Medical writing for *in vitro* diagnostics: A different approach for the 'hidden' side of healthcare

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Abstract

Medical writing for *in vitro* diagnostics differs from writing for pharmaceutical products in several ways. The shorter development time and lifecycle of diagnostic assays, different regulatory requirements and approval times, and upcoming changes to European Economic Area regulatory requirements are a few challenges. In addition, the type of data from *in vitro* diagnostic studies and relevant forums for presenting scientific diagnostic data (independently from patient data) can significantly differ from data collected in pharmaceutical clinical trials.

Keywords: *In vitro* diagnostics, Publication planning, Diagnostic assays

Introduction to *in vitro* diagnostics

The category 'medical devices' covers a wide range of non-pharmaceutical healthcare products. The world of *implantable* medical devices and the world of *in vitro* diagnostic medical devices (IVDs) are different. The IVD industry supplies laboratory tests (assays and instruments) used by healthcare professionals, healthcare institutions, or patients themselves to evaluate human samples of various kinds for abundance of any number of biological analytes. The key distinction between IVDs and medical devices is location: while many medical devices are implantable, IVDs by definition are *in vitro* or outside of the human body.

In practical terms, an IVD could be the instrument at your doctor's office used to measure a selection of variables (electrolytes, lipid profiles, blood cell counts) using only a drop of blood; it could also be a battery of automated instruments filling a room, processing thousands of blood samples every hour in large, centralised laboratories or blood banks. It has been reported and widely cited that laboratory tests are responsible for up to 70% of medical decisions.[1] Traditionally, one would think of many IVDs as having two basic components: the platform or instrument that performs testing, and the assays or actual tests that can be used on a given platform. It is similar to an inkjet printer in a basic way: the printer accepts ink cartridges and the ink cartridge has to be replaced when it is empty for the printer to continue functioning. In addition, the system needs a software component to tell the platform what to do. Just as technology develops at a rapid pace in the communication and information technology industries, so it develops for IVD and laboratory testing software.

What are some important facts about the IVD industry that have relevance for medical writing in comparison to the pharmaceutical industry? First of all, the lifecycle of most diagnostic assays is much shorter than for a pharmaceutical compound, meaning there is a constant cycle of platform, assay, and software updates, with varying frequency. This is comparable to the major version releases for computer operating systems. Indeed, as so much of diagnostics depends on software architecture, the platforms have to keep pace with the breakneck speed of advancement for other digital technologies – no small feat when next generation platforms have to be approved by regulatory authorities. Another important aspect is regulatory approval itself. The requirements in the USA and in other countries are significantly different – at least for now. More on this can be found in the section 'IVD registration timelines'. The study design for IVDs yields a different kind of data to those produced during a Phase II or III clinical study. More on this in the section 'What are IVD data?' below. Finally, IVD data present a special challenge in finding the appropriate scientific information portal for dissemination,

as discussed in the section 'Who wants to know about IVD data?'.

Contrasts with writing for the pharmaceutical industry

IVD registration timelines

Have you ever wondered what the abbreviation 'CE' means? You will find it on most electronic items in your home, as well as many other everyday items. The European Commission website explains CE marking as follows:

> The CE marking indicates a product's compliance with EU legislation and so enables the free movement of products within the European market. By affixing the CE marking to a product, a manufacturer declares, on his sole responsibility, that the product meets all the legal requirements for the CE marking….[2]

Basically, the manufacturer can 'self-validate' an item that qualifies for CE marking by ensuring the item passes a conformity assessment. Only in special cases of 'high-risk' IVDs does the assessment have to be performed by a notified body. Once an IVD manufacturer can prove a product has passed conformity assessment, the product can be CE marked and made commercially available. Producing the required data via external validation studies can take <1 year. While the situation in the USA is very different, requiring more data generation and FDA review and approval, the total timeline could still be only a few years.

Contrast this to the situation for pharmaceutical products, which take several years or more than a decade to complete all trial phases, with interim analyses and safety data, before a product can be available on the market. Needless to say, the challenges in publication planning around registration timelines for IVDs are very different from those for pharmaceutical products. However, change is looming for IVD registration in the European Economic Area, due to the recommendation to the EU parliament in response to the scandal over silicone breast implants in France in 2012.[3]

What are IVD data?

Another significant difference to pharmaceutical products is the type of data used to describe IVDs. Where pharmaceutical endpoints will focus on efficacy, safety, pharmacokinetics, and pharmacodynamics, the diagnostic data landscape will focus on precision, accuracy, and lot-to-lot variability. In addition, the IVD manufacturer should offer data regarding comparability to similar or predicate (pre-existing) commercial IVDs, so that laboratories are aware of what must be considered if they plan to change platforms or assay manufacturers. These data typically take the form of linear regression analyses comparing two sets of measurements from the same set of test samples.

In addition, testing laboratories themselves often have to undergo certification by participation in quality assessment schemes. These are independent studies run by academic or hospital centres where samples are sent to participating laboratories every month or several times per year. Participating laboratories measure the samples and report the platform type and results to the study centre. All results are analysed for mean and median concentrations determined according to assay type or measuring principle, platform type, whether the sample was a patient blood sample or a 'spiked' sample, etc. Data from these schemes are a very helpful and unbiased measure of how well platforms and assays perform in the field in different laboratory environments and are an important part of evaluating any new platform or assay.

On the other hand, there are areas where IVD and clinical data may overlap. Pharmaceutical documents or publications may include diagnostic data from haematology and clinical chemistry assays as required for safety data, as well as laboratory qualification data described above. However, unless diagnostic criteria are critical for defining a claim for a product, this information is likely to be in the background where patient outcomes are the primary focus. One other similarity to pharmaceutical trials is the comparison to a 'gold standard' method, which is comparable to the 'standard of care' concept for clinical trials. Any new platform or assay must demonstrate acceptable or improved performance when compared to the gold standard method. This can often be challenging due to the rapid changes in biomedical and imaging technology, making an adequate comparison between newer and older methods difficult even when the gold standard method is inferior.

Who wants to know about IVD data?

As mentioned above, laboratory technology and clinical chemistry results are often 'hidden' behind the treatments that are prescribed as a result of these tests and the associated patient outcomes. Not surprisingly, diagnostic data are generally not headline-grabbing. There are a number of journals with a focus on 'medical laboratory technology', with the Thomson Reuters Journal Citation

Reports© Science Edition (2012) listing 32 journals in this category (http://thomsonreuters.com/journal-citation-reports/). The impact factors of 27 of these 32 journals are below 3, indicating the high degree of specialisation in this field. However, a different breed of diagnostics known as companion diagnostics or personalised healthcare has been pushing the boundaries of how IVDs are perceived. Here, assays such as assessments for specific genetic mutations can be used to identify patients who will benefit the most from a pharmaceutical product with a very specific mode of action related to the mutation in question. Such IVDs may be required for prescription of a pharmaceutical product and garner attention from much higher profile journals, as they are used for a specific intervention and affect patient outcomes. This trend, as well as more emphasis from the healthcare industry in general on preventative medicine, health economics, and healthcare payers, may mean that publication of diagnostic assays and data alone in connection with patient outcomes will become more important in the near term.

Conclusion and parting thoughts

While the opportunity (or burden?) to write lengthy clinical study reports, patient narratives, and outcome publications still remains in the pharmaceutical realm, an understanding of diagnostics and their impact on healthcare will become increasingly important for pharmaceutical writing, as personalised healthcare or targeted cohort selection will rely on more and more sophisticated assays. Who knows, as you dive into the world of IVD data, you might discover a passion for instrumental precision lying dormant within.

Author information

Alisa Davis obtained her PhD in Biophysics and Biophysical Chemistry from The Johns Hopkins University in Baltimore, MD, USA. After several years of postdoctoral research and writing at the University of Zurich and the Swiss Federal Institute of Technology (ETH) in Zurich, Switzerland, she fully transitioned to a career in medical writing in 2010.

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Conflicts of interest

Alisa Davis is an employee of Roche Diagnostics International, Ltd. All views and opinions expressed in this article are solely those of the author and do not necessarily reflect those of her employer.

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