

Medical Devices

SECTION EDITOR



Beatrix Doerr

Beatrix.doerr@coriuvar.com

Editorial

This issue is about careers in medical writing. Despite the recent scandal, the medical device sector is certainly a sweet spot to be in as there is an increasing need for medical writers due to the new European regulations. Sarah Choudhury and Gillian Pritchard have prepared the featured article “Career opportunities in medical device writing: Employee and freelance perspectives” that is available in this issue and is worthwhile reading (see page 46).

To prepare you for a career in the field, the Medical Device Special Interest Group (MD-SIG) has launched several workshops:

- Introduction to Medical Devices
- From Pharma to Medical Devices (new since November 2018)
- Literature Review for Medical Devices (new since May 2018)
- Writing Clinical Evaluation Reports for Medical Devices (an update according to MDR2017/745 and MEDDEV 2.7/1 Rev4 will be provided in May 2019)
- Writing Clinical Investigation Plans (alias Clinical Study Protocols) for Medical Devices (will likely start in November 2019).

In addition, several webinars on medical devices are available in the webinar archive and an Expert Seminar Series on medical devices is planned for May 2019 during the Spring

Conference in Vienna.

For this issue on careers in medical writing, I am particularly happy that I was able to enlist Monica Meyer to review the medical device articles and provide practice-based input. Monica has more than 30 years of experience in the medical device industry, as Director Clinical Research Europe and as Director of a Global Medical Writing Team, an expertise that was particularly useful to the “Medical device files’ article I wrote for this section.

In closing, if you have any comments or suggestions for the MD-SIG or would like to contribute an article to the Medical Device section, please contact me

Beatrix

The next medical device scandal: Medical device files – my personal view (Part 1)

During a visit to Greece more than 15 years ago when I was involved in an animal protection campaign, I met a journalist who was investigating prohibited fishing methods that local fishermen were using. When he was asked by the animal protection organisation if he could write about the ongoing spaying campaign, he responded with “... good news doesn’t sell”. I remember well how I thought this is quite sad as it leaves a falsely negative picture of the world. Moreover, positive news can also be important, such as in this case, where the intent was to increase public awareness of best practices to ensure a healthy and manageable dog population and provide information on adopting dogs from abroad.

Some years later, when I worked in clinical research, I was very concerned about an article in *Der Spiegel*, at this time a respectable German magazine that I trusted to contain reliable information. The journalist reported that people in Africa are abused as “guinea pigs” for clinical research as medical data are more easily retrieved in Africa than in Europe. This was only partly true. Certainly, it was less complicated to do research in Africa than in Europe, but what the journalist forgot to mention was that – to gain commercial approval in Europe or in the US – the

research population has to be representative of the patient populations in Europe and the US. As there are known variations in substance metabolism between European Caucasians and Asians or Africans it is unlikely that a company would do a research study solely in Africa simply because it would be nearly impossible to get approval in Europe or in the US with this data alone.

Shortly thereafter the next scandal was in the news – that coronary stents are worse than coronary bypass grafts as they lead to thrombosis and that they are used because “bad companies” and “bad physicians” are only interested in “making money” and not acting in the best interest of the patients. Well, again partly true. Indeed, first generation stents had elevated stent thrombosis rates, but at the time the article was published, third generation stents were already on the market that had overcome the elevated stent thrombosis issue.

It made me wonder if journalists ever

consider that they are jeopardising patient lives with such articles as patients may choose to refuse life-saving therapies based on biased information. Certainly, my trust in the media was shaken.

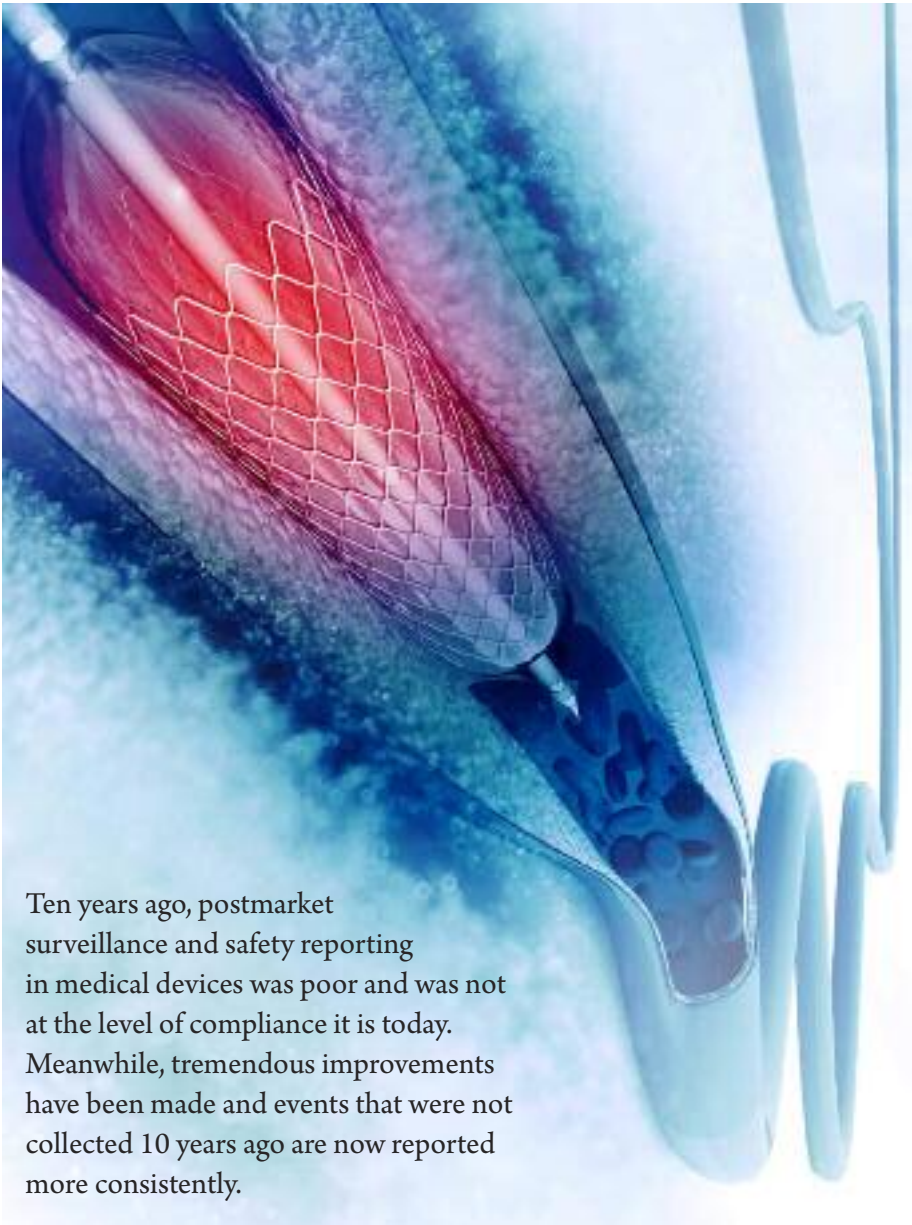
This form of reporting occurred even before online media became the major source of public

information. Today journalists are under even greater pressure to attract readers and produce catchy headlines, so the situation has certainly become worse. I am not speaking about fake news or misinformation, but about a substantial bias in reporting.

Now to the latest scandal, the implant files.¹ One of the most respected German newspapers, *Süddeutsche Zeitung*, published a summary identifying “10 facts to know about the implant files”,² which I would like to comment on. I am giving my personal view built on my experiences after nearly

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15 years in the cardiovascular medical device sector, including more than 10 years in clinical research, several of them in leadership positions.



Ten years ago, postmarket surveillance and safety reporting in medical devices was poor and was not at the level of compliance it is today. Meanwhile, tremendous improvements have been made and events that were not collected 10 years ago are now reported more consistently.

Reported “Facts”:

1. The number of injuries and deaths in conjunction with medical devices is increasing.

I can imagine that the reported numbers are increasing, but the numbers need to be seen in context. The increase is not necessarily due to more events, but these events are now more consistently reported. This has several reasons:

- Ten years ago, postmarket surveillance and safety reporting in medical devices was poor and was not at the level of compliance it is today. Meanwhile, tremendous improvements have been made and events that were not collected 10 years ago are now reported more consistently.
- The number of postmarket medical device clinical studies is increasing. The importance

of collecting and reporting events to evaluate longer-term results and identify late events, their causes and device relationship is now key in maintaining commercial product availability. Potential incidents are thoroughly monitored and hence more events are reported.

- The definition of device relationship has slightly shifted: 10 years ago, events were mostly classified as “device-related: Yes/Unknown/No”. Only events with a reasonable likely device relationship were reported. Currently, there are five categories: “Not related/ Unlikely/ Possible/ Probable/ Causal relationship”. According to German BfArM guidelines, events now have to be reported as device-related as soon as a

relationship cannot be ruled out – a much more conservative approach that has increased the number of events.

- Ten years ago, only device-related events were commonly reported; now procedure-related events are also taken into consideration.
- There has also been an increase in the number of new medical devices used over the past 10 years as device-related therapies have been developed for patient populations where previously only medical therapy was possible. For instance, transcatheter heart valve therapy for severe aortic disease was initiated in elderly, high-risk patients with multiple comorbidities that prevented aortic valve surgery.

Therefore, the large increase in events is most likely due to new therapies, refined definitions, and more thorough reporting. It is anticipated that the numbers will increase even further as there will be more studies and postmarket surveillance will continue to improve.

The authors also mention that not all cases in which a medical device might have caused a life-threatening situation have been reported to the authorities. This is certainly true when it comes to cases outside of clinical studies. I can imagine that after a long working day, physicians would only report cases for which they believe there is an unexpected and likely relationship to the device. From personal experience, my dog suffered from auto-immune hemolytic anaemia that started 4 days after a vaccination. I am sure none of the treating veterinarians has taken the time to fill in a complaint form because the timely association was probably thought to be attributed to a random occurrence rather than to a causal relationship. However, since a relationship could not be ruled out, I completed and submitted a complaint form. This is something very important the journalists forgot to mention – that patients can complete such notifications themselves. I am not an expert here, but I think there are already attempts to allow simple notifications via social media in the pharmaceutical industry. Furthermore, in the new Medical Device Regulation (MDR), which will be fully applicable in 2020, devices will receive a unique device identifier. This will make such reporting even easier.

The authors also claim that there are no reliable facts on how many devices have been implanted. Well, according to MEDDEV 2.7/1 rev 4, the product clinical evaluation report must be regularly updated and submitted to the notified body, including information on “whether the device is currently on the market in Europe or in other countries, since when, number of

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devices placed on the market...” Furthermore, many countries have also established national registries to document the use of various medical devices.

2. Many implants are only tested in men.

I can only speak for the cardiovascular field, but I have never seen a study in which female gender was an exclusion criterion. I also doubt that such a study would receive approval from the ethic committees or competent authorities. Furthermore, it would not make sense to exclude one sex in disease states that affect both men and women, as rapid study enrolment is always desired. Even if impaired outcomes are encountered, e.g., in girls or women, a statistical subgroup analysis could be performed to account for it.

Notwithstanding the above comment, there are of course, diseases that are more prevalent in one sex, such as coronary artery disease.

3. There is no national certification for medical devices and implants in Europe.

This is correct. In fact, I think it is good that there is not a national, but a European certification programme (CE – an abbreviation of *Conformité Européenne*), as registering a device per country would be more complex and time consuming and

companies might not seek approval in certain countries. In many countries, however, European CE certification does not guarantee access to new devices until reimbursement negotiations in the countries take place.

The authors further claim that there is no possibility for patients to see if a device is CE-certified or not. Actually, a medical device cannot be commercially distributed or sold in the European market if it is not CE-certified, which means all devices that patients receive are CE-certified. There are a few exceptions, though, such as devices in pre-market clinical studies or in cases of compassionate use. In these cases, the device must be labelled as an investigational device; patients must be adequately informed about the status of the device, and they must sign an informed consent form that also indicates that they are aware that the device is not CE-certified.

4. Private entities decide if a product may be implanted or not.

The authors state that, unlike the US with the FDA, private entities such as TÜV, BSI, or DEKRA (“notified bodies”) may decide if a device receives certification or not. A manufacturer can change the notified body in case they are unsatisfied with the respective work. In the

past 8 years, only 84 medical devices have been rejected.

Frankly speaking, I do not have the insights to judge the benefits of one system over the other. But clearly, although notified bodies are private entities, they cannot act in a legal vacuum. They are designated and supervised/audited by the national competent authority, which then reports CE approvals to the European Commission. For those who live in Germany: remember your car does not necessarily get the certification even though you pay “TÜV” or “DEKRA” for the inspection.

The low rejection rate of new devices compared to the approval rate might be due to the fact that most of the certifications are re-certifications. (Similar to cars, the certification for medical devices has to be regularly renewed, generally every 3 years). Furthermore, for novel devices, companies usually discuss with the notified bodies in advance as to what data the notified bodies want to see. If the device does not meet the pre-specified success criteria (commonly, a statistical-based sample size has to be calculated based on an expected endpoint), companies would rarely invest the time and money in a submission. And lastly, yes, in the past, approvals were easier. But this has changed

with revision 4 of MEDDEV 2.7/1 released in 2016 and approvals will become even more difficult in 2020, when the MDR is fully in force.

The new MDR also has more stringent requirements for notified bodies and hence the number of notified bodies has already been reduced and will probably be further reduced once the MDR is fully in force. Joint audits of the notified bodies with competent authorities are currently pending following submission of applications to meet the new directives.

5. The certification system is lax and prone to errors.

The authors report that an undercover investigation successfully attempted to get a hip implant device certified that was faulty and which was similar to a hip implant that had been retracted from the market.

When I read this, I suspected that this case occurred prior to the new regulations (revision 4 of MEDDEV 2.7/1). After searching the internet, I found that the respective publication is from 2012,³ long before the new regulations. As stated earlier, it is true that some notified body certifications were too lax in the past, but this is exactly the reason why revision 4 and the new MDR were released that have significantly more stringent requirements.

Part 2 will be published in the next issue of *Medical Writing*.

Conflict of interest:

The author, Beatrix Doerr, acts as a medical writer and consultant in the medical device industry and owns shares from Edwards Lifesciences.

References

1. Implant Files: Health authorities across the globe have failed to protect millions of patients from poorly tested implants, the first-ever global examination of the medical device industry reveals. [cited 2018 Dec 08]. Available at: <https://www.icij.org/investigations/implant-files/>.
2. Was Sie über die Implant Files wissen müssen [cited 2018 Dec 08]. Available at: <https://www.sueddeutsche.de/politik/implant-files-fakten-ueberblick-1.4225363>.
3. Cohen D. Faulty hip implant shows up failings of EU regulation. *BMJ*. 2012;345:e7163.

November meeting of the MD-SIG

During the autumn conference in Warsaw, the MD-SIG met and the following items were discussed:

1. Next MD-SIG meetings

To allow everybody to join the MD-SIG meetings, these meetings will become regular parts of the conference programme.

2. Educational needs

We performed a gap analysis between the current educational content and the members' interest as assessed through the Spring 2018 Conference survey. It seems that we are on track:

- "More workshops on medical devices" – there has been a new workshop on medical devices during the 2018 autumn conference, at the spring conference in May, we will likely have a workshop on Clinical Evaluation Reports and one on literature review for medical devices, and another new workshop is planned for the Autumn Conference.
- "Medical device regulations in the EU and US" – this will be part of the Expert Seminar Series (ESS) at the spring conference this year.
- "Combined products" – this will be part of the ESS this year.
- "Clinical Evaluation Reports" – this workshop is currently updated and will be available at the spring conference this year.
- "Risk benefit analysis" – it is unclear if this suggestion refers to the part of the Clinical Evaluation Report or rather refers to risk management itself. But certainly, risk management is a topic of further interest.

In 2020, we also plan to start to offer trainings for the new in-vitro device regulation that will be fully in force in 2022.

3. Best practice

We discussed the following topics related to writing clinical evaluation reports (CER):

- Table of Contents: The structure provided in the MEDDEV guideline is somewhat inconvenient. Several members have worked with different tables of content, but all agreed that it is best to adhere to the MEDDEV's table of contents unless the sponsor has a different template.
- A tip from one member was to use the Clinical Evaluation Assessment Report (CEAR) checklist to verify that the CER contains all required information.
- There is a white paper that compares the Essential Requirements of MDD 93/42/EEC with the Safety and Performance Requirements of MDR 2017/745: Macomber L, et al. General Safety and Performance Requirements (Annex I) in the New Medical Device Regulation: Comparison with the Essential Requirements of the Medical Device Directive and Active Implantable Device Directive. Available at <https://bit.ly/2AYmaeI>.
- All members do two separate literature searches for the CER, one for state-of-the-art and guidelines, and one for the device in question.
- For weighing of literature, the Oxford Centre for Evidence-Based Medicine (OCEBM) Levels of Evidence may be used, available at <https://www.cebm.net/2016/05/ocbm-levels-of-evidence/>.

We are looking forward to seeing you at the next MD-SIG meeting in Vienna!