

Regulatory Requirements for Clinical Trials in Zambia – What Researchers Need to Know for Local Development of Medical Products.

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Abstract

Clinical trials are a fundamental requirement for drug development and establishing safety and efficacy of medical products. This article describes the regulatory requirements and the key institution in Zambia that govern or oversee research for the conduct of clinical trials.

Key words: Clinical trials, regulatory requirement, compliance

Introduction

Clinical trials are a fundamental requirement for a new drug under development to establish its safety and efficacy [1]. As such, a Marketing Authorisation cannot be issued in any country without this evidence submitted to regulatory Authorities [2]. Additionally, any authorised medical products that seek changes to licensed indications, target populations, route of administration, and dosage regimens also require evidence of safety and efficacy through a clinical trial. In contrast, generic medical product(s) seeking Marketing Authorisation are supported by safety and efficacy data in the form of bioequivalence and bioavailability studies.

Clinical trials must meet the acceptable standards of Good Clinical Practice (GCP) to generate reliable data [3]. In Zambia, the Zambia Medicines Regulatory Authority (ZAMRA) established under the Medicines and Allied Substances Act no. 3 of 2013 has the mandate to regulate and

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control the conduct of clinical trials. However, various health institutions play key roles in the conduct of clinical trials in Zambia. As such, several regulations, guidelines, and standards have been published by ZAMRA and various health institutions to guide the conduct of clinical trials in Zambia. This article describes the regulatory requirements and the key institutions in Zambia that govern or oversee research for the conduct of clinical trials. This information is important to institutions and companies that wish to conduct clinical trials in Zambia. Locally generated clinical data offers population-specific safety and efficacy information on a medical product seeking Marketing Authorisation or amendments to approved clinical data such as indications and safety profile.

Governing Institutions

The Zambia Medicines Regulatory Authority is the national medicines regulatory authority in Zambia which ensures that all medical products being made available to Zambian people and animals consistently meet the set standards of quality, safety, efficacy and performance. ZAMRA grants clinical trial certificates for the conduct of clinical trials in the country. Its ambit extends to the inspection of clinical trial sites, inspection of manufacturing, storage and distribution facilities, and testing of health products among various other roles, responsibilities and functions [4]. The other key institution is the National Health Research Authority (NHRA). The NHRA is mandated with the responsibilities of regulating health research in general, health research ethics committees' registration, research institutions, health researchers, biological material for health research and ethical approval for the conduct of clinical trials. Health research institutions are required to constitute health research ethics committees, which should be registered with, and accredited by, NHRA. Ethical approval from NHRA or accredited health research ethics committee is required for the conduct of health research involving human participants or animal subjects in Zambia [5]. Depending on the nature of the investigational products and clinical trial or other facilities involved in the trial, authorisation may be sought from additional institutions such as the National Biosafety Authority for products that are genetically modified [6]. Others include the Office of the Data Protection Commissioner [7] and the Zambia Information and Communications Technology Authority to regulate the processing of personal data [8] and the Zambia Metrology Agency which

provides for consumer protection, health, safety and environmental management through legal metrology measures [9].

Key documents in clinical trials

The Medicines and Allied Substances Act no. 3 of 2013 is the principal Act in Zambia for the conduct of clinical trials. Sections 49 – 50 of the Act provide the framework for the regulation of clinical trials. These include the need to obtain a clinical trial certificate before one conducts any clinical trial, the application process, the procedure for granting the clinical trial certificate and the inspection of clinical trial sites. To support the Principal Act, ZAMRA has published guidelines on regulating the conduct of clinical trials in human participants [10]. The document provides detailed guidance to applicants on the application processes, responsibilities of parties involved in trials, ethical clearance, insurance of trial participants, key documents for the study, requirements for the informed consent, reporting of adverse events from clinical trials, submission of progress reports and inspection of clinical trials. For a generic medical product seeking Marketing Authorisation in Zambia, the Authority has published bioavailability/bioequivalence guidelines which must be complied with to establish the safety and efficacy of a generic (multisource) medical product [11]. These guidelines require that studies (clinical trials or bioequivalence) are conducted in line with the principles of ethics, GCP, GMP and applicable regulatory requirements. Therefore, these guidelines must be consulted by any company that wishes to design and conduct a clinical trial or bioequivalence study.

Regulatory requirements

For a company or research institution to conduct a clinical trial in Zambia, there are a number of requirements that must be complied with as provided in the above-stated key documents and other documents.

a) Clinical Trial Application Documents

Before applying for clinical trial authorisation, the research institution is required to prepare application documents in line with the clinical trial guidelines. These documents

includes information such as the application form, insurance for trial participants, study protocol, informed consent forms, investigational product dossier, investigator’s brochure, ethics clearance or evidence of submission to an ethics committee and proof of payment of application and GCP inspection fee [4, 10].

b) Regulatory Fees

The Medicines and Allied Substances Act (fees) Regulation, 2016 (Statutory Instrument No. 38 of 2016) provides the regulatory fees for the application for authorisation to conduct clinical trials in Zambia. The fees were deliberately set to promote local production of medical products. The application fee for locally manufactured investigational products (IPs) are about 5 times lower than fees for imported products. Similarly, the GCP inspection fee for local clinical trial sites are much lower compared to foreign clinical sites as presented in Table 1.

Table 1. Application fees for Clinical Trials

	Locally manufactured IP		Imported IP	
	Veterinary	Human	Veterinary	Human
With MA	K9,800	K14,000	\$2,000	\$2,000
Without MA	K10,300	K14,500	\$2,100	\$3,000

IP: Investigational Product, MA: Marketing Authorisation

c) Application process

Once the application documents are prepared, the research institution makes an application through the online portal. An applicant needs to create an account, complete the required fields and attach the necessary documents.

d) Evaluation of clinical trial applications

The submitted application is assessed internally by ZAMRA staff and members of the experts committee on clinical trials and pharmacovigilance appointed by the ZAMRA Board. Following the review, ZAMRA may approve the application and issue a clinical trial certificate if the application meets all the requirements or defer the application and request the applicant to submit additional information. ZAMRA can also reject the

application if it does not meet the requirements. In some circumstances such as a clinical trial being conducted in Zambia and multiple countries, ZAMRA may conduct the review of clinical trial application in collaboration with other regulatory and/or ethics committees.

e) Conduct of clinical trials

Once the clinical trial certificate is issued, the investigator must ensure that the clinical trials is conducted in compliance with the approved protocol, GCP and applicable regulatory requirements. The investigator must obtain clearance for any amendments to the approved protocol from the ethics committee and ZAMRA [10].

f) Importation of Investigation Products (IPs)

If the IP has to be imported from another country, the IP can only be imported following the approval of the clinical trial application. The procedure for the importation of IPs follows the same procedure as for the importation/export of all other medical products by obtaining an import permit from ZAMRA [12].

g) Inspections of clinical trial sites

ZAMRA conducts inspections of clinical trials to ensure that the trials are conducted in compliance with the approved protocol, GCP and applicable regulatory requirements. The clinical trial may be inspected at least once depending on the risks involved [4, 10].

h) Reporting from Clinical Trial Sites

The investigator is required to notify ZAMRA of any safety concerns that arise during the conduct of the study. The investigator must submit to ZAMRA all reports of adverse events arising from the study. Reporting of serious adverse events must be expedited while non-serious ones are submitted as a line list together with the biannual progress report. At the end of the clinical trial, the investigator is expected to submit a close out report and later on the final study report to ZAMRA [10].

CONCLUSION

Zambia has an established regulatory framework for the conduct of clinical trials with regulatory requirements aligned with international standards for GCP and GMP. ZAMRA is the main regulatory agency responsible for regulation of clinical trials in the country while ethical clearance is provided by NHRA or a delegated ethics committee. Favorable requirement, in the form of regulatory fees, exist that favors development of medical products locally.

References

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