

Harmonising SOPs for Global Clinical Trials: Myth or Reality?



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Nicky Dodsworth is currently Director of Quality Assurance at Pharm-Olam International (UK) Ltd, UK, a CRO specialising in the set-up, monitoring and project management of international clinical studies. She has been involved in clinical research and quality systems activities since the mid-1980s in pharmaceutical and CROs, and her experience ranges from laboratory research across Phase I to IV studies in many therapeutic areas, to clinical and medical writing, training and quality assurance. Nicky has been actively involved in developing quality systems and has written numerous standard operating procedures (SOPs), including a system for ISO 9002 accreditation. She has also audited extensively across Western and Eastern Europe, Russia, Africa and Asia.

The pharmaceutical industry places high priority in keeping costs to a minimum and in the constant struggle to accelerate the development of profitable new drugs. Increasingly, a growing percentage of trials are being conducted in areas outside of the US and Western Europe. Continual changes in regulatory and ethical standards, as well as logistical and operational issues, need to be addressed. To execute and manage trials on a global basis requires harmonisation of standard operating procedures (SOPs), but is this achievable in reality?



Despite current attempts at harmonisation of the regulatory, ethical and working practices relating to clinical research in the European arena, it is becoming increasingly obvious that this has not been entirely successful. In a world where there is no standardisation of regulatory practices or ethical considerations, despite recent and ongoing attempts, and where the technological infrastructure and cultural differences need to be considered, the pharmaceutical industry needs to ensure its working practices, as defined by standard operating procedures (SOPs), achieve the required conformity.

Guidelines and standards in the field of clinical research continue to develop and the list of regulations and guidelines that govern SOPs grows. It is important that pharmaceutical companies continue to update their policies for trial conduct in line with new developments during this ongoing evolution. This continuous improvement mechanism to ensure SOPs follow the latest relevant legislation and current best practice is a heavy burden – both costly and time consuming. The implications of not developing or maintaining critical SOPs hang heavily over us all.

The concept of true global SOPs, which benchmark current working practices but still allow for a degree of flexibility and for continual improvement of standards of practice, would ideally bring people in a large global organisation together when all around them is a sea of disharmony.

SINGLE CENTRE VERSUS MULTICENTRE GLOBAL STUDIES

The challenges we face are magnified when considering large global studies. Not only do you have to consider local legislation and its interpretation, but you also often have added logistical and operational issues to consider. Understanding local customs and communication channels can only be appreciated by staff working in this environment.

Addressing cultural issues in countries can be a major issue; local expertise is essential to overcoming these barriers. For example, importation of investigational medicinal products can be particularly daunting to anyone without local

knowledge. These local practices need to be documented for local operational staff to follow. The key to resolving cultural differences is by communication and setting standards – and what better way to do this than by SOPs? SOPs that are developed by local expertise have the added advantage of involving staff who need to use them in their daily work, and their input means that you have the necessary ‘buy in’.

STANDARD OPERATING PROCEDURES

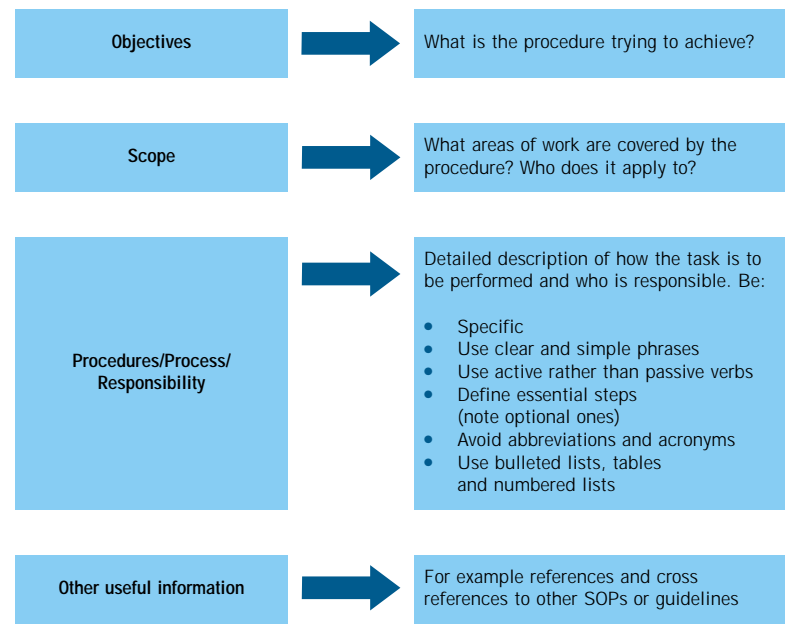
There are, therefore, two options open to us. Global SOPs that have the advantage of bringing together and standardising practices within an organisation may have the disadvantage that they are not detailed and specific enough for staff to follow. On the other hand, locally developed SOPs that compliment the global SOPs will provide the necessary information, but do move away from the standardisation that companies so often seek. To consider the use of country-specific or global SOPs is therefore not entirely straightforward. Before we can make any conclusions, it may be useful to remind ourselves of some of the basic concepts behind SOPs.



SOPs must document your working practices; they must be user-friendly; they must be compliant with all relevant regulations; and they must be up-to-date. SOPs are written to help staff in their daily activities; this reasoning can sometimes be lost in the process. The old adage, ‘if it isn’t documented, it wasn’t performed’, is still true.

SOPs vary in content and structure with different organisations, but all SOPs should cover the essential points of ‘who,’ ‘what,’ ‘where’ and ‘when.’ There is no need to be prescriptive on how to write SOPs, but the aim is to ensure good practice is achieved at all times, to clarify roles and responsibilities, and to follow the natural flow of work.

Figure 1: An Example of an SOP Format



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SOPs, whether global or country-specific, need to be written by staff who are familiar with the daily working practice being described. It is a good idea to involve as many people in the review process as is practical; that way you are well on your way to achieving acceptance.

Bad SOPs are wordy and complicated. Bad SOPs are also too vague, but when writing global SOPs, you have to make some exceptions. Don’t use lots of words; use shorter sentences, especially when your audience’s first language may not be English. Flow charts can be a good idea, and are especially helpful when linking SOPs to e-learning programmes. The use of generic role names produces more stable SOPs. They do not require modification as an organisation evolves unless this affects the processes being followed.

Undoubtedly, when working in a contract research organisation (CRO), well-written SOPs that our sponsors are happy for us to use facilitate the transition between our clients. Operational staff that are used to working to the same SOPs do not have to



Inspectors and auditors use SOPs to verify that results can be reconstructed and that the essential steps in the execution of a procedure are traceable.

Many organisations prepare and operate using standard, core SOPs, and for practices that cannot be standardised additional country-specific SOPs are provided. For example, labelling of investigational medicinal product may be outlined in the global or core SOPs, but this could not cover all individual country requirements without making the SOP unworkable and unreadable. This type of local issue is far too specialised to be handled effectively in a global procedure. Country-specific SOPs are therefore extremely valuable documents, as they provide detailed knowledge on how to perform a certain task at this level. If using this 'two-tiered' approach, global SOPs will rely heavily on referencing country-specific procedures. This can improve readability, as the reader is focused on the essential activities. It also increases flexibility by allowing global SOPs to accommodate individual local issues.

spend any additional time training, with associated costs, in order to familiarise themselves with further SOPs. This leaves staff more time to spend on concentrating on the project, where the only variation may be with study-specific forms.

GLOBAL VERSUS COUNTRY-SPECIFIC SOPS

So, is it possible to undertake the structuring of global SOPs to ensure they are compliant at all locations? Truly global SOPs must use terminology that is vague enough to cover most situations. The general process can be outlined in the global SOP, with additional statements added. For example, when preparing document X, the terminology used must also contain a phrase such as: 'ensure document X follows any local national guidelines/regulations' (or similar wording). This is fine as a general overview of working practices, but it does not go far enough in informing local staff on how they should prepare document X to follow national guidelines or regulations.

For all SOPs, defining the right level of detail is a subject of considerable debate. ICH GCP guidelines state that SOPs are written to provide, 'detailed, written instructions to achieve uniformity of the performance of a specific function'.

Maintaining both global and country-specific SOPs, although more of an administrative burden, should therefore enhance compliance. It is especially important in this case to minimise risks in using documents at both the global and local level by involving quality assurance in early audits of both new SOPs and new procedures. This consistent feedback loop will ensure the SOPs are workable and are not creating more problems than they resolve.

CONCLUSION

Today, there is an SOP for almost any practice. From January 2005, pharmacy departments in the UK have been working to SOPs. There are SOPs on the stock market, fire prevention, water purification – the list is endless. The whole range of SOPs to cover clinical research activities are here to stay – of that there can be little doubt. How they are categorised and developed within individual organisations varies, and at present no-one has a set of guidelines or regulations that defines the 'right' way to structure your SOPs. Consistency is key. The use of a comprehensive set of global SOPs enhanced with highly specialised, country-specific SOPs delivers maximum clinical trial quality, efficiency and speed at every location, ensuring that global project deliverables are met. ♦

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