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Full Length Research Paper

Assessment of pharmacy professionals' knowledge and practice on the management and dispensing of investigational drugs in clinical trials

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In quality approach for the development of clinical research in Africa, the level of knowledge and practices of professionals influences the quality of the trial, the confidence of the sponsors in the performance of sites. We evaluated the management and dispensing of experimental drugs in Burkina Faso. From January to June 2018, we conducted a descriptive cross-sectional study with a sample of pharmacists and state pharmacy assistants. Proportions were used to calculate their knowledge levels on management and compliance with good dispensing practices in clinical trials. A total of 30/41 targeted professionals participated in the study. Only 26% said they had clinical trial training, 54% never participated in the conduct of a clinical trial. Less than half of the staff had knowledge of the pharmaceutical file. Staff knowledge on the correct prescription validation procedure varied between 60-76 and between 56-76.6% on good treatment delivery and advice. The level of knowledge of pharmacy professionals in trial drug management was average. The knowledge and practical experience of professionals is relatively low in the management of the investigational drug. Respect for good clinical practices which should add value to the quality and safety of trials must be improved. The major challenges are the continuous training of staff, the strengthening of the regulatory framework on good clinical practice in order to increase the competitiveness of hospitals in the conduct of clinical trials.

Key word: Pharmacy professional, experimental drug management.

INTRODUCTION

In the conduct of clinical trials, authors have shown that there are invisible barriers that impact on implementation

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Indeed, David and Alan (2021) listed four types of barriers that cite: procedural, structural, infrastructural, and synchronicity. The interactive effects of these barriers contribute to increasing inefficiency of the process (David and Alan, 2021; Colinand Alan, 2021). In addition of these barriers it is important to identify the barriers associated with the pharmacy professional knowledge and practices. The organization of the management and dispensing of pharmaceuticals in clinical trials must be based on a quality assurance system. Pharmacists, as they take on the increasing responsibilities required by these new roles, should actively seek to improve their professional skills (Agence, 1997). In some northern countries like France the regulatory and legislative framework places the holding and dispensing of investigational medicinal products for clinical trials under the responsibility of the hospital pharmacist unlike developing countries where regulation is weak (Philippe and Solange, 2000).

Burkina Faso is a developing country with hospital facilities that can contribute to training and research into new therapies through clinical trials. There is, however, a low level of involvement of hospitals in the conduct of clinical trials.

According to the 2013 report, only 25/495 European & Developing Countries Clinical Trials Partnership/EDCTP clinical research projects in 2013 were conducted in research centers (European and Developing Countris Clinical Trials, 2013).

The same observation is made in most African countries (Julien, 2015). The literature surrounding the development of standardized quality measures to assess site performance in clinical trial consortia is sparse (Marius et al., 2021).

There is in general a lack of data on the knowledge, and practices of health workers in the management and dispensing of medicines and other practical aspects of care in African countries and in Burkina Faso in particular (Susannah et al., 2013; Hervé et al., 2013) .

With the aim of creating a specific unit for the management of clinical trials in our hospitals, like the hospitals in the north, we evaluated the level of knowledge and practice of pharmacy professionals in the management and dispensing of experimental medicines. This evaluation of the organisation and pharmaceutical performance is part of the self-evaluation.

MATERIALS AND METHODS

Study type and duration

This was a cross-sectional study that took place from 15 January 2018 to 30 June 2018 in three university hospital center (CHU) in the city of Ouagadougou (CHU Yalgado Ouédraogo, CHU pédiatrique Charles De Gaulle, CHU de Tingandogo). The validation phase of the questionnaire from January to February, then the data collection phase took place from March to April and the data analysis took place from May to June 2018.

Study sample

The study population was hospital pharmacy staff. A census of all available qualified personnel such as specialist pharmacists, general pharmacists and state pharmacy assistants was carried out beforehand in each university hospital.

Inclusion criteria

These included:

1. Be a pharmacist or pharmacy technician
2. Be staff in the hospital pharmacy of the hospital surveyed
3. Be present in the hospital during the survey period
4. Have at least three months of service in the hospital

Exclusion criteria

These included:

1. Staff who are not pharmacists or pharmacy technicians
2. Pharmacist or pharmacy technician with less than 3 months of service in the hospital
3. Pharmacist or pharmacy technician refusing to participate in the study
4. Professionals on leave or secondment not included.

Questionnaire development, validation

Data were collected using a physical questionnaire and the technique of self-administration of questionnaires was used. The questionnaire was validated after a pre-test. The questionnaire was developed with reference to hospital pharmacist quality manuals and good dispensing practice processes in pharmacology. The items on operating procedures in part A of the questionnaire were intended for pharmacy managers. The items in part B of the questionnaire were intended for staff and managers. Closed questions were used to facilitate the exploitation of our results regarding staff knowledge and attitude on dispensing (appendix).

Study variables

These included:

1. Socio-professional characteristics (qualification and years of professional experience)
2. The number of participations in clinical trials, etc,
3. The list of regulatory documents available in the UHC.
4. The level of knowledge of staff in the practical management of investigational medicinal products (dispensing process and management of the pharmaceutical file)
5. The availability of management procedures, dispensing procedures for trial medicines and quality manuals

A descriptive analysis of the data was conducted. Proportions were used to estimate levels of knowledge about clinical trial management and good practice in dispensing investigational medicines during clinical trials.

Ethical and regulatory considerations

Authorization was obtained from each director of the three university hospitals. Data relating to personnel were collected

Table 1. Socio-professional characteristics of the agents surveyed.

Profile	CHU-YO	CHU-PCDG	CHU-Tingandogo	Total staff	Number of respondent
Specialist pharmacists	5	2	2	9	4
General pharmacists	5	0	3	8	9
State Pharmacy Preparers	9	5	10	24	17
Total	**19**	**7**	**15**	**41**	**30**
Seniority 1-5 years	-	-	-	-	11
Seniority 6-10 years	-	-	-	-	6
Seniority 10 years and more	-	-	-	-	13

Source: Study data

Table 2. Level of experience and field of clinical trials (n=30 respondents).

Pharmacy staff experience	Frequency	Percentage
Trained in clinical trial management	8	26
Staff who participated in a clinical trial	14	46
Phase 2 trial	3	10
Phase 3 trial	11	36
Medical field of clinical trials		-
Infectious diseases	8	57.,2
Cardiology	3	21.4
Nutrition	3	21.4

Source: Study data

anonymously according to a code assigned to each.

RESULTS

Socio-professional characteristics of the staff surveyed

A total of 30/41 staff meeting the inclusion criteria participated in the study. The majority of the staff had been in the profession for more than 10 years (Table 1).

Staff experience in conducting a clinical trial

Approximately 35% (14/41) of staff reported having been involved in the conduct of a clinical trial. About 21.4% (8/41) of staff reported having received training on clinical trials Only 10% of staff had ever been involved in the selection of a site for a clinical trial and 25% in the closure of the trial. Thirty percent of staff reported having participated in trial set-up meetings (Table 2).

Assessment of the level of knowledge of the clinical trial pharmaceutical record

Less than half of the staff surveyed had knowledge of the various mandatory documents that should be available in the hospital pharmacy during the conduct of clinical trials. The individual level of knowledge of each document in the trial pharmaceutical record varied from document to document (25-60%) (Table 3).

Evaluation of the knowledge and practice of dispensing medicines

All hospital pharmacy staff had a good command (56.6 to 76.6¨%) of the different stages of the act of dispensing medicines. The rate of compliance with good dispensing practices varied. Thus, for systematic compliance with each of the dispensing procedures, the proportions were disparate (validation of prescriptions after a pharmaceutical analysis (60-76%); provision of prescribed medicines to patients (56.6-76.6%); advice and pharmacovigilance practices (60-76.6%); management of treatment returns (60-76.6%).

Availability of medication management and dispensing procedures

The various management and dispensing activities were not subject to written standard operating procedures previously available in the hospital pharmacy (Table 4).

Table 3. Assessment of staff's knowledge of the pharmaceutical dossier.

Documents who must be available at the hospital pharmacy	Head count (N=20)	Percentage
Unblinding procedures	5	25
Certificate issued by the insurer	6	30
Undertaking the responsibilities of the principal investigator	6	30
Financial agreement	8	40
The investigator's brochure	9	45
Task delegation form	9	45
Management document and accounting	9	45
Opinions and authorisations from competent authorities	11	55
Pharmaceutical circuit with traceability documents	11	55
Copy of the letter sent to the hospital director	9	45
Information notice and consent	12	60
The protocol	12	60
The clinical trial prescription	12	60

Source: Study data

Table 4. List of clinical trial management procedures.

Name of the procedure	Available on days	Available not updated
Procedure of procedures	0/3	0/3
Procedure for dispensing clinical trial medicines to outpatients	0/3	1/3
Batch acceptance procedure for clinical trials	0/3	0/3
Batch manufacturing procedure for clinical trials	0/3	0/3
Procedure for destruction of clinical trial batches	0/3	0/3
Procedure for recording the ambient temperature of batches for clinical trials	0/3	0/3
Storage procedure between 2 and 8°C	0/3	0/3
Procedure to be followed in the event of a temperature excursion in the storage of clinical trial batches	0/3	0/3
Procedure for recording non-conformities	0/3	0/3
Monitoring follow-up procedure	0/3	0/3
Procedure for conducting the annual review	0/3	0/3
Procedure for using the SOFTWARE	0/3	0/3
Procedure for editing production sheets	0/3	0/3
Training procedure for new interns	0/3	0/3

Source: Study data

DISCUSSION

The pharmaceutical professionals were pharmacists and state pharmacy technicians managing the experimental medicines in the country's university hospitals. The organisation of the hospital pharmacy implies the definition of a profile of the personnel necessary for the proper functioning of the clinical trial. The qualities of the staff should be related to the profile and level of activity. This same profile is observed in hospitals in northern countries (Agence, 1997; Chistel et al., 2019).

However, more than half of the staff have never been involved in conducting clinical trials. This could be explained by the scarcity of clinical trials in our hospitals but also by the regulatory environment compared to developed countries (Les Entreprises du Médicament, 2016, 2018; Vincent et al., 2008). Studies have demonstrated the importance of pharmacist involvement in the success of clinical trials. Indeed, according to Destrumelle et al. (1997), 93% of investigators rated the participation of pharmacists in clinical trial set-up meetings as positive and 65% were satisfied with the pharmaceutical activities during trial closure (1997). According to ICH E6 R1, the pharmacist or other appropriate person designated by the investigator/ institution should maintain records of product delivery to the trial site, inventory at the site, use by each subject, and return to the sponsor or disposal of unused product

(International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, 2016)

Some hospitals use the expertise of the in-house pharmacy in the management of experimental research to ensure the coordination of international multicenter clinical trials, but also the subcontracted manufacture of experimental drugs (Jihyun et al., 2016; Farshid, 2008). In our context, there are ministerial decrees and orders governing the granting of clinical trial authorizations. However, the texts framing the role of hospitals and hospital practitioners in clinical trials, such as the good clinical practice guidelines, remain limited (Ministère de la Santé, 2010a, b, 2013). The level of individual knowledge of each document in the trial's pharmaceutical dossier varied from document to document. Trial documentation should be filed, with an individual file for each trial. The storage of files and their indexing comply with the rules of confidentiality and archiving of clinical trials. All documentation must be known by the users and the various participants (Agence, 1997). Dispensing is an important time for the drug specialist to better inform the patient about their treatment. Compliance with procedures ensures that the right medicine is given to the right patient at the right time. Analysis of the responses on good dispensing practice showed that the risk of error was between 24.4 and 40% during prescription validation and between 23 and 43.4% during the provision of experimental drugs to patients at the time of advice and pharmacovigilance. Dispensing a medicine to a patient involves: Reviewing the prescription, collecting, counting and packaging the medicine, and dispensing it to the patient. The dispenser must explain to the patient precisely and clearly how to take the medicine. This is crucial. Medicines are only effective if they are taken correctly (Flaubert, 2005). Authors assessing the knowledge and practices of hospital practitioners have found the same pattern (Mohamed et al., 2013). In contrast, a study in an Asian school setting showed that pharmacy students had basic knowledge of clinical research (Natsuko et al., 2017). The lack of standard operating procedures for dispensing and managing investigational medicinal products in accordance with the rules of good clinical practice and the lack of experience with clinical studies could explain the respondents' level of knowledge (Ministère de la santé et des solidarités, 2006). Written procedures are a requirement for quality and performance testing according to ICH E6 (R1) (International council for harmonisation of technical requirements for pharmaceuticals for human use, 2016).

Conclusion

At clinical research site all persons involved in the implementation of any aspect of a clinical research study must be appropriately qualified to perform their tasks in accordance with good clinical practice of ICH requirements. The various hospital pharmacies surveyed meet this requirement but the knowledge and practice experience of staff is relatively low. The drafting of procedures and guides, as a support for good practice, is necessary to improve the management and dispensing of experimental medicines. Ongoing training of staff in addition to training appropriate to their field is necessary before receiving protocol-specific training on the activities related to each study. These actions will form a good basis in the process of creating a clinical research unit in our hospitals.

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CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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APPENDIX

Questionnaire

This questionnaire has two parts and is intended for hospital pharmacy managers (part A+ part B) and one part is intended for all hospital pharmacy staff (part B).

I-Collection Sites

		Identification of the site	Please mark here
A1	1	**CHU-YO**	☐
A2	2	**CHUP-CDG**	☐
A3	3	**CHU –BC**	☐

Part A (Pharmacy managers)

II-Description of Legal Farmwork By Pharmacy Manager

Elements on the regulatory framework for the management of clinical trials in hospitals in Burkina Faso		Yes	No
A4	Does your hospital pharmacy participate or has it ever participated in clinical trial activities?	☐	☐
A5	If not, why?		-
A6	Are you aware of the national regulations governing clinical trial activities**?**	☐	☐
A7	If yes, can you name some?		
A8	Is there a decree or internal regulation in the hospital that determines the conditions for authorising "the preparation of medicinal products made necessary by the testing of medicinal products?	☐	☐
A9	Is an agreement between the pharmacy department and the sponsor signed or any other document before a study is started?	☐	☐
A10	If yes, please specify		

III. Quality of Human Resources of Hospital Pharmacy

Characteristic of the pharmacy's staff		Number	1-Permanant ; 2-Contractual
	Profile		
A11	Pharmacist		
A12	State Pharmacy technicia		
Qualification			
A13	Generalist Pharmacist		
A14	Specialist Pharmacist		
A15	Trainee Pharmacist (intern)		
A16	Trainee State Pharmacy technician		

IV. Quality Assurance in the Hospital Pharmacy Department

	List of available procedures that your hospital pharmacy has	Available and updated	Available and not up-to-date	Not available
A17	**A quality manual for the pharmacy**			
A18	Procedure of procedures			
A19	Procedure for dispensing clinical trial medicines to outpatients			
A20	Receipt procedure for clinical trials batches			
A21	Batch manufacturing procedure for clinical trials			
A22	Procedure for destruction of clinical trial batches			
A23	Procedure for raising the ambient temperature of batches for clinical trials			
A24	Storage procedure at 2 to 8°C			
A25	Procedure to be followed in the event of a temperature excursion in the storage of clinical trial batches			
A26	Procedure for recording non-conformities			
A27	Monitoring follow-up procedure			
A28	Procedure for conducting the annual review of clinical trials			
A30	Procedure for the training of interns			

V-Evaluation of Knowledge and Practice

PART B (for all pharmacy staff)

	Identification of the site		Please mark here
B1	1	**CHU-YO**	☐
B2	2	**CHUP-CDG**	☐
B3	3	**CHU –BC**	☐
Respondent Code			

	Respondent characteristics	Yes	No
B4	Generalist Pharmacist	☐	☐
B5	Specialist Pharmacist	☐	☐
B6	Trainee Pharmacist (intern)	☐	☐
B7	Trainee State Pharmacy technician	☐	☐
B8	Years of experience in hospital pharmacy		
B9	Have you followed a specific training in clinical trials (DIU, Specialisation...etc)?	☐	☐
B10	If yes, please specify	……..	

Experience in conducting clinical trials		Response modality	
		Yes	No
B11	Have you ever participated in the conduct of a clinical trial?	☐	☐
B12	Which phase of the clinical trial you participated in (phase 1 or 2 or 3)? please specify		
B13	Medical fields concerned (Specify)	☐	☐
B14	Trainee State Pharmacy technician	☐	☐
B15	Years of experience in hospital pharmacy		
B16	Have you followed a specific training in clinical trials?	☐	☐
B17	If yes, please specify		
B18	Type of sponsor of the clinical trial: institutional "University, research center"	☐	☐
B19	Type of sponsor of the clinical trial: private "name of pharmaceutical company)	☐	☐
B20	Have you ever been involved in the selection of the site?	☐	☐
B21	Have you ever been involved in the set-up phase of the clinical trial at the site?	☐	☐
B22	Have you ever performed or conducted all stages of the clinical trial at the site?	☐	☐
B23	Have you ever been involved closing the trial in the site?	☐	☐
B24	Have you ever been involved at creation or drafting of documents for (accounting, allocation, receipt, dispensing)?	☐	☐
B25	Have you ever been involved in management of stock movements of medicines: (Receipt and placing in stock, orders)?	☐	☐
B26	Have you ever been involved in dispensing to patients (prescription, advice)	☐	☐
B27	Were you trained before the start of the trial?	☐	☐
B28	Have you ever been involved in the monitoring and audit visit?	☐	☐
B29	Have you ever been involved in the re-labelling of medicines?	☐	☐
B30	Have you ever been involved in the development of the hospital's manufacturing sheet?	☐	☐
B31	Have you ever been involved in the pricing of pharmaceutical procedures	☐	☐
B32	Have you ever been involved in the management and accounting of returns (compliance)	☐	☐

VI-Evaluation of Practice for Dispensing Medicines

For each dispensing of an investigational medicinal product, should the pharmacist or staff perform the following operations or acts?		Response modality	
		Yes	**No**
B33	Preliminary verification and identification of the patient?		
B34	Identify the protocol of the clinical trial in which the patient is participating before dispensing (sponsor, study)?		
B35	Provide patient counselling if necessary?		
B36	Invoice the patient for treatment?		
B37	Check for investigator's signature on prescription?		
B38	Record quantities and allocation of treatment numbers given to the patient?		
B39	Counseling the patient: patient recognition of treatment in clinical trials?		
B40	Check the patient's knowledge of the method of administration?		
B41	Check the patient's knowledge of when to take their medication?		
B42	Advise on monitoring and expected adverse effects?		
B43	Provide patients with information on precautions for use, storage?		
B44	Tracking returns of used treatments?		
B45	Track returns of unused treatments?		
B46	Give prohibited or contraindicated drugs?		
B47	Check treatment duration (next visit date)?		

VII-Evaluation of staff knowledge on document

		Response modality	
B48	**What documents do you know that should be available to the investigator (clinical trial pharmacist)?**	YES	NO
B49	The Investigator's Brochure (IB)		
B50	The study protocol		
B51	Opinions and authorizations from the competent authorities		
B52	Copy of the letter sent to the hospital director		
B53	Certificate issued by the insurer		
B54	Information leaflet and consent		
B55	Commitment of responsibilities of the principal investigator (or contract)		
B56	Delegation of task form (list of co-investigators and collaborators) + curriculum vitae of all collaborators		
B57	Financial agreement when the investigator is paid, on the part concerning the site		
B58	Pharmaceutical circuit with traceability documents		
B59	Management and accounting document for experimental drugs		
B60	Unblinding procedures and sample unblinding card if required		
B61	Register of eligible and non-enrolled patients		
B62	The clinical trial order		