Regulatory Writing

Medical writing in China and Japan

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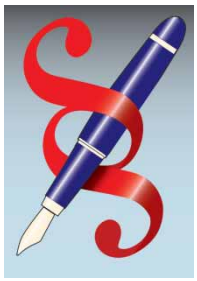

Abstract

This article introduces aspects of the regulatory writing profession in China and Japan. Although regulatory medical writing is at an early stage of development in China, the ever-growing research and development activities in this country have led to an increasing need for regulatory medical writing. In Japan, the Ministry of Health, Labour, and Welfare has made significant changes in recent years in order to address a downward trend in new drug applications due to the lengthy and expensive processes for clinical studies and approvals, and to shorten the lag in the availability of drugs compared to other developed countries. The changes introduced by the Ministry of Health, Labour, and Welfare include a more simplified and efficient approach to clinical studies while improving infrastructure and introducing global standards, such as the International Conference on Harmonisation/Good Clinical Practice. Accordingly, the increased demand for clinical studies has led to an increasing need for medical writing support for regulatory documents in Japan. Both China and Japan have their own regulatory authorities equivalent to the United States Food and Drug Administration, but there are also marked differences leading to challenges and opportunities for regulatory writing.

Keywords: Chinese writer, Japanese writer, Regulatory writing, SFDA, PMDA, Challenges

Introduction

China is gaining increasing exposure to the profession of medical writing ever since *Provisions for Drug Registration* first became effective in 2002.[1] Virtually a monolingual non-English-speaking country, China has its own standalone health regulation system, with marked differences from the United States (US) and European Union (EU): different language, different regulations, and bureaucratic system, etc.; however, China's pharmaceutical regulation largely adheres to ICH. In Japan, medical writing is being recognised as a professional field, although this is a relatively recent development. Due to the increasing number of global studies, the expectations for local medical writers are expanding and are becoming more important in China and Japan. This article aims to give readers a better understanding of the present state of medical writing in China and Japan, as well as the challenges and prospects.

Status quo

Regulatory writing as a profession is not well recognised

Most people in China equate medical writing with medical manuscript writing for submission of biomedical research to journals. There is little public knowledge about regulatory writing for clinical trials leading up to drug registration. This is no surprise since China is ranked second in the world in terms of quantity of scientific research papers published between 2002 and 2012.[2] Although language is one challenge faced by Chinese researchers, this obstacle can be overcome with the support of translators and authorship support. According to an editorial review titled *Concept of Medical Writing* from the *Modern Medicine Journal of China*,[3] medical writing is described as medical activities ranging from writing medical books and papers, drafting patient case histories, and completing medical examination application slips, but no mention is made of regulatory writing. It is therefore understandable that the term medical writing in China has little if any emphasis at all on regulatory writing.

In Japan, regulatory medical writing is also misunderstood or not well recognised. Before medical writing was established as a function, regulatory documents prepared by medical writers today, such as protocols, informed consent forms, and clinical study reports, were actually written by other functional groups, such as clinical operations. The role of the medical writer, as a professional dedicated to the preparation of regulatory documents, was not acknowledged at that time. Now

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that pharmaceutical companies are becoming aware of the need for high-quality documents that can no longer be handled as a side activity, and now that they have established their own medical writing groups, the role of the medical writer has become clearer and is better understood.

Regulatory authorities and requirements for regulatory documents in China and Japan

The equivalent of the US FDA (Food and Drug Administration) or European Medicines Agency in China is State FDA (SFDA), which directly reports to the Ministry of Health. In Japan, the regulatory authority for drug approvals is Pharmaceuticals and Medical Devices Agency (PMDA), working together with the Ministry of Health, Labour, and Welfare. The functions of SFDA and Pharmaceuticals and Medical Devices Agency are mostly similar to that of FDA. Among the differences, the two most relevant to medical writing are: working language (see below) and country-specific regulatory requirements, which are described in the table below (Table 1).

Challenges

Language issues

China

Regardless of whether the studies are international trials involving China or local trials, all documents submitted to Chinese regulatory authorities must be in local language. For this reason, all regulatory documents like protocol, investigator's brochure (IB), informed consent form, and clinical study report, although perhaps drafted initially in English, will need to be translated into local language eventually. There are many translation vendors in China to which pharmaceutical companies and contract research organisations (CROs) frequently outsource translation work; however, the translation quality can vary greatly among the vendors, requiring some translation drafts to be almost completely re-worked in-house. This is partly because some vendors tend to hire part-time student translators. Careful evaluation of the potential vendors and on-going review of translation quality are necessary for reliable translation services.

Japan

Even though English is the common language for global studies, a Japanese translation is required for the protocol and IB (at least a summary). In addition, all study personnel may not understand English and may not be able to conduct clinical studies only with English documents. As more global studies are conducted in Japan, there has been a growing demand for Japanese-translated documents. Medical writers in Japan are expected not only to write a document in Japanese and English, but are also expected to translate and fact check the document to ensure consistency between the languages. When translations are outsourced to external vendors, quality is often compromised. Even though the vendor translators are experts in the language, they may not be experts in clinical studies and may not be familiar with the regulatory requirements and proper wording. Medical writers are expected to fill in the gap, providing input from the regulatory perspective and re-writing the translated document as needed. The process from translation to finalisation of a document can be time consuming.

For both China and Japan, the English language can be a daunting barrier for local medical writers. English documents are an inevitable aspect of the working life of a medical writer. Native English speakers have the natural advantage of preparing the English documents. This barrier can only be overcome by intensive training and long-term self-improvement.

Medical writer's role in the local pharmaceutical/CRO industry

Although the role of the medical writer can be unclear to anyone not directly connected to the pharmaceutical industry, there is also misinformation about the role of medical writing from within the industry. The general impression is that 'writing' implies that a medical writer drafts anything and everything. In a professional organisation, a medical writer has a clear job description and SOPs to follow for every document they are assigned to create. In a well-run medical writing department, the medical writer is trained first before taking on a new document type as required by the Japanese GCP but not stated clearly in Chinese GCP, and a process for quality control is in place. When a CRO works together with a partner, such as pharmaceutical company, it is important that both entities have the same understanding of the medical writer's role. For example, a common misunderstanding is that the medical writer will do statistical analysis of the data.

Current talent pool is small

Although China is one of the largest pharmaceutical markets in the world, it is still expanding its relatively small pool of medical writers. This is in contrast to India, which has had its own medical writing association since 2007.[7] Training a new recruit from entry level to an experienced medical writer requires time and money, but writers in

Table 1: Country-specific regulatory requirements

Document	China	Japan
Protocol ICF	ICH GCP (ICH E6) compliant Generally comply with ICH GCP (ICH 4.8). Now in practice, adolescents/children are also recommended to sign the ICF. No age threshold is specified for signature by adolescents/children, as long as they can understand the ICF	ICH GCP (ICH E6) compliant Although the requirements follow the ICH GCP (ICH 4.8), more detailed information is required for Japanese ICF. For example: • Explain what a clinical trial (in general) is about • Include actual data on adverse drug reactions from previous studies, the package inserts of similar products and the IB In order to be 'visually friendly' to the patients: • Table, charts, and pictures are often used • Font and font size are carefully considered
CSR and appendices	Generally ICH GCP (ICH E3) compliant, but China's SFDA requires also for appendix: • Approval letter of each EC for the study; a list of study site qualification is needed • Approval letters from EC for all protocol amendments • Principal investigators' qualifications (e.g. GCP and SFDA training certificates and medical licenses) • Certification of analysis and preproduction record for investigational product(s) (including placebo) • Package insert sheets of comparator and investigational product (if marketed) • Individual by-site summary table for multicentre clinical trials • Statistical report	ICH GCP (ICH E3) compliant
CTD (Module 2.7.3, 2.7.4, and 2.7.6)	Previously China has only its own drug registration system, following *Provisions For Drug Registration* and did not accept CTD format. Currently, two systems are applied in parallel: other than *Provisions For Drug Registration*, a China's own CTD format system is being developed. The system is developed largely based on ICH M4. China's CTD format system is only provisionally applied now and still under development. The content could change greatly[4]	ICH GCP (ICH M4) compliant
Safety Report	China's SFDA has a special SAE report form[5] equivalent to CIOMS form. The PSUR guidelines issued by China's SFDA (latest version dated 6 September 2012[6]) are mainly based on ICH E2C. The major differences are: • Except line listings and summary tabulations, all the other parts are to be submitted in Chinese or with Chinese copy • Any differences in China's situation from other countries, e.g. drug indications, formulations and dosages, and any safety information, need to be addressed and explained • Updates are required once every year in new drug monitoring period (3–5 years); then every 5 years thereafter	For marketed products, a post-marketing Safety Periodic Report is to be submitted every 6 months for the first 2 years of marketing, then annually until re-examination (drug re-examination system: a part of the PMS to examine safety and efficacy data collected during a certain period of time). The post-marketing Safety Periodic Report includes the post-marketing survey reports explain briefly what these are, overview and analysis of the survey, ADRs reported, individual case report of the ADRs, actions taken for safety reasons including any changes to the drug labelling, the package insert, and an analysis of safety The PSUR is attached to the post-marketing Safety Periodic Report
	For non-marketed products, no periodic safety reports are required so far	For non-marketed products, a 6-month periodic report on serious ADRs is to be submitted. The 6-month periodic report is applicable to all serious ADRs reported in and outside Japan DSUR has not been introduced in Japan yet

Abbreviation: EC, Ethics Committee; CTD, common technical document; SAE, serious adverse event; CIOMS, Council for International Organisations of Medical Sciences; PSUR, Periodic Safety Update Report; PMS, post-marketing surveillance; ADRs, adverse drug reactions; DSUR, Development Safety Update Report.

China will gain the necessary experience when it gears toward more international trials.

Although there are quite a few medical writers in Japan, writers' knowledge and capabilities can vary regardless of their years of experience in the role. A medical writing association (Japan Medical and Scientific Communicators Association (JMCA)) was established in Japan in 2002, with 390 members and 37 supporting organisations (as of February 2013).[8] The JMCA is relatively new compared to the American Medical Writers Association and the European Medical Writers Association. The JMCA has provided workshops to medical writers, and the Union of Japanese Scientists and Engineers[9]

has provided medical writing training courses; however, there is no certificate course established, unlike American Medical Writers Association and European Medical Writers Association.

Prospects

Potential talent pool is large

Though the current pool of trained regulatory writers in China is small, the potential pool could be fairly large. Firstly, there are many manuscript writers and translators in biomedical fields who could switch to regulatory writing fairly easily with the appropriate training. In addition, there is an increasing trend for young Chinese to study or work overseas and gain biomedical knowledge, a bilingual advantage and even with some pharmaceutical experience to move back to China. For Japan, medical writers are experiencing more and more global studies and are exposed to global standards; accordingly, they are learning how to better serve internal and external clients, as well as regulatory needs. Although medical writing in Japan is still 'developing' compared to the US or Europe, more stable and effective infrastructure and standards are being implemented. In addition, it is also important to train younger writers to accommodate future demands and to continue to provide long-term quality services in the region.

Language advantages

SFDA requires documents to be submitted either in Chinese only or in English but with a Chinese translated version appended for submission. Most international organisations in China write first in English and engage a translation agency; however, quality control of the translation by a native speaker with the necessary background in clinical trials is necessary. This is where a Chinese regulatory writer can help given their familiarity with the required terminology and document content.

Another advantage for Chinese regulatory writers is the ability to communicate with Chinese sponsors, colleagues, and local investigators in their native language. With the expansion of China's pharmaceutical companies into new markets, in the near future there could be a need for Chinese medical writers to lead global document preparation for submissions to both SFDA and FDA on the behalf of their companies.

The above-mentioned language advantages also apply to Japanese medical writers, both in writing and communication. Local medical writers will play an increasingly significant role in document for global studies in the future.

Growing market

The Japanese pharmaceutical market has been rapidly expanding and the need for local medical writers is expected to grow further in the future. China has a huge market and the cost of drug development is relatively low. At the same time, more Chinese pharmaceutical companies are becoming interested in generic drugs. The SFDA plans to accelerate the approval of ANDA registrations.[10] This will in turn lead to more demand for regulatory medical writers to support the expansion of generic drug approvals-related document development.

The continued growth of pharmaceutical corporations within China and Japan, coupled with each country's respective global market expansion, suggests a promising future for medical writers in this region. But any writers who speak and write Chinese/Japanese will not only have to be familiar with the local regulatory requirements but also have the capability to formulate sentences the way that is expected by the local regulatory.

References

1. 药品注册管理办法 (试行) (局令第35号). Available from: http://www.sda.gov.cn/WS01/CL0053/24478.html [current English version: http://eng.sfda.gov.cn/WS03/CL0768/61645.html].
2. 2012中国科技论文统计结果发布. Available from: http://www.istic.ac.cn/EducationDetail.aspx?ArticleID=94468
3. Editorial. Mod Med J China 2012;14(6):90.
4. Hui Y, Lihua S. China's drug registration document and ICH CTD: a comparative study. Asian J Soc Pharm 2012;7(3):155–9.
5. 表2严重不良事件报告表(SAE). Available from: http://www.sfda.gov.cn/WS01/CL0058/9317.html
6. 药品定期安全性更新报告撰写规范. Available from: http://www.sfda.gov.cn/WS01/CL0844/74864.html
7. All India Medical Writers Association. Available from: http://aimwa.webs.com/
8. Japan Medical and Scientific Communicators Association. Available from: http://www.jmca-npo.org/
9. Union of Japanese Scientists and Engineers. Available from: http://www.juse.or.jp/e/
10. SFDA将加快新药临床审批. Available from: http://news.pharmnet.com.cn/news/2012/09/17/366441.html

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