than three, including lenalidomide and a proteasome inhibitor. The company is also required to submit the final results of the pivotal phase 2 clinical trial.

EMA alerts EU patients and healthcare professionals to reports of falsified Ozempic pens

October 18, 2023

The EMA has been notified by relevant national competent authorities that pre-filled pens falsely labelled as the diabetes medicine Ozempic (semaglutide, 1 mg, solution for injection) have been identified at wholesalers in the EU and the UK. There is no evidence that any falsified pens have been dispensed to patients from legal pharmacies and there are no reports of harm to patients in relation to the falsified medicine.

The pens, with labels in German, originated from wholesalers in Austria and Germany. The pens have batch numbers, 2D barcodes, and unique serial numbers from genuine Ozempic packs. In the EU, each medicine pack has a unique 2D barcode and serial number so that it can be tracked in an EU-wide electronic system. When the packs of the falsified Ozempic were



scanned, the serial numbers were shown to be inactive, thereby alerting operators to a potential falsification.

There are differences in the appearance between the falsified pen and the original pen. A picture of the falsified pen has been published by the German medicines agency (please note that the picture of the falsified pen is an example and

falsified pens with other features are also likely).

The issue is currently being investigated by EU medicines regulatory authorities and the police. EMA is assisting national authorities in their investigations. Wholesalers and pharmacies in the impacted countries have been warned about the suspicious offers of Ozempic to wholesalers. In addition, parallel distributors across the EU have been alerted.

In the meantime, the German and Austrian regulatory authorities have issued statements of non-compliance with good distribution practices (GDP) to the concerned wholesalers in their countries for not following required procedures, including compliance with security measures. EMA is monitoring the situation closely and will provide updates as appropriate.

The latest reports of falsification come in the wake of an increase in demand for Ozempic which has also led to a shortage situation.

EMA takes further steps to address critical shortages of medicines in the EU

October 24, 2023

Today, EMA published details of the newly created solidarity mechanism developed by the EMA Medicines Shortages Steering Group (MSSG). This voluntary mechanism allows Member States to support each other in the face of a critical medicine shortage.

The solidarity mechanism, which is based on an informal setup during COVID-19, will enable any Member State facing a critical shortage that has been escalated to the MSSG for coordination at European level to request assistance from other Member States in obtaining medicine stocks. This mechanism can only be used under very

limited conditions and was developed as a last resort for Member States after they have exhausted all other possibilities.

The solidarity mechanism complements a number of actions that the MSSG can carry out to address critical shortages in the EU. These were also published today as part of the MSSG Toolkit.¹ The toolkit includes recommendations for monitoring supply and demand, an approach that was used to tackle the widespread critical shortages of antibiotics in the autumn and winter seasons of 2022/2023. The toolkit also provides guidance on interactions with marketing

authorisation holders and manufacturers to increase and redistribute existing stocks and the implementation of regulatory flexibilities, such as the exceptional supply of certain medicines that may not be authorised in a particular EU Member State, or full or partial exemptions to certain labelling and packaging requirements for medicines.

The two documents published today are part of a clear set of actions announced by the EC today to protect Europe against medicines shortages in the future.

The MSSG was established under Regulation (EU) 2022/123, which reinforces the role of the Agency in crisis preparedness and management for medicines and medical devices in order to monitor shortages and ensure a robust response to major events or public health emergencies and to coordinate urgent actions on the supply of medicines within the EU. The regulation formalises and strengthens the governance structures EMA had put in place to ensure swift and coordinated action during the COVID-19 pandemic.

Reference:

1. MSSG Toolkit on recommendations on tackling shortages of medicinal products. First published October 24, 2023; EMA/899955/2022. Available from: https://www.ema.europa.eu/en/documents/other/mssg-toolkit-recommendations-tackling-shortages-medicinal-products_en.pdf





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Digital Communication

Editorial

As the end of 2023 approaches, we're wrapping up projects and reflecting on the year that was. Like most, this is usually the time I start thinking about my goals for the new year and how I plan to achieve them. Building on an activity I started early on in my career to boost my efficiency and improve the quality of my communications, I'm motivated to expand and optimise my digital workspace by learning new tools. After all, it's difficult to succeed in the digital era without being tech-savvy. However,

I have to admit that the rapidly evolving technology and digital landscapes make it difficult to keep up with the latest and greatest. So, I'm left somewhat confused about which tools to tackle next and whether the effort is worth leaving my old faithfuls behind. Federica Angius is a freelance medical writer who enjoys keeping up with the latest developments and tools suitable for medical writing, not to mention everything else it takes to succeed as a business owner. In her article, she shares what her digital workspace looks like, highlighting tools

SECTION EDITOR



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she uses every day – some familiar to many of you and others you've probably never heard of. Hopefully, you're inspired to broaden your horizons and expand your digital toolkit to take your medical writing to the next level in 2024. Happy holidays!

Best, Nicole

From the well-known to the cutting-edge: Tools to revolutionise your digital workspace in 2024

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doi: 10.56012/wkmb1498

In today's digital era, we're more connected than ever, with endless opportunities at our fingertips. Yet, it was the sudden global pandemic that truly thrust us into the heart of this digital transformation. As medical writers, we found ourselves at an interesting intersection: our profession, rooted in evidence and detail, meets the ever-evolving world of digital tools.

Three years since the pandemic began, it's time to ponder: How has our digital work environment changed? How have we adapted, grown, and maybe even thrived in this new setting? While many of us smoothly transitioned into the digital world, some faced a steep learning curve, diving into unfamiliar tools and technologies. As 2024 nears, an important question remains: How can we optimise our digital workspaces? We need to ensure we're not just equipped with the basics but also with the latest innovations suited for our profession and work-life interface.

Chasing productivity is a tricky path. Think about it: If we add up all the hours, we spend nearly a decade of our lives working. So, it's

natural for us to want to make every moment count. But sometimes, our desire to be ultra-productive can lead us astray, especially when we're lured by the siren call of "productivity porn" – that endless stream of hacks and tips promising to turn us into efficiency machines.

But here's the catch: this constant chase for the ultimate productivity hack can set us up for disappointment. It's like we're being sold a dream of endless energy and focus, often by self-styled experts who say they've cracked the code. Yet, many of these "miracle" methods don't hold up in the real world. They play on our hopes, making us chase after goals that might not even be right for us. And in a twist of irony, our quest for productivity can become a distraction in itself, keeping us from our actual work.

Being medical writers, we value truth, evidence, and authenticity. We can't be swayed by every new trend that promises the moon. What we need is mindful productivity – a thoughtful approach that addresses our real challenges and encourages self-awareness. It's about knowing our strengths and weaknesses, being smart about what advice we take, and, most importantly, enjoying the journey rather than just fixating on the destination.

This article dives deep into the digital tools that have become a staple in my workspace

between the well-known and the cutting-edge. These tools are handpicked to boost my efficiency and speed as a freelance medical writer. Let's journey through this digital exploration, always remembering that when it comes to personal productivity, we are our best guides.

Project management and collaboration

Every morning, as the world is just waking up, I sift through my emails, scanning for any overnight updates. This ritual sets the tone for the day, giving me a clear view of immediate tasks.

Then, **ToDoist** jumps in.¹ It's not just a task manager; it feels like having a personal aide. Whenever I set a task, ToDoist sends gentle reminders, ensuring I stay on top of the day's priorities. While I use calendars for specific appointments or meetings, ToDoist serves as a repository for my thoughts, both personal and work-related. Tasks range from "read 8 literature papers for project X" to simple reminders like "water the plants." Each morning, I tackle the highest-priority tasks, gradually moving to those with lower priorities.

Mornings are also reserved for client meetings. The platform you use can set the mood, be it the ever-present **Zoom**, **Google Meet** with its smooth integration of Google tools, or

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THE DIGITAL WORKSPACE of a Medical Writer

Microsoft Teams, which many businesses prefer for its robust security and teamwork features. Sometimes, if the meeting is a more demanding one, I use **Descript** to capture every word, pause, and nuance, ensuring I don't miss out on valuable insights.² It does more than just transcribe; it allows for structured playback, letting me revisit any part with precision. This ensures that when I weave these discussions into my work, the essence remains pure.

Previously, I juggled Calendar, **ToDoist**, and various meeting tools separately, which became tedious. That changed when I discovered **Fantastical**.³ It integrates all these applications (apps) together, providing an overarching view of my day. Its intuitive design showcases my appointments, meetings, and reminders in a visually pleasing manner. Its ability to merge both personal and work calendars, along with Todoist, Zoom, Google Meet, and Teams, is invaluable. Whether it's a formal virtual meeting or a relaxed coffee chat, Fantastical keeps me on track, avoiding double bookings and ensuring I take those much-needed breaks.

Cardhop fits right in, acting as my digital address book.⁴ Be it sending an email or joining a meeting, Cardhop ensures all my contacts are just a click away, proving more efficient than traditional address books, like those in Microsoft Excel.

For deeper collaboration, especially with colleagues abroad, **Google Drive** and **Notion Projects** are my go-to.^{5,6} They're not just storage apps; they're dynamic platforms that foster collaboration. Google Drive allows for real-time document collaboration, while Notion Projects is where the magic of project management happens. Every project, no matter how complex, has its space, allowing for task breakdowns, role assignments, milestones, and even dedicated discussions. I found Notion Projects to be superior to **Trello** (another project management tool). While it retains Trello's board structure, it adds task dependencies, Gantt chart visualisations, artificial intelligence (AI)-generated summaries from simple bullet points, and project prioritisation. Its integration with other Notion templates streamlines my workflow. Depending on the project and client, I occasionally revert to Trello boards.⁷ They're visually engaging, interactive, and super flexible. Each card represents a task or a sub-project, moving fluidly across columns, marking its journey from idea to completion.

At the end of the day, **Clockify** acts as a mirror, showing me how I've spent my time, offering insights into my time management, and highlighting areas for improvement.⁸ It was my first time tracking app, and it remains user-friendly. I activate it daily, allocating every minute to distinct projects. Its year-end breakdown proves invaluable for client interactions and freelance business management.

As a project winds down, **Zoho Invoice** takes over the financial side of things.⁹ Its ability to integrate with platforms already part of my digital workplace, like



MANAGE & COLLABORATE

- ToDoist*
- Fantastical
- Cardhop
- Google Drive*
- Notion Projects*
- Trello*
- Descript
- Zoom
- Microsoft Teams
- Google Meet*
- Clockify*
- Zoho Invoice*



DIVE DEEP INTO RESEARCH

- Zotero*
- Scite
- Pubmed*
- Google Scholar*
- MEDLINE*
- Microsoft Excel



DRAFT & REFINE

- Microsoft Word
- Google Docs*
- Scrivener
- ChatGPT-4



VISUALISE

- Microsoft PowerPoint
- Keynote*
- Canva*
- Biorender*
- Visme

*The primary features of this app are available free of charge.

Google Drive, ensures all my invoices, expense reports, and financial documents are neatly organised and ready for any audits. What endears me to this app is its exceptional value, especially given its free status.

Deep dives into research

When it's time for in-depth research, everything changes. The room feels calmer, my coffee stronger, and my digital tools become more specialised. **Zotero** has been my trusty sidekick, making referencing easy with its vast library and citation features.¹⁰ Every piece of information I gather from sources like **Pubmed**, **Google Scholar**, or **MEDLINE** is neatly organised and tagged. Zotero stands out for its simple collection of references from websites. It often allows PDF downloads alongside references, streamlining access to full texts. I value its feature of saving webpage snapshots with references, preserving original content that might change. It's compatible with many word processors, such as **Microsoft Word**, **Libre Office**, and **Google Docs**, which is handy for collaborations. Despite Zotero's 300 MB free storage seeming limited, it's straightforward without needing special memberships. Additionally, its citation style language (CSL) visual editor is intuitive, even for those new to such formats.

But research is an ever-evolving field. Recently, **Scite** has piqued my interest.¹¹ It bridges the gap between old-school citation and modern analysis using AI to determine whether articles mention, support, or contrast the claims of each cited article. By showing how specific research has been cited, it provides context. It's like having a magnifying glass that doesn't just zoom in on the reference but also shows its wider impact. While there's a learning curve to it, its capabilities go beyond what most traditional reference managers offer, making its potential benefits worth every bit of effort.

When data analysis beckons, **Microsoft Excel** is my tool of choice. It's an oldy but a goody, and if you know how to use it, it can be more than just a spreadsheet; it can become a storyteller. With its vast array of formulas, pivot tables, and visuals, Excel turns raw data into insights that enrich my articles. Every formula, cell, and chart guides my research, ensuring it's both informed and impactful. While Excel boasts immense capabilities when fully leveraged, learning this app can be daunting given the vast

array of available features and the endless list of formulas one needs to memorise. However, Microsoft's release of **Copilot**, an AI assistant powered by the large language model generative pre-trained transformer 4 (LLM GPT-4), promises to diminish the learning requirements for all its apps, including Excel, improving user capabilities and experiences.^{12,13}

From research to writing

The shift from research to writing is always thrilling. Depending on the project, I might use a classic like Microsoft Word or Google Docs or turn to a more modern app like **Scrivener**. Scrivener is like having a personal writing studio.¹⁴ While most word processors prioritise presentation, Scrivener zeroes in on content. Picture the creative process: we scribble initial ideas on bits of paper and index cards, pinning them to a corkboard, unsure of their final position. As our thoughts evolve, a structure emerges, highlighting which sections have organically developed and which require more refinement. Scrivener digitally integrates this methodology. While Word simplifies the typing process compared to a typewriter, Scrivener elevates the experience by seamlessly integrating planning, writing, and structuring for extensive texts as a white paper.

But writing isn't a one-and-done process. Lately, I've been turning to **ChatGPT-4**, a LLM-based chatbot.¹⁵ I prefer it over traditional tools like Grammarly and Hemingway for polishing my work. ChatGPT-4 isn't merely an editor; it's a dynamic feedback loop. It pushes me to dig deeper, refine my writing, and even play out potential feedback scenarios. Engaging with

ChatGPT-4 feels like a stimulating conversation. Beyond just refining my writing, these interactions with ChatGPT-4 have sharpened my communication skills, preparing me to anticipate and adeptly navigate real-world discussions, whether it's about the direction or structure of a paper.

Visual storytelling

Turning my research into presentations feels like crafting a visual story. Every slide, image, and narrative element must weave together to share the essence of my findings. The platform I choose plays a pivotal role. Whether it's Microsoft **PowerPoint** with its classic layout, **Keynote's** modern design flair, **Canva's** vast visual library,

Biorender's detailed scientific illustrations, or **Visme's** animated infographics, each has its unique strength.^{16,17,18,19} Just as a movie director sets the scene's mood, I tailor my presentations to resonate with my audience's preferences and expectations. Gone are the days when you need to be an expert at illustration software. The tools outlined here are easy to use and provide a vast array of visually appealing, accurately depicted scientific and other artwork to create beautiful illustrations with minimal effort.

The value of lesser-known tools

Sometimes, we gravitate towards familiar tools, thinking they're more efficient. However, we might be overlooking hidden gems that, while requiring an initial time investment, can save us much more time in the long run. Consider my experience with time tracking. My bookkeeper initially wanted me to manually log every minute I worked in an Excel file, which meant noting down start and end times for every task. But with Clockify, the process became seamless, and I automatically got a detailed report. I've done the math: using Clockify over Excel saves me at least an hour every week.

And then there's PowerPoint. It's a staple for many, but have you explored Biorender? It's a game-changer for medical writers, offering specialised scientific illustrations. Similarly, while Word is a go-to for many, Scrivener offers a refreshing approach to writing, particularly for extensive documents.

Exploring lesser-known tools can provide a unique advantage, allowing us to address specific challenges that mainstream tools might overlook. So, even if there's comfort in the familiar, venturing into new territories can yield unexpected and rewarding results. Why not give it a try? You might find a tool that becomes an essential part of your digital toolkit.

Looking ahead to 2024

The only constant is change. As we journey deeper into the digital age, it's essential to keep an eye on the horizon, spotting emerging trends that might reshape our professional world in 2024. A prime example of this is AI. It isn't just a buzzword for the future; it's already woven into our daily lives, changing the way we work.¹³

Generative AI is advancing at a breakneck pace thanks to significant investments. This has paved the way for groundbreaking tools capable of creating text, videos, images, and audio. And multimodality can blend them to deliver richer, more accurate results, setting the stage for immersive experiences. The progress in AI technology is also democratising its access,

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essence of my findings. The platform I choose plays a pivotal role. Whether it's Microsoft **PowerPoint** with its classic layout, **Keynote's** modern design flair, **Canva's** vast visual library,

allowing more people to tap into intuitive AI apps that effortlessly blend into their daily routines.

AI's influence is particularly pronounced in areas like literature analysis, data interpretation, and content optimisation. It's enabling more precise research curation from vast databases like PubMed, streamlining the synthesis of complex medical data, and even suggesting content structures tailored to specific audiences. Personalisation is taking centre stage, with AI enabling tailored interactions across various channels. Digital twins are gaining popularity, especially as our interactions become more virtual. These digital replicas are proving invaluable in areas like online meetings and medical consultations.

As AI's footprint expands, the call for ethical AI and regulation grows louder. This urgency arises from several considerations. Medical writing often conveys information with direct implications on patient care, drug development, and public health policies, making the accuracy and reliability of AI-generated or AI-assisted content paramount. The sensitive nature of medical data demands that AI tools processing this information adhere to the highest ethical standards, safeguarding patient confidentiality and informed consent. Furthermore, AI models used in medical writing must be trained on diverse and representative data sets to prevent the introduction or perpetuation of biases, ensuring the information remains unbiased and universally applicable. The mechanisms behind AI tools should be transparent, especially when these tools are used to explain medical phenomena or provide recommendations, ensuring accountability in the information presented. Lastly, to maintain the integrity of the profession, AI-assisted medical writing must consistently align with established medical standards and guidelines.

In the professional realm, AI isn't just boosting productivity; it's reshaping job roles. This shift means we need to be on our toes, constantly learning and adapting. Are you ready to venture out of your comfort zone and explore new digital tools?

Disclosures and conflicts of interest

The author declares no conflicts of interest.

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Medical Communications and Writing for Patients

Editorial

Dear all,

As I'm sure you are aware, EMWA's Special Interest Groups (SIGs) have been hard at work hosting "Meet & Share" sessions throughout the year. These sessions aim to encourage open and honest discussion between medical writers on a variety of topics (usually identified ahead of the session). It's an invaluable resource for EMWA members, since we are lucky enough to have a lot of very experienced and talented medical writers in our community, so I strongly encourage you to look out for the Meet & Share sessions and get involved!

The Communicating with the Public SIG's latest Meet & Share session delved into the

issues surrounding the roles and responsibilities of ethics committees in the UK and US. This was the first of a two-part series on "Protecting the public from undue harm during research studies", and was developed in response to a need to educate medical writers about how ethics committees function and how effective medical writing can really make a difference to an ethics committee submission. It's a fascinating area of medical writing, and is often overlooked, so it's a great honour to have presentations from Alison Rapley and Art Gertel, who are both hugely experienced in this area, and were able to compare and contrast the UK and US ways of doing things. A special thanks to the SIG's ever-trusty and talented reporter Sam Rappaz, for another engaging and very readable article.

SECTION EDITOR



Lisa Chamberlain James

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The session could have continued for a lot longer than we had, so I encourage you all to join Part 2!

As 2023 draws to a close, I hope that it has been a good year for you all, and that you and your loved ones remain healthy and happy. Enjoy the upcoming Christmas break – may you dodge the snowballs, and may Santa be kind.

See you in 2024!

Bestest,
Lisa

Meet and Share session on protecting the public from undue harm during research studies: A report

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doi: 10.56012/qxky3990

In September 2023, the Communicating with the Public Special Interest Group (SIG) held a Meet and Share session on the roles and responsibilities of ethics committees in the UK and the US, the first of a two-part series on "Protecting the public from undue harm during research studies". The purpose of the series is to educate medical writers about how ethics committees function and how effective medical writing can add value to a submission to an ethics committee. Freelance medical writing trainer and consultant Alison Rapley gave an introduction to Research Ethics Committees (RECs), which review submissions for studies in the UK. She was followed by Art Gertel (principal consultant of MedSciCom LLC), who introduced the US-

centric ethics review committees, the Institutional Review Boards (IRBs). The session was moderated by SIG Chair Lisa Chamberlain James.

The ethics committees' main objectives, irrespective of where they function, is to protect the public by:

1. Thoroughly reviewing the background information of and justification for a proposed research study that is provided to them by the investigators, funders, or sponsors; and
2. Ensuring that participants can truly understand what they are agreeing to when they sign an Informed Consent Form (ICF).

Effective and ethical writing of study documents helps ethics committees fulfil their objectives, making the approval process easier and leading to a useful and successful study. Below are highlights of the information presented.

Research Ethics Committees

How are RECs organised?

There are 60 RECs currently active in the UK,

co-ordinated by the Health Research Authority. The REC is made up of volunteers. Each REC must have a minimum of 7 members and can have up to 18 members; the average membership size is about 8 to 10. One-third of the membership must be "lay" and the rest "expert". Lay members are currently defined as those who are not registered healthcare professionals and whose primary professional interest is not in clinical research. (This means that medical writers are considered lay members, despite having extensive specialist knowledge!) Expert members include specialists, such as doctors, hospital medical staff, other healthcare professionals, statisticians with expertise in clinical research, and others. While there is no legal requirement for the membership to be culturally diverse or to include members with varied perspectives, (such as patient advocates, research staff), an REC functions best when its membership includes people who are representative of the participant community and general population.



What are the roles of the REC?

The REC has two main roles:

1. Balance the rights, safety, and wellbeing of research participants against the wishes of researchers. At times, researchers seek information that may not be ethically justified, so the REC steps in on behalf of potential participants to make researchers reassess their goals.
2. Ensure “true” informed consent has been sought. The REC will check if the potential participants know everything that will happen to them during the course of the study and what that means to their health and wellbeing.

What does the REC review?

RECs review the following aspects of a study:

1. **Social or scientific value:** Does the research support the study objectives? Is the study necessary? Will the outcomes be useful?
2. **Recruitment:** Is the participant selection fair? Is any community excluded? Are there any barriers for participation, such as language, technology? Why is a certain vulnerable community (such as children, pregnant people, people with cognitive problems) being recruited, or not being recruited?
3. **Informed consent process:** Is the information adequate and complete?
4. **Risk-benefit ratio:** What are the anticipated

benefits? What are the risks and have they been clearly explained? Are adverse effects explained using clear, accurate language?

5. **Care and protection of participants:** Is the welfare and dignity of the participants being prioritised? Will study expenses be paid? Is the language coercive? Will the participants be provided with the trial results?
6. **Suitability of applicant and supporting staff:** Will the trial be conducted by capable and competent people?
7. **Suitability of supporting information:** Is the language in the Patient Information Sheet, posters, participant diary, etc., appropriate and understandable? (Ms Rapley highlighted that this is a common objection raised by RECs as the language is often not appropriate.)

Institutional Review Boards

How are IRBs organised?

An IRB is a committee that reviews and approves research in accordance with US federal regulations and institutional policies. The Common Rule (45 CFR 46, Subpart A, effective from 2018)¹ requires that an IRB reviews and approves certain studies involving human participants. Only “non-exempt” studies require an IRB review, and some “exempt” categories require a “limited IRB review”. Ethics review in the US is two-tiered: Submission is reviewed by

an IRB that is affiliated with the institution whose staff will conduct the study or where the study will be conducted and by an independent IRB that is non-affiliated. An independent IRB review is required; however, an institutional IRB review could be done in addition to the independent review. The purpose of an independent review is to mitigate bias and corruption; the review is done upon payment and these IRBs work on a for-profit business model.

An IRB must have at least 5 members. The membership has varied background and qualifications; however, as in the UK, there are no legally required diversity quotas that need to be met. There are central IRBs that provide a national perspective and local IRBs that provide a local one, and these perspectives may not dovetail. Single-gender memberships and single-profession membership are not allowed. There is no guidance yet on how to classify people who are undergoing a gender transition. Each IRB must consist of at least one member who is not in any other way affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution. A member who has a conflict of interest must not participate in the review. When an IRB’s membership does not have the expertise to conduct a thorough review, it can bring in an expert as a non-voting member.

What are the roles of the IRB?

The overarching role of the IRB is to protect the study participants. IRBs are heavily regulated; they follow the FDA's Criteria for IRB Approval of Research (21 CFR §56.111).² Their review is continuous. To approve the research, IRBs must determine in its initial review that all of the following criteria are met:

1. Participants give their time and put their wellbeing at risk for benefits that may not be realised. Hence, the risks to participants must be minimised and be reasonable in relation to the anticipated benefits and the importance of resulting knowledge.
2. Selection of participants must be equitable, and thus must consider language, socio-economic, and technological barriers to participation.
3. Informed consent must be sought and appropriately documented. The ICF must be understandable.
4. Research plan must include a data monitoring plan to record data signals on risk.
5. Privacy of the participants must be protected.
6. Vulnerable participants must be protected by installing appropriate safeguards.

When new information is available that affects the IRB's prior finding on the research, the IRB conducts a continuing review in accordance with the above criteria (21 CFR §812.64).

What does the IRB review?

IRBs review the following materials:

- Protocol and informed consent document(s) in use at the study site and any proposed modifications to these documents
- Summary of amendments to the research since the last review
- Investigator's Brochure, including any modifications
- New and relevant information, especially about the risks associated with the research. This could be gathered from various sources, such as new information on competitors' products, newly described relevant syndromes, and other published and unpublished sources.
- Relevant regulatory actions that could affect safety and risk
- Other significant information, such as reports from data monitoring committees
- Summary of withdrawal of participants from the research since last review

- Summary of complaints by the participants about the research since last review

Ethics review of decentralised clinical trials

During the peak of the coronavirus disease 2019 (COVID-19) pandemic, regulatory authorities and trial sponsors were motivated to establish and follow decentralised trial processes to mitigate virus spread. Although presently only used in a few cases, decentralised clinical trials (DCTs) have many advantages that could make them the "new normal".³ A DCT, also called remote clinical trial, is defined as: "A clinical trial utilising technology, processes, and/or services that create the opportunity to reduce or eliminate the need for participants to physically visit a traditional research site."⁴ So, when participants do not visit a site what information does the ethics committee review?

Ethics committees scrutinise all patient-facing information for understandability.

Good Clinical Practice (GCP) guidelines (ICH E6 R2)⁵ require the written information that is provided to patients to be submitted for ethical review. This would include the electronic ICF and screenshots of the patient-facing screen. But, if adaptive design is used, the information on the screen can change from one day to the next. Dr Gertel

noted that if every possible screen had to be reviewed it would greatly increase the effort and time required by ethics committees to adequately review all material. So the initial library of screenshots submitted for review may not be the full library. Dr Gertel confirmed that the IRBs are not given a software demonstration, only screenshots. As for RECs, Ms Rapley said that they are lagging behind in how to carefully review DCTs. Both agreed that screenshots are not adequate to understand the patient perspective. Ms Rapley said that RECs are sometimes sent weblinks to help them experience the platform, but there is no clear guidance on how to submit such information.

Both the speakers highlighted the questions raised by ethics committees concerning equity and digital literacy when reviewing DCTs, such as "Will the participants be provided with a device?", "Do the participants know how to use the device?", "Can they access the internet?", "Do they have an option to use a facility to access the program?". Ms Rapley suggested that it is good practice to provide options so as to not inadvertently hinder participation.

Problems facing ethics boards

The speakers agreed that one of the main problems faced by ethics committees is diversity, both when considering study recruitment and its own membership. The participant population should be a representative one, but participation is hindered by cultural norms and historical injustices that have eroded trust in clinical research for some communities. Also, it is difficult to balance benefit and risk when it comes to deciding if vulnerable participants should be recruited. While these issues would benefit from having an ethics committee that represents the participant community, organising such a committee has proved difficult.

Not enough people are volunteering to join ethics committees as it requires a large time commitment, a good understanding of clinical research and related issues, and possibly some qualifications. Being a member of an ethics committee entails a lot of reading and may require travel although most of the committee meetings are now virtual for the sake of convenience. Even so, as Ms Rapley pointed out, membership mainly consists of White, older people, who have the time and luxury to participate. Also, as there are no legal requirements in the UK or in the US to have an adequately diverse membership, there is less motivation to persuade people from underrepresented communities to volunteer.

An attendee raised the question of whether ethics committees can offer remuneration to its members. Dr Chamberlain James, who had been an REC member, said that ethics committees run on a small budget so they cannot offer compensation. Dr Gertel explained that ethics committees need to be careful about receiving and making payments as it may lead to a conflict of interest. People participate in ethics committees "out of the goodness of their heart", according to Ms Rapley. She noted that a REC's chair and vice chair do get a small annual payment as they have a lot more work than the others.

Role of medical writers in ethics review

Writing in plain language

Medical writers must use plain language principles⁶ when developing written materials for patients. Ethics committees scrutinise all patient-facing information for understandability. A plain language glossary is a needed resource when translating complex scientific terms into the more understandable and familiar terms that a study participant will encounter. A widely recommended plain language glossary is the

Multi-Regional Clinical Trials (MRCT) Center Clinical Research Glossary,⁷ which is now being expanded and maintained in collaboration with Clinical Data Interchange Standards Consortium (CDISC) as one of its global clinical research standards.⁸ Dr Gertel, who along with Dr Chamberlain James is one of the current workgroup members for the MRCT glossary, gave an overview of how the glossary was developed. He spoke about the extended discussions the workgroup had on defining “plain”; the problem is that what is “plain” for one person may not be for another. He advised medical writers who wish to write in plain language to let go of some precision while embracing accuracy and understandability. What is important is to not be misunderstood. A glossary is especially useful to achieve these goals, as it ensures that terms are used accurately and consistently across all communications. Giving patients information in plain language empowers them to participate in decision making, which leads to them making informed decisions.

Becoming an ethics reviewer

Speakers strongly encouraged medical writers to join ethics committees. Medical writers would bring valuable insight to the review. They understand clinical research and know the ethical principles that govern it. Those who are trained in plain language writing are especially suited to reviewing the appropriateness of written materials for patients. Medical writers in turn would benefit professionally as they would learn the intricacies of how an ethics review is conducted, what documentation is needed, and how discussions take shape. You can learn more about ethical practices in the EMWA workshop “DDF17: Ethical considerations in clinical trials”.

If you live in the UK, you can join an REC. More details can be found on the Health Research Authority website: www.hra.nhs.uk/about-us/committees-and-services/res-and-recs/.

Thank you

The Communicating with the Public SIG thanks the speakers and all those who attended the Meet & Share session. The SIG welcomes you to join the next Meet & Share (the second part of the series), which will cover sections of an ethics submission in the UK that require writing for the public, specifically what RECs want to see in the Lay Summary, the Application Form and participant facing documents such as the Patient Information Sheet, ICF, recruitment posters, etc.



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The author declares no conflicts of interest.

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Veterinary Medical Writing

SECTION EDITOR



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Editorial

This edition of Veterinary Medical Writing is a bit of a departure from the usual format. I have invited Caroline Frith, veterinary surgeon, amateur athlete, and good friend from vet school, to share extracts from her blog “Here We Go Again”. Here, she details her experiences as a patient undergoing treatment for stage 4 breast cancer and the impact it has had on her and her family. Why did I ask Caroline if she would like to share excerpts with a medical writing audience? Firstly, because I think you will agree, the prose is beautifully written and an excellent example of the genre of patient testimonial, containing rare insights provided by Caroline’s

veterinary medical training. Secondly, it is an opportunity to be reminded that whatever domain you work in, be it regulatory writing, medical communications, medical education or beyond, ultimately, it is all about the patient, and each patient is a unique individual. This is something that is easily forgotten in the discourse of population means, statistical significance, and power calculations. And if you are wondering why the title seems familiar, it is inspired by one of Caroline’s favourite music tracks: *Everybody’s Free (To Wear Sunscreen)* by Baz Luhrmann, itself a paragon of reflective thinking. This is probably also the first time that a veterinary *Medical*

Writing article comes with a content warning, or “steer clear”, as Caro says, as it does cover challenging topics, including living with incurable disease, descriptions of medical interventions, and the ultimate taboo, death. On the other hand, if an audience of medical writers can’t engage with these themes, who can?

In this edition of *From the Horses’ Mouth*, we have good news in the global fight against rabies, a spotlight on a study that challenges preconceptions about inbreeding (or feline blood bank), and some new evidence in the controversial issue of feeding cats a vegan diet.

Louisa

Trust me on the sunscreen

Caroline Frith

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Editor’s note - Caroline Frith graduated from Glasgow Veterinary School, UK, in 2000 and had settled into a busy career as a small animal veterinarian when she was diagnosed with primary breast cancer in 2014. She went into remission after treatment, but unfortunately, in February 2022, the cancer returned and is now incurable. Caroline started a blog documenting her experiences of the countless interventions and treatments she had received. Whilst undergoing treatment, Caroline has completed Ride London, the London Marathon, and Swim Serpentine, and in doing so, she not only completed the gruelling London Classics challenge, but also raised a phenomenal sum for Maggie’s - a charitable organisation providing emotional and practical support to patients with cancer across a network of centres in the UK, Barcelona, Hong Kong and Tokyo. Caroline lives in London with her husband, Ian, and their two children, Matilda and Eric.

Just keep on running (February 13, 2022)

I hope this isn’t depressing, either for me or you – that is not my aim. Being diagnosed with a life-threatening illness definitely makes you do a lot of soul-searching and evaluate the important things in life. However, I will admit the past couple of years have been really hard, and if I have regrets, I’d say I have sweated the small stuff more than is good for me, mostly about work. So, if you can forgive my self-indulgence, then join me on the cancer rollercoaster – most of you will be lucky enough to just be spectators, but some of you are already riding alongside me, and as you have probably realised, once you’re strapped in you can never get off.

Hold on – it’s going to be a bumpy ride.

Protocols (April 1, 2022)

Medicine is not straightforward. It’s not like taking your car to a garage, the mechanics plugging it into a computer, running some diagnostics, coming up with an answer, and fixing it. Some things in medicine are less complicated than others, and often, there are protocols in place which are evidence-based, tried and tested.

This time, I have a locoregional recurrence, and it is unusual in that it appears to be solely confined to one lymph node in my neck. Whilst I am aware that everything I read on Google needs to be taken with a pinch of salt, one thing I know for certain is that in the UK, there is no



Photo: Caroline Frith



specific guidance for how patients like me should be managed. There is even a study – the MARECA study – which was only started last year, whose aim is to determine the frequency, current management, and prognosis of patients diagnosed with my type of recurrence in the UK. I am willing to be part of that study, but it won't help me. It will help those who come after me. So, at the moment, it feels like the treatment chosen for me will be a bit of guesswork – albeit very educated guesswork.

I know I am not an easy patient. I am completely incapable of just accepting what I am told – I have to understand every course of treatment offered, why it has been chosen, and know that it is right for me before I will agree to it. The list of questions I bring to every appointment probably seems infinite to the poor person at the receiving end. But, at the end of the day, I am a medic too – albeit for different species – and I need to know that if the treatment doesn't work, that I was happy with the decisions I made. At some point, I know I just need to trust that the oncologists do know what they're talking about and let them do their job.

A taboo subject (April 29, 2022)

In my job, I facilitate death. It is not the first thing people think about when I tell them what I do – I think the assumption is I play with puppies and kittens all day – but one day, all those puppies and kittens become “senior pets”, and sadly, no one's dog or cat lives forever. Owners come to me, and we talk about death. Often in a roundabout way, because people don't like talking about death even though we all know it is one of the few

certainties in life. Years of experience have taught me to interpret what the owners are trying to say, and so I am the one to bring it up because somehow, if it is me who suggests it, then the guilt the owner feels for even thinking such a thing is lessened.

Yet, as a society, we don't talk about death; we use expressions like “tempting fate” if we dare so much as mention it, despite the fact we are all hurtling towards the same inevitable destiny at an unknown moment in time, and facing cancer for a second time before my mid-40s means accepting my own mortality and staring death right between the eyes. Do I want to die? Of course not. Does thinking about these things make it any more likely that I will die? No. So why aren't we better at preparing for the unavoidable conclusion of life?

Ride London ✓ (May 30, 2022)

The past week has definitely been a mixed bag. When I wrote my last post, I was cautiously optimistic that I was over the worst for this round, but I couldn't have been more wrong. On Sunday evening, after coming back from a scheduled MRI scan at the Royal London Hospital, I came down with a headache and sore throat, and a bug had unfortunately taken advantage of my weakened immune system – I knew from bloods taken a couple of days previously that my neutrophil count was a mere 0.2.

By Tuesday, I could no longer talk or swallow my own saliva; I was in so much pain. By

lunchtime, out of desperation, I wrote a note (being unable to speak) and headed down to my GP to do battle with the receptionists. First, I was told to come back in an hour (it had taken every ounce of energy to get there in the first place,) then I was offered a telephone consult (I can't talk in case you hadn't noticed), then finally when I flashed my chemo alert card, she gave me an actual in-person appointment with an actual GP. I was prescribed amoxicillin, and within 24 hours, I was a new woman and eternally grateful to Alexander Fleming.

I now had three days to eat all the food and get my strength up for the little matter of a 100-mile bike ride. Mentally, I never doubted myself, and I would have been absolutely devastated if I hadn't been able to do it after months and months of training. It is not in my nature to give up, and cancer wasn't going to win this one. My cycling isn't fast at the best of times; all I had to do was keep fuelling and keep pedalling – and that's what I did for 7.5 hours.

I had a really good appointment with my oncologist this morning – I finally feel like we understand each other, which is so important in my mind. For once, I was seen pretty quickly, and when I went into the consulting room, the waiting room was still half empty. However, when I came out, it was bursting at the seams, and I felt really bad that I had definitely used up more than my allotted five milliseconds of his time with all my questions. I hate that this makes me feel guilty.

In my job, I facilitate death. It is not the first thing people think about when I tell them what I do – I think the assumption is I play with puppies and kittens all day.

Breast Cancer Awareness Month and me (October 29, 2022)

October is Breast Cancer Awareness Month, which, as hard as I try, is difficult to ignore.

During the month of pink, there is one day, October 13, dedicated to secondary or metastatic breast cancer – that is, breast cancer that has spread to other parts of the body – the type of breast cancer that kills people. I often forget how much (or little) the general public understands about breast cancer because when I was first diagnosed in 2014, I made sure I learned as much as possible about my disease, and with my medical background, I suppose I already had a head start with the terminology.

Did you know that every year, around 11,500 women and 85 men die from breast cancer in the UK? That's nearly 1000 deaths each month, 31 each day or one every 45 minutes.

I have been on drugs for so long I no longer remember the Caroline without them. I

LONDON MARATHON RUNNER FOR MAGGIE'S NAMED TOP FEMALE FUNDRAISER BY JUSTGIVING

Tuesday 25 April 2023



45-year-old Caroline Frith, who ran the London Marathon for us on Sunday while living with stage 4 cancer, has been named "Top Female Fundraiser" by JustGiving.

Source: <https://www.maggies.org/about-us/news/london-marathon-runner-for-maggies-named-top-female-fundraiser-by-justgiving/> (with permission)

sometimes wonder what I would be like if none of this had happened to me – both physically and psychologically. There is no doubt in my mind I would be a different person because all of us are changed by life events. This obviously gives me a perspective on life that I wouldn't otherwise have, but I cannot go down the rabbit hole of wishing this hadn't happened to me because then I would just spiral into despair.

So, back to awareness. Why is it so important? Because if you catch it early, breast cancer is completely curable. Despite having male breast cancer in a close relative, no one told me this increased my risk. I didn't know women in their thirties got breast cancer, and I rarely, if ever, checked myself. Again, I can't go down the "what if" scenario, but if I'd found it earlier, would my story be different?

However, over the years, several friends have said that because of me, they went to their doctors when they found something that concerned them, so if me telling my story is doing my bit for breast cancer awareness, then I won't bury my head in the sand every October – although I draw the line at wearing pink.

Did you know that every year, around 11,500 women and 85 men die from breast cancer in the UK? That's nearly 1,000 deaths each month, 31 each day or one every 45 minutes.

Step out of the vehicle (February 21, 2023)

Cancerland is a really sad, scary and dark place at the moment. I don't recommend it for a holiday. Just when I thought it couldn't get any worse, guess what? The rollercoaster fell off a cliff.

I appear to have several "metastatic deposits" in my brain, including the original tumour they found before Christmas, which has grown marginally to 2.5mm.

Brain tumours mean an automatic driving ban – that's it, gone. I can no longer get behind the wheel of a car, just like that. I have my bike, which I absolutely will still ride, but I have been cautioned because of the slight risk of seizures.

The plan of action is an MRI of my spinal cord to see if it's opened up shop there as well, cyberknife radiotherapy of the lesions in my brain, followed by a different systemic drug called Enhertu, which is a combination of chemo and targeted treatment. On paper, it sounds like an amazing drug, really clever. I just wish I didn't have to have it. It's given IV every three weeks, and from reading other people's reports on the dedicated Enhertu Facebook group (yes, there

really is a Facebook group for everything), nausea and constipation seem to be the main complaints. My further research tells me it's partly a monoclonal antibody derived from Chinese hamster ovary cells. The mind boggles.

I guess my 3:30 marathon is out the window as well, but I really hope I can still do it. I cycled 100 miles on chemo last year, so I can damn well run/walk a marathon!

The "I" word (April 29, 2023)

Many, many years ago, at the London Marathon Expo, I bought a hoodie. In large letters on the front, it says RUN. Then, in very small writing underneath are the words "Be the Inspiration". The irony is not lost on me, given that I have been described as inspirational an infinite number of times over the past few weeks, particularly by people who've never met me.

I ran a marathon on Sunday in under three and a half hours and, in doing so, achieved a long-standing goal of mine, which has made me very happy. Along the way, I somehow raised an extraordinary amount of money for a charity that has come to mean a lot to me over the past year – but I didn't set out to do that. Training for and running the London Marathon was far preferable to me than chucking myself out of a plane or abseiling down a skyscraper, and it gave me a real sense of purpose over the past few months, as opposed to a 5-minute adrenaline rush.

So what now? The only concrete thing in the pipeline is Swim Serpentine in September – a 2-mile open water swim that I have to do in order to get my London Classics medal – the medal awarded to people who've completed the marathon, Ride London and the swim. My marathon time was good enough to qualify for the Boston Marathon next year – a pretty high accolade in running circles – but I would have to enter in the autumn, many months before the event, with no way of knowing what shape I will be in this time next year. In the meantime, I shall enjoy last weekend's marathon success a bit longer and know that I am happy today, whatever tomorrow may bring.

On and on and on ... (August 4, 2023)

Things have been pretty rubbish, to be honest, and when you're well and truly fed up with something, regurgitating it for others to read about isn't conducive to making you not think about it. But I may as well put pen to paper and hope this has the cathartic effect it usually does.

I've now had two doses of Enhertu, the supposed wonder drug, but have no way of knowing if it's working or not. In the last month or so, I feel like I have been in hospital all the

time, had at least 4 MRI scans, 1 CT scan and more appts than I can remember, so when the poor neurooncologist got me yesterday, he didn't get the usual resilient version of Caroline that just gets on with it, he got the crying version of Caroline who really didn't want to be there any more. We all have our limits, I guess. But I don't get to have a limit; I can't say stop enough, I want to get off. The rollercoaster doesn't have an off switch.

The chemo itself isn't too awful – of the three I've had, I'd say it's the least bad so far. If you follow me on Strava, you'd be forgiven for thinking nothing's going on. I'm swimming and cycling as much as ever, resting a leg injury whilst training for Swim Serpentine in September. I don't feel well; I just don't feel as bad as I thought I would. My hair seems to be shedding a fair amount, and I'm not sure how effective the cold cap is being this time around. My hair itself feels like wire wool and has the much sought-after style of Worzel Gummidge these days, but I still prefer the scarecrow look to boiled egg. The Maggie's Centre has been a godsend these past few weeks, especially yesterday when I was at Bart's for over 8 hours. Just having it there makes such a difference.

Tomorrow, we go on our long-anticipated holiday to Greece, and I don't feel like I've ever needed a holiday as much as I need this one. I'm going with a suitcase full of drugs, expensive travel insurance, a bikini, sun cream, two books, and the people I love.

Caroline's blog, *Here We Go Again*, can be accessed at <https://breastcancerrunner.wordpress.com/>

Disclaimers

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



From the Horse's Mouth

The quarterly pick of the news from the veterinary world

To coincide with World Rabies Day, September 28, the World Veterinary Services (WVS) has announced that 2 million dogs have been vaccinated against rabies through their Mission Rabies initiative, it was reported at MRCVS Online on September 26, 2023. Rabies continues to present a significant health burden globally, being the cause of death of a child every nine minutes and at a cost of \$8.6 billion to the global economy annually.

It is estimated that dogs are responsible for up to 99% of all rabies transmissions to humans, and, as a result, dogs are indiscriminately and inhumanely killed in many parts of the world due to fear of the disease.

Veterinarian Luke Gamble, founder and chief executive of WVS, which became part of the Dogs Trust charity in May 2023, said: "Our pledge is to halve the number of human rabies deaths in the next five years and protect hundreds of thousands of dogs". In the wake of the largest-ever rabies vaccination drive in Cambodia, where 75,000 dogs were vaccinated over ten days, the group's aim to vaccinate 70% of dogs in any given project zone seems eminently achievable. The ultimate goal is to eliminate rabies, thereby saving countless human and canine lives.

On September 25, 2023, *The Veterinary Times* reported on a study recently published in the *PLOS One* journal, which claims that cats fed a vegan diet are healthier than their meat-eating counterparts. Data from the study conducted by researchers at the University of Winchester in the UK, which was derived from owner-reported outcomes, indicated that the 127 cats (9% of the study population) fed on a vegan diet recorded risk reductions for a range of health outcomes, including veterinary visits, medication use, therapeutic diet prescription, and reduced number of health disorders per cat. The authors reported that only one difference was statistically significant; nevertheless, the authors claim the results are evidence that cats fed vegan diets tended to be healthier than those on meat-based diets. These results challenge long-standing "reservations" about feline vegan

diets in the veterinary profession that are based on the currently accepted physiological principle that cats are obligate carnivores and a meat-free diet is detrimental to them. However, any actual health benefits notwithstanding, there is a sustainability argument for feeding pet cats a plant-based diet. In response to this ongoing research, along with similar studies in dogs, the British Veterinary Association has set up the companion animal feeding group to help steer the profession in future policy based on emerging evidence.

The Dog Control Coalition has published its response to the announcement by the UK government of its intention to impose a ban on the ownership of XL bully dogs, it was reported on bva.co.uk on September 15, 2023. The statement by Prime Minister Rishi Sunak was made the day after a fatal attack on a man in Staffordshire, UK, allegedly by two XL Bullies, as well as an attack on an 11-year-old girl in Birmingham, UK, the same week. Although details of the law which would enforce such a ban were yet to be provided at the time of this writing, it is speculated that it will have a similar function and reach as the controversial, "unworkable" Dangerous Dogs Act. This breed-specific legislation came into force in the UK 32 years ago. The Dog Control Coalition argues that the Dangerous Dogs Act is not working, as the incidence of dog attacks on people and other animals has increased over the last three decades. They contend that instead legislation should focus on unscrupulous breeders and irresponsible owners and call for the UK government to engage with them and other stakeholders to implement properly evidence-based legislation and avoid future tragedies.



Regulatory Matters

SECTION EDITORS



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Editorial

As young medical writers still learning the craft, we may be more than eager to prove ourselves to our bosses, managers, or clients.

We may take on work beyond our capacity, be afraid to speak up, or be afraid to ask questions because that may indicate weakness or inexperience. In this issue, Tiago Silva offers

medical writing tips to writers new to the job and important things to think about when starting a project.

Clare Chang

I did it so you don't have to: Lessons learned as a young writer struggling with a regulatory document

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Medical writing is not easy, especially for new writers still learning the ropes. We are exposed to new documents, therapeutic areas, procedures, and challenges regularly and the fast-paced and ever-changing environment can be stressful. Nowadays, there are resources and initiatives available to equip writers with the right tools to get started, which is a tremendous development.¹⁻³ Nevertheless, mistakes will happen, regardless of experience, and it is part of our professional journey to acknowledge, learn, and grow from them.

In this reflection article, I share the story of one of my earlier regulatory writing projects, the lessons I learned, and how they improved my craft. I hope it will be valuable for other regulatory writers who are starting their journey.

The story

Back in my early years as a medical writer, I was tasked to write a protocol for an investigator-initiated clinical study (i.e., a study conceived, developed, and sponsored by an independent investigator) that assessed a new ocular surgical

technique. I received an outline from the principal investigator, which included the study objectives, design, endpoints, and schedule of assessments. I was assigned a team of subject matter experts within various functions such as operations, regulatory, and biometrics with whom I would work. I was also tasked with completing the document under aggressive timelines. I did not attend the kick-off meeting and only joined the project afterwards.

I was still a bit inexperienced in regulatory documents at the time and, considering that I was leading several other projects in parallel, I was overwhelmed. Still, I wanted to prove that I could get the job done without support. In discussion with the team and management, I was clear that the study design was final so I did not dive deeper into its contents. This meant that after receiving the operational and statistical information, I would focus on putting the document together from an editorial perspective. This allowed me to meet the timelines and still work on my other projects. After some quick drafting and reviewing, the team was happy with the final output. However, at the very end when I was preparing the document for approval, I noticed one problem in the design: it allowed for treatment to both eyes of the same patient on the same day (assuming both were eligible for surgery). This raised all sorts of concerns related to biases and patient safety. Even though we were on the verge of

approval, I could not let it slide, so I asked the team about it. It turned out that everyone missed this, leading to a redesign of the study and the timelines being extended. The team was frustrated with this delay and I felt terrible for not having noticed this problem earlier (even though I realise now that the fault was not mine alone, as nobody else noticed it either). Still, we were able

to finish the protocol after adjusting the design and the study ran its course.

As medical writers, we must place ourselves at the centre of the collaborative effort and communicate openly with all team members.

Lessons learned

Embrace and clarify the role of the medical writer

Regulatory documents are mostly cross-functional. Medical writers work with teams of various technical and scientific subject matter experts, who provide the content from their line function

and make the final decisions regarding content and document approval. However, unlike the name suggests, the scope of the medical writer goes beyond just writing. We are tasked to lead the process as efficiently as possible, along with critically appraising and incorporating input from subject matter experts and literature into a cohesive document that clearly delivers the right message to the target audience. This means that understanding, synthesising, analysing, and discussing information are part of our scope, not just writing and editing.

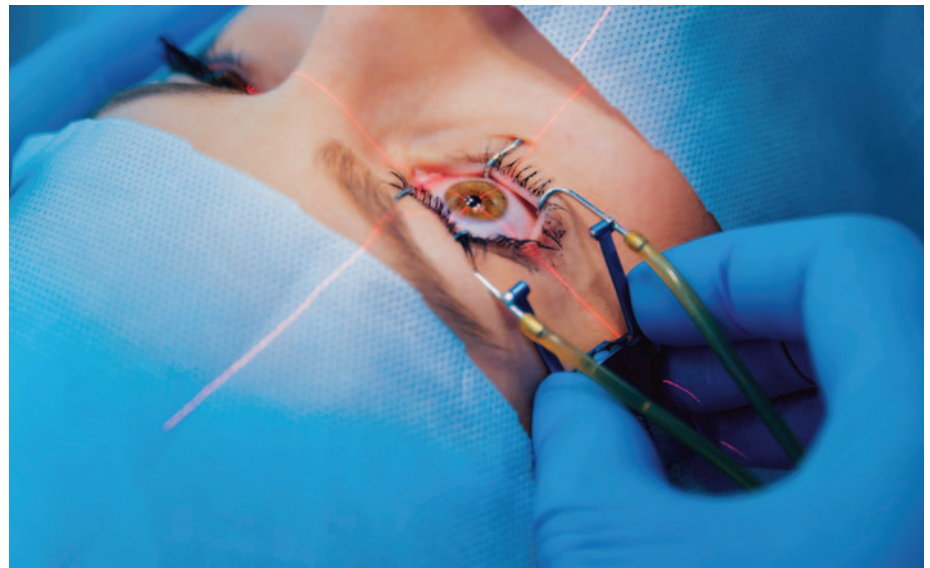
To do this successfully, as medical writers we must place ourselves at the centre of the collaborative effort and communicate openly

with all team members (Figure 1). We must clarify our role as consultants who advise the team on the best practices to ensure document quality and compliance. We must also be ready to challenge the team when needed, by openly discussing potential concerns raised by contradictory or incomplete input or review comments and offer solutions and alternatives that will help the team make the best decisions.

Doing this requires strong leadership and teamwork skills, which have already been identified as important skills for the medical writing profession.^{4,5} These skills can be gained by formal training, but must be nurtured with experience. Thus, it is normal for inexperienced writers to feel insecure about leading teams right away (which I do not think is an entry level task). Writers starting out can work alongside more experienced colleagues, to see how they write and run the process, and to become more familiar with the documents. With time and experience, younger writers will be able to start leading their own projects and take their place in the team as an equal brain in the brainstorm.

The kick-off meeting is key

Expectation management is vital in medical writing. My experience taught me that we cannot assume teams will know what our roles as medical writers are or how the process works in the first place. This is why we should have well-structured kick-off meetings at the start of every document: to ensure the whole team is on the same page and to set clear expectations



(Table 1).^{5,6} However, it is important to communicate continuously after kick-off to ensure that the project is going as planned, and that everyone is up to speed with any shifts in scope and timelines. Sometimes, the plan can deviate, and everyone needs to stay in the loop.

In the example I gave, I did not attend the kick-off meeting and was only later introduced to the team. This had a negative impact, as I was not able to establish myself as the process lead or even an equal team member. This is why I believe that lead medical writers should lead all kick-off meetings concerning their documents. It allows us to introduce ourselves as the process leader

and the main contact for questions, concerns, or updates that may impact the document. This meeting is also an excellent opportunity to create a good first impression. A well-planned and well-led meeting will make the team feel safe and trust the writer to lead them.

Writers not yet experienced in leading these calls may ask senior colleagues to attend one of theirs and see how they lead the discussion and establish a working relationship from the very start.

After kick-off, the writer should prepare and circulate the meeting minutes, so that everyone (including non-attendees) can stay on the same page.

Do not underestimate document complexity

Regulatory documents are complex by default:

- They require a cross-functional team to provide input and review the contents.
- They include a high density of scientific information condensed into strict templates that must adhere to numerous regulations, templates, and guidelines.
- There is a large variety of regulatory documents available, each with unique characteristics and challenges.
- Regulatory timelines can be stressful.

Writers who are starting out on a new type of document should ideally start by supporting experienced colleagues on their projects. Getting formal training (hands-on and theoretical) either from the employer or another way is also important to gain familiarity with these documents.

In addition, writers should always confirm they are following the correct standard operating procedures, style guides, and templates when

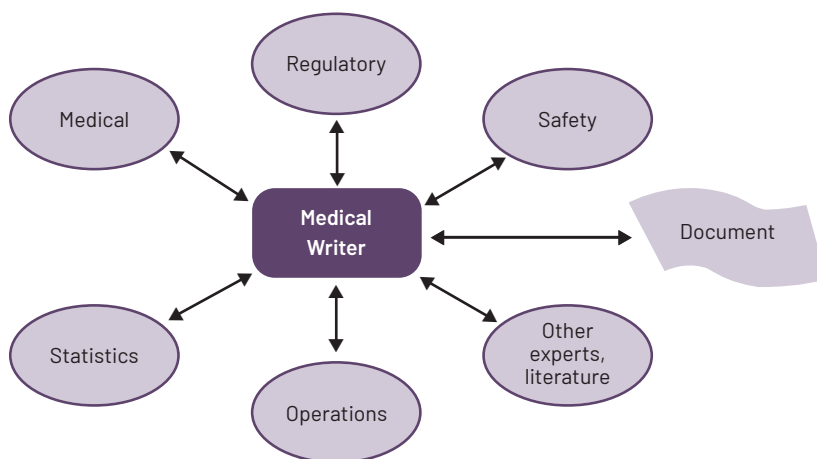


Figure 1. The role of the medical writer in cross-functional documents

Medical writers are at the centre of the collaboration: collecting and triaging all input and comments received from subject matter experts. They are tasked with critically analysing, discussing, and incorporating all comments and information in order to achieve a high-quality, fit-for-purpose document.

Table 1. Topics to discuss at kick-off meetings

| Topic | Considerations |
|------------|---|
| Background | <ul style="list-style-type: none">● Provide background information so that everyone has a clear understanding of the project and its scientific/regulatory environment. |
| Team | <ul style="list-style-type: none">● Identify all team members by line function, including the lead writer and other supporting writers. Make sure all line functions are included as per standard operating procedure.● Clearly identify authors, reviewers, viewers, approvers, and other tasks (e.g., separate tables for each task).● Ensure that the team has time to check the list and identify any mistakes, missing personnel, or potential delegates, if necessary. |
| Process | <ul style="list-style-type: none">● Provide an overview of the process as per standard operating procedure.● Clarify your role as the lead medical writer and any supporting writers involved.● Clarify the role of the team members, including other authors/contributors, reviewers, and approvers.● Clarify how the document will be drafted, reviewed, approved, and published, including any specific software and document management platforms, if applicable.● Establish a communication plan with the team, including preferred communication methods (e.g., email, phone, chat) and, if needed, regular catch-up calls. |
| Timelines | <ul style="list-style-type: none">● Timelines should include all tasks required by the standard operating procedure, including drafting, reviewing, and approving periods, as well as slots for important meetings (e.g., comment resolution meetings after each draft review), and publishing steps, if applicable.● The team should confirm their agreement with the with the proposed timeline and their availability when needed. In case of absences, delegates should be assigned to ensure line function involvement. |

writing a document. I also suggest asking the team for examples of similar, recently finished documents. I do this regularly as an agency writer, as each client has preferences that may not be clear by using templates and style guides alone. This allows me to achieve consistency between documents from the same client and better understand their expectations.

In my example, I underestimated the complexity of a clinical study protocol. These documents are particularly challenging, because study designs depend on the full alignment of many items (Figure 2), and even a small change can have a profound impact in the whole document, just like a game of Jenga. In my case, a seemingly tiny oversight resulted in the study being redesigned.

Ensure appropriate timelines

In my example, timelines were a major issue. I felt uncomfortable raising my concerns, as I thought I was seen as a service provider instead of an equal member of the team. I also assumed that the pressure was considered the norm in medical writing. In retrospect, if I was more assertive in ensuring proper timelines, the whole situation



could have turned out differently.

Medical writers should, whenever possible, have an active role in defining the timelines for their projects. We should also raise concerns as soon as possible when faced with an unfeasible timeline. It is true that the regulatory environ-

ment we work in will sometimes put us in tight spots, but a high-quality document needs time for its development; this may include time to think and discuss the strategy with the team, to draft, to review, and to further align everything at the end. If this is not done, the quality will be

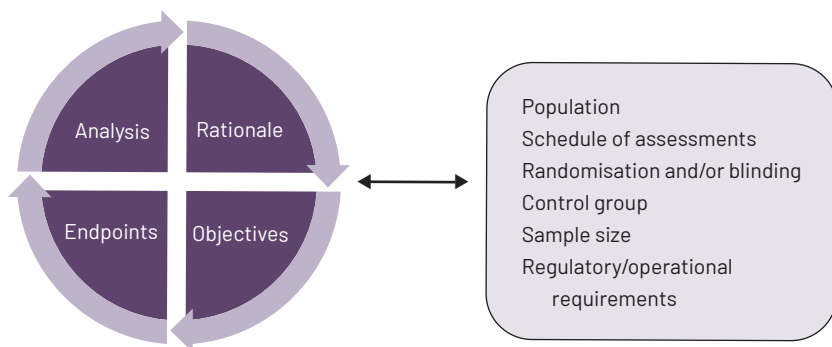


Figure 2. Requirements to write a clinical study protocol

Protocols require full consistency between the rationale, proposed objectives, endpoints, and statistical analysis, to answer the questions proposed by the study. Moreover, several factors (see box) must also be aligned with the methods proposed. Changes made to a single topic may have a profound impact on all others, making protocols particularly sensitive documents.

subpar and result in forced timeline extensions or even amendments/addendums, leading to further delays, additional costs, and increased risk of quality issues.

Also, timelines are not always “non-negotiable”. Knowing the context of the document and the programme it is in may help understand if there is flexibility. In my experience, if there is no strong reason to push a document forward at breakneck speed (e.g., a regulatory deadline), teams will likely be fine with an extension. In my example, no reasons were provided for the timelines proposed; it is possible that the timeline was initially proposed by someone unfamiliar with the writing process and assumed to be reasonable, hence why medical writing input when setting up timelines is important. If I had spoken up at the beginning and highlighted the importance of having adequate time required to draft and review the document, either I or the team would likely have spotted the error earlier and addressed it without the need for a late-stage rewrite.

Writers feeling overwhelmed with a difficult timeline can ask a senior colleague or manager for assistance (if possible), and never make promises they cannot keep. It is important to keep an open line of communication with the team, so that expectations can be managed properly.

If not comfortable, speak up!

It is tempting, especially for those starting out, to try to prove their worth and gain as much experience as possible. However, this can be overwhelming, so writers should not underestimate the job. The regulatory environment (including document strategies) can change at any time, leading to shifts in timelines and scope

of work. So, if possible, writers should avoid working on too many documents in parallel.

If the writer feels that a project is too much to handle, or a shift in a timeline is going to give them a difficult time, and support is available, they should reach out for help. A colleague sharing the workload, overseeing the project, or just providing advice or a sanity check, may be a huge relief.

In the example I provided, I did not voice my concerns over my workload because I saw that as a failure on my part, even though my team (and management) never gave me reasons to be concerned. Knowing when to reach out when necessary is not a sign of weakness. Instead, it shows strong foresight and project management skills. Writers who do this are adapting their work to improve efficiency and to attain high-quality output.

Conclusion

As medical writers, our work is about protecting patients and public health, while helping the advancement of medical science. It is a high-responsibility and high-pressure job, and mistakes can happen. However, writers can improve their chances of success by understanding and clarifying their place in the project and establishing clear roles, expectations, and communication lines. Writers uncomfortable with a new document type, timeline, or excessive workload should be comfortable asking for help. In my experience, medical writers are a friendly and supportive bunch, and always love a new challenge.

Acknowledgements

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Disclaimers

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

Disclosures and conflicts of interest

The author declares no conflicts of interest.

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Good Writing Practice

Syntactic punctuation distraction

Slash: usage and misuse

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Introduction

In research writing, non-distracting usage of the slash are (1) “per”, (2) semantic synonyms, (3) alternatives, and (4) possibly parts of a whole.

Non-distracting slash usage

(1) Per

Example

Moles/hr/skin

Notes

The most explicit and conventional usage of the slash is to symbolise the mathematical-like prepositional meaning of *per* as in a numerator-to-denominator relation.

(2) Semantic Synonyms

Example

Solidus/virgule

Notes

Each term on either side of the slash is acknowledged to be an equivalent of the other. Being equivalent to the equal sign, the slash is often applied when the nomenclature is undecided for a recently identified entity.

(3) Alternatives

Example

And/or

Notes

The protein occurs in the cytoplasm and/or the nucleus vs. the wordy: the protein occurs in the cytoplasm, the nucleus, or both.



(4) Parts of a whole

Example

0.5 M NaOH/0.5 M NaCl

Notes

The slash denotes the presence of NaCl in the solution, being equivalent to *and*, *containing*, or *plus*.

Slash misuse

In contrast to non-distracting slash usage, there are distracting examples of slash misuse: (5) contrasting abstractions, (6) inexplicit coordinating conjunction *and*, and (7) inexplicit inclusive conjunction *or*.

(5) Contrasting Abstractions

Example

(Results section: results statement)
A venous/arterial concentration difference was observed for plasma free fatty acids.

Revision

A venous-to-arterial concentration difference was observed for plasma free fatty acids.

Notes

The contrasting *to* meaning, as in *cell/cell interaction*, effectively conveys a tangible physical relation. But in the example, this meaning is

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inexplicit when the contrasting constituents are intangible as in *venous/arterial*. In the Revision, the athwart (i.e., on both sides) hyphenated “to” is explicit.

(6) Inexplicit coordinating conjunction “and”

Example

(Methods section)

At each physician appointment, blood/urine tests were performed.

Revision

At each physician appointment, a blood and a urine test were performed.

Notes

In the example, it is confusing whether there is more than one test for blood and for urine. The coordinating conjunction *and* is clearer by focusing on individuality. Furthermore, the repeated *a* avoids the unintended plural meaning *tests*.

(7) Inexplicit inclusive conjunction “or”

Example

(Introduction section: research objective)

In this study, the Tinto model and other derived models are reviewed to understand freshman persistence/exit from two-year colleges.

Revision

In this study, the Tinto model and other derived models are reviewed to understand freshman persistence or exit from two-year colleges.

Notes

This usage of the slash is intended to convey that instances of *persistence* and *exit* each occur, but as alternatives. However, the relation between opposite alternatives is confusing, compared with slash demarcation of synonyms, justifying usage of the inclusive coordinating conjunction *or*. A frequent example of the inclusive *or* is when a moderator of a meeting asks the attendees whether there are any questions or comments. The moderator is not saying an attendee can only ask a question or state a comment (the exclusive *or*) for which *either ... or* would be explicit.

The Crofter: Sustainable Communications

SECTION EDITOR



Kimi Uegaki
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Editorial

Greetings from the croft. I recently attended the Green Health (Groene Zorg) Festival here in the Netherlands, which was organised by the Green Health Alliance (Groene Zorg Alliantie).¹ It was inspiring to hear about the different sustainability initiatives taking place in hospitals and clinics and efforts to include planetary health in professional education curriculums and embed it into the daily practice of public health. These actions make me hopeful.

There were also a series of panel discussions on Green Deal-related healthcare topics. During one of these, the moderator shared her

experience with how she has encountered two camps when it comes to thinking about sustainable healthcare and how discussions can derail if this difference in perspective is not recognised: those who think about its environmental impact and those who think about how its “future-proofness” in terms of affordability and access to resources. Hearing this made me hope that these two camps will come to see that it is not “or-or” but “and-and”. To this end, I am very excited by this issue’s contribution by EMWA member Sarah Kabani and her colleagues Virginie Chasseigne and Sihame Chkair. They share how they created a multidisciplinary sustainability team in hospital

and how their research projects have demonstrated that healthcare practices that are not only eco-friendly but are also future-proof. Happy reading!

Best,
Kimi

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Growing and nurturing a grassroots sustainability team in a clinical centre

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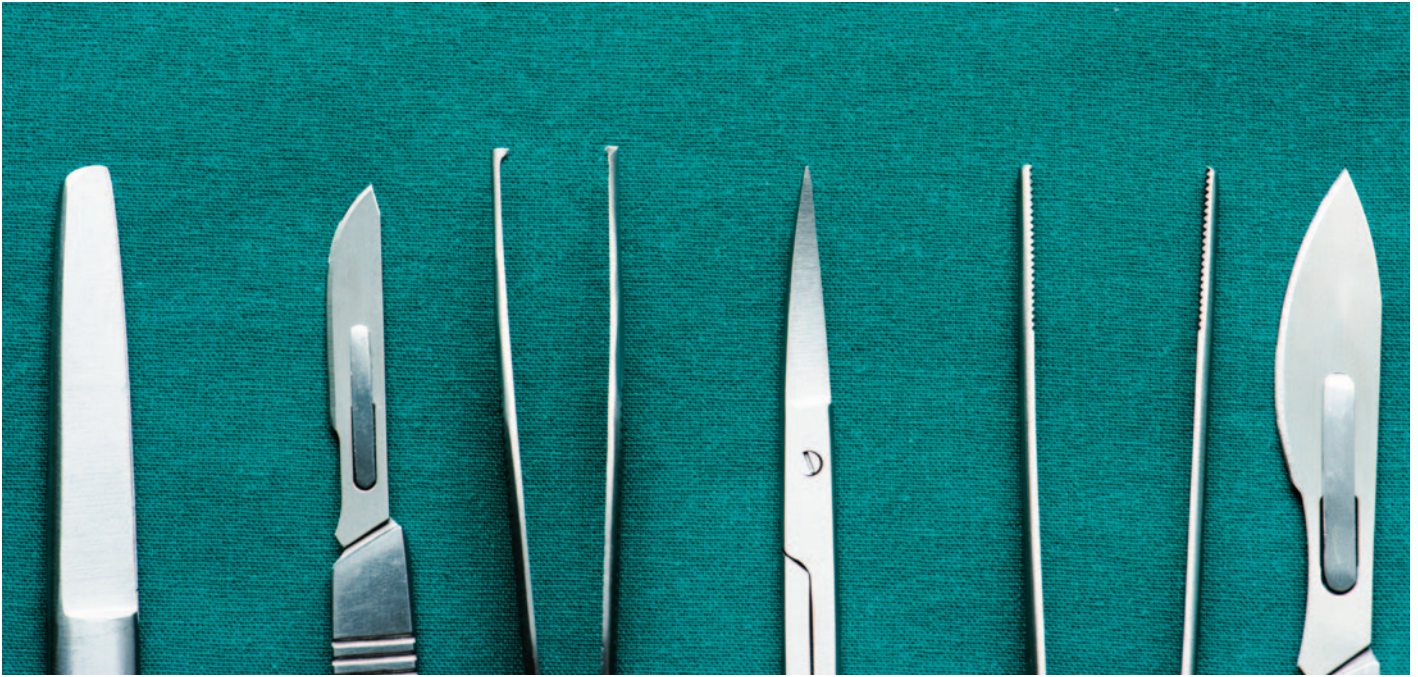
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How can medical writers get involved in sustainability projects?

In an age of rapid climate change, it can be easy to despair. Even when following recommendations to improve personal sustainability, such as giving up the car, reducing or eliminating meat from one’s diet, and avoiding flights, the powerlessness as an individual can lead to eco-anxiety. As a medical writer in a teaching hospital, I (Sarah Kabani) did not feel that I had the capacity to drive sustainability practices at work, so I focussed on improving the carbon footprint in my personal life. I wished to do more, but did not feel qualified to influence





people. I felt lonely in my drive for change, but I soon found out that I was not alone. People at work had noticed that I arrived each day by bike, went for the vegetarian options, and took the train to conferences rather than fly (even to Prague from the South of France!). This led to general conversations with colleagues about climate change, which snowballed into us creating a team with this common interest, with a range of backgrounds and expertise. With an organically created team of researchers and a shared passion in sustainability, it did not take us long until we started thinking about the research that we could perform.

Health economics meets eco-responsibility

Our team's first project was led by hospital pharmacist Virginie Chasseigne, who, with vast experience in the management of sterilisable and implantable medical devices, was at the forefront of observing numerous ways to reduce waste in the operating room. A preliminary study highlighted the extent of waste in surgery and the potential for improvement,¹ prompting Chasseigne to launch the DURABLOC project, which aimed to broaden the range of eco-friendly actions in the operating room.² The project team selected 13 initiatives to target, identified through staff surveys, literature reviews, and suggestions from societies. Sihame Chkair was asked to perform an

You don't need to be an expert on climate action to initiate a sustainability team.

economic analysis of the sustainable practices that they wished to target, and I became involved at the publication stage of the article. The integration of sustainable measures in operating rooms has important ecological benefits, with positive economic outcomes. This more eco-responsible approach should be considered in all healthcare establishments that generate a significant annual volume of waste.

Following this, the DURABLOC working group performed an ecological and economic impact evaluation of switching from single-use to reusable laryngoscope blades.³ They performed a life-cycle assessment (LCA), whereby the ecological impact of the blades was measured from cradle to grave, taking into account the materials used (e.g., metal), and the resources to manufacture (e.g., chemicals), transport, and dispose of the blade. The LCA showed that the reusable blades were better for each of the ecological indicators, from lower CO₂ emissions, toxic chemical production, and water use. These benefits were observable after just three uses, and the economic analysis also showed some considerable savings (estimated at around €5800 per year). These compelling results prompted the key players, i.e., the anaesthetists (technical feasibility), the sterilisation unit manager (human resources feasibility), and the purchasing department to make the decision to switch over to the reusable blades. Importantly, this project was entirely spearheaded by the

pharmacy team, without institutional request, although the direct benefits to the institute are manifold. Today, in our hospital, the DURABLOC working group is very active, holding meetings every two months with different hospital departments to discover which processes staff members believed could be made more environmentally friendly.

Many organisations are keen to lower the environmental impact, but *all* organisations are keen to save money. This is where the input of a health economist is transformative. Indeed, budgetary and financial constraints weigh heavily on organisations, and implementing certain actions can generate significant expenses. In our studies, we have been able to demonstrate that we are not only reducing expenses, but also initiating eco-responsible actions. However, this is not the rule in all situations, and in such cases, it is important to calculate the initial cost to fully inform the decision-maker.

Expanding the network: Europe and beyond

After working with the pharmacy team on their eco-responsibility project, we had a list of other projects as well. For example, we have an ongoing collaboration with a like-minded biostatistician to calculate the economic effects of mitigation strategies for a hospital that had recently been flooded. We also have started a mixed-methods study on the effects of extreme heat events on emergency room management. In addition to the economic impact, the HOTPOINT study will compare focus groups

before and after the summer to describe the expectations and reality for the hospital management team and the clinicians during a heatwave. It will also consider the impact of ambient temperatures on hospital admissions and ambulance call-outs. Such large-scale projects might once have seemed out of reach to us as none of us are formally trained in sustainability. However, it has been gratifying to experience how, with teamwork and a strong will to apply our skills to environmental research topics, we are succeeding.

Even more ambitiously, we next found a Horizon Europe grant programme, Water4All (<https://www.water4all-partnership.eu>), offering funding to projects on water security. Our hospital is in the South of France, an area at risk of water scarcity, so this subject is a pressing concern for us. As a nascent sustainability group, our network was limited, yet the grant emphasised the importance of a global team. European partners were easier to find among contacts-of-contacts and some successful cold-calling, but the grant also covered South Africa. A previous Crofter article⁴ had published an interview with Gomotsegang Fred Molelekwa, PhD, whose biography listed interests in environmental health and environmental management. He is also a member of EMWA's Sustainability-Special Interest Group (SUS-SIG), so I did not hesitate to contact him and suggest a collaboration. This project, called PHOENIX 2, now comprises members from five countries (France, Netherlands, Spain, Lithuania, South Africa, and Turkey). The study aimed to optimise management of healthcare organisations during hydrometeorological stress events, evaluate the cost-benefit analysis of preparing for these extreme events, and perform a LCA of extreme heat events on hospital water consumption. We also wished to perform qualitative

analysis to learn hospital workers' perspectives on how to conserve water. Finally, we would work with specialists in green nudge techniques to develop ways to encourage water saving methods at work and home. Although we passed to the second round of selection, unfortunately, the project was not successful in the final round. However, the positive feedback we received has encouraged us to maintain this new collaboration and we will continue working together on other projects in the future.

The positive outcomes of this collaboration between members of the SUS-SIG and our hospital has inspired us to create a portal where researchers with interests in sustainability can find each other, share knowledge, and work together. Launching this portal is one of the aims of the SUS-SIG for this year, and I hope it will lead to many more fruitful collaborations.

Towards a greener future

It is hard to imagine how, in just a couple of years, we have gone from concerned citizens with climate-anxiety to piloting projects at different stages of completion with a global team of experts. ability changes, initiated by staff members. In a recent issue of the *British Medical Journal*, Florence Wedmore reported a number of initiatives that were discussed at the 2023 Royal College of Physicians conference. These initiatives ranged from switching from pre-packaged saline to offering patients telemedicine meetings rather than in-person consultations for those with stable symptoms, and demonstrated the capacity to save money and staff time whilst also providing a direct benefit to patients.⁵ At the end of this article, Wedmore lists suggestions for

It is hard to imagine how, in just a couple of years, we have gone from concerned citizens with climate-anxiety to piloting projects at different stages of completion with a global team of experts.

climate-friendly gestures in the workplace and offers resources for further information. If you are feeling powerless about climate change, the chances are that there are others around you feeling the same. From something as simple as a chat around the coffee machine, you might find the collaborators you need to start your own green projects in your workplace. Don't forget that these projects often save money and lead to publications, in addition to their environmental credentials, making them attractive prospects to employers. And keep an eye out for the SUS-SIG portal – we would love to have you join us.

Disclosures and conflicts of interest

The authors declare no conflicts of interest.

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Sihame Chkair, PhD, has been a health economist for a French teaching hospital since 2013, a health economics lecturer at University of Montpellier since 2013, and a sustainable development expert at the Agence Nationale d'Appui à la Performance des établissements de santé et médico-sociaux since 2022.

Virginie Chasseigne, PharmD, is a hospital pharmacist at a French teaching hospital. As head of the DURABLOC working group, she is currently conducting a local study as part of her doctorate to promote sustainable development actions in relation to medical devices.



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Serbia

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If you have ideas for themes or would like to discuss any other issues, please write to mew@emwa.org.



Upcoming issues of **Medical Writing**



March 2024: **Translation**

Medical translation is a complex and demanding field requiring specialised knowledge, skills, and expertise. In this issue, we explore a range of topics, including the role of medical translation in clinical trials and regulatory affairs, the importance of terminology management, the use of technology and machine translation, ethical and legal considerations, the impact of cultural differences, quality assurance and risk management, and the emerging trends and challenges in the field.

Guest Editors: Ana Sofia Correia and Claire Harmer

The deadline for feature article has now passed.

September 2024:

Clinical Trial Transparency and Disclosure

The clinical trial transparency and disclosure space continues to grow at pace. With the EU Clinical Trial Regulation being applicable since the 2022 launch of the Clinical Trials Information System comes increased requirements for public-facing documents. Provision of a summary of clinical trial results in lay language is also now mandatory in the EU. Challenges continue in balancing protection of personal data of trial participants with transparency, especially in the wake of the COVID-19 pandemic. All of these bring opportunities for medical writers to drive best practice in authoring clinical trial documents with disclosure in mind.

Guest Editors: Holly Hanson and Alison McIntosh

The deadline for feature articles is June 1, 2024.



June 2024:

Soft Skills for Medical Writers

Medical writing is a highly specialised field that requires a unique combination of technical knowledge, writing skills, and soft skills to produce high-quality work. While technical knowledge and writing skills are undoubtedly important, it is how one interacts with people that can truly set medical writers apart and enable them to succeed in their careers. This issue will focus on how soft skills are used within the different areas of the medical writing industry, and we hope it will provide valuable insights and inspiration for medical writers at all stages of their careers.

Guest Editors: Clare Chang and Nicole Bezuidenhout

The deadline for feature articles is March 1, 2024.



December 2024:

Medical Writing Around the World

Medical writing transcends geography, demography, language, or culture. To date, EMWA has more than 1400 members from 48 countries on 6 continents. This issue of the journal celebrates our diversity and will focus on medical writing activities around the world.

Guest Editor: Raquel Billiones

The deadline for feature articles is September 1, 2024.



<http://journal.emwa.org/>