

Pharmaceutical Good Manufacturing Practice Regulatory Affairs in Sudan: Continuous Debate between Regulatory Authority and Manufacturers

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Abstract

Background: The implementation of GMP requirements in Sudan as developing country imposes pressure on both the manufacturers and regulatory authorities since resources are limited and additional regulatory and manufacturing facilities are required.

Objective: The study aimed to assess the regulatory affairs of pharmaceutical good manufacturing practice in Sudan.

Method: A structured questionnaire was given to the secretary general of the Sudanese National Medicines and Poisons Board (NMPB). Other different questionnaire was conducted to get information from manufacturers. The study questionnaire was validated and analyzed using SPSS software version 20.

Results: The study findings from authority displayed a satisfactory relation between the manufacturers and regulatory authority. In contrast majority of manufacturers (5 out of 7) were not satisfied. Four of manufacturers were strongly agreed and agreed with the Sudanese drug registration guidelines. Two of manufacturer's complaints on delay of medicines release. It was found that there is a lack of local GMP regulatory documents. There is an absence of regulations regarding the reporting of the side effects of medicines by doctors or pharmacists. Capacity shortage is considered as the main problem faced by the Sudanese authority. Controlling the price of medicines is one of the functions of the NMPB.

Conclusion: To strengthen the relation between the manufacturers and regulatory body there is need to enhance the efficiency of meeting. Local GMP guidelines are necessary to improve the application of current regulations. Lack of training personnel and shortage of facilities in pharmaceutical factories exert difficulty in implementation of require GMP. Adoption of a law to report the side effects improve the safety of medicines. NMPB pricing system helps in minimizing escalating GMP implementation costs, but it affected by economic instability. Government support, enhancement of technical cooperation and information exchange with other authorities in different countries will speed up improvement in the GMP regulatory status in Sudan.

Keywords: Good manufacturing practice; National medicines and poisons board; Registration; Auditing; Pricing

Introduction

According to the World Health Organization (WHO), Good Manufacturing Practice (GMP) is part of quality assurance which ensures that products are consistently produced and controlled according to the quality standards suitable for their intended use and as required by the marketing authorization [1]. According to the current GMP, the modern quality systems include quality, quality by design and product development, quality risk management, change control, quality unit as well as corrective and prevention action (CAPA).

Compliance towards GMP requirements minimizes the contamination risk, mix ups or any sort of error. International regulatory authorities such as WHO established its GMP guidelines initially in 1967. Later in 1972 Pharmaceutical Inspection Cooperation Scheme adopted its guidelines [2], and followed by authorities at country level such as United States Food and Drug Administration (FDA), Malaysian National Pharmaceutical Control Bureau (NPCB) and Chinese State Food and Drug Administration (SFDA). The regulations are adopted to safeguard consumers, provide information for medical practitioners and improve the quality standards of the medicines produced by manufacturers [3].

WHO estimates that 25% of the medicines supplies in the developing countries are substandard [4]. About 10% of the supplied medicines in developed countries and approximately 30% in the

developing countries are counterfeit medicines. The challenge faced by the regulatory authorities is in combating counterfeit, substandard, fake, contaminated or adulterated medicines that threaten public health however, without impeding the registration of lifesaving drugs.

Pharmaceutical field is a dynamic field and involves different stakeholder's interests; therefore, establishing an efficient and professional law is a difficult job [5]. The balance between accessibility and safety of drugs squeezes both the regulators and manufacturers and causes problems to emerge even in developed countries.

Pharmaceutical authorities and manufacturers play a crucial role in the implementation of Good Manufacturing Practice guidelines and requirements to ensure the quality, safety, efficacy, affordability and accessibility of medicines.

The role of the regulatory authorities is to ensure the quality, efficacy and safety of medicines and that they are appropriately manufactured. Other aspects include, advertisement control, accessible information about the rational use of drugs as well as the storage, distribution and dispensing in addition to the enhancement of the affordability and accessibility of medicines as documented in the 13th International Conference of Drug Regulatory Authorities in Berne 2008.

GMP inspection is one of the essential tools to ensure that manufacturers comply with the requirements adopted by the regulatory authorities. According to WHO, there are six areas to be inspected which include quality management, facilities and equipment, production, packaging and labeling, materials management and laboratory control. According to recent study conducted in 2010 the growth rate of the total pharmaceutical market value in Sudan was 52% with a total expenditure of 1.349 million USD, making up 36% of the total health expenditure. This reflects the workload or burden to the regulatory authorities. In order to perform their roles efficiently, regulatory authorities should have adequate capacity besides having qualified and sufficient number of staff [6]. WHO survey findings in 2006/2007 showed that most regulatory authorities in the African countries lack qualified human resources and adequate facilities [7]. Therefore, the aim of this study is to assess the impact of implementation of Good Manufacturing Practice (GMP) on the regulatory status in Sudan.

Sudan has the National Medicines Policy (NMP) which was formulated in 1983 and updated in 2005 [8], covering matters such as selection of essential medicines, medicines pricing, procurement, distribution and regulation, pharmacovigilance, rational use of medicines, human resource development, research, monitoring and evaluation as well as traditional medicines [9]. The Sudanese Governmental Regulatory Body named the National Medicines and Poisons Board (NMPB). It was established to ensure the safety, efficacy and quality of pharmaceutical products, medical devices and cosmetics under the authorization of the Sudanese Medicines and Poisons Law 2009. It was formerly known as the Federal Pharmacy and Poison Board (FPPB) established under the Pharmacy and Poison Act 2001 [10]. The main sections operating under the NMPB as shown in Figure 1 are Registration, Inspection Department and the National Laboratory. The main activities carried out by the Board are the registration of medicines and cosmetics through certain processes and guidelines, pricing of medicines through technical teams and the pricing committee, inspection of pharmaceutical factories as shown in Figure 2 as well as testing and retesting of the pharmaceutical products after they are marketed.

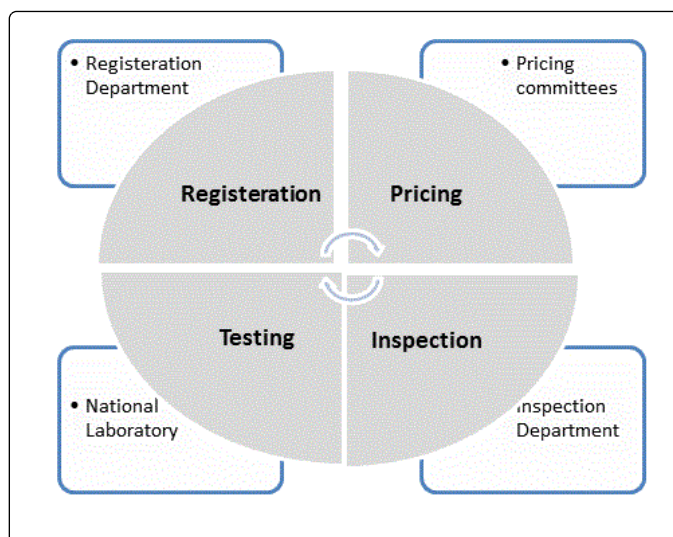


Figure 1: The main activities of National Medicines and poisons board (NMPB) in Sudan.

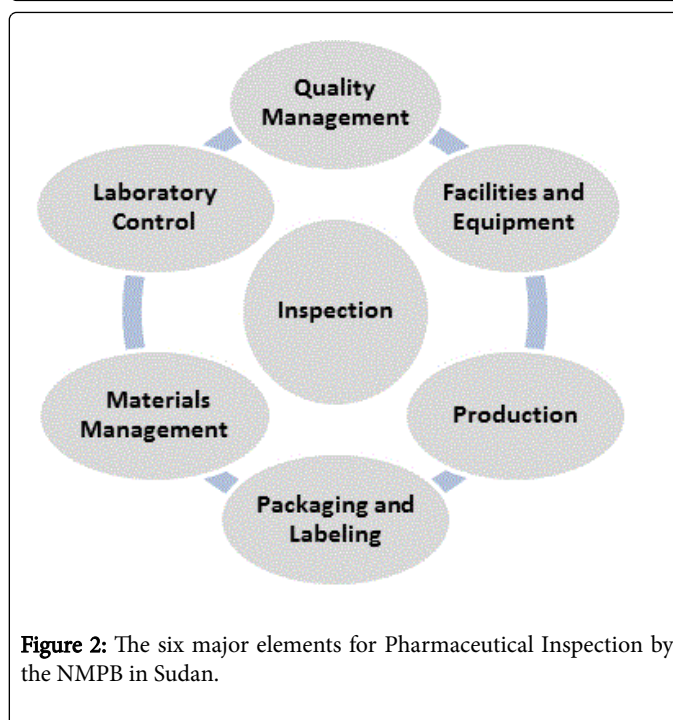


Figure 2: The six major elements for Pharmaceutical Inspection by the NMPB in Sudan.

Methodology

This study has been approved by secretary general of NMPB and Medical Ethics Committee of University of Malaya. A self-administered questionnaire was distributed to seven biggest manufacturers in the country out of 19 currently working manufacturers. The questionnaire include, opinion of manufacturers on GMP regulations, perception of manufacturers on GMP guidelines, relationship between authority and manufacturers, adequacy of manufacturing facilities.

Structured questionnaire was conducted to obtain information from the representative of secretary general of NMPB. The information

given were collected from answers of a structure questionnaire replied by the respective heads of departments. Questions which considered as confidential were excluded such as questions about the auditing reports. The questions were formulated using the Likert scale. Information required by manufacturers was categorized into four sections which included the relationship between authority and manufacturers, opinion of manufacturers on GMP regulations, awareness and perception of manufacturers on GMP guidelines, adequacy of manufacturing facilities. A previous study was conducted using questionnaires as a tool to assess the advantage and disadvantage of certain system or to see the effect of an intervention (impact study) through analyzing manufacturer's perspectives [11]. Content and face validity was conducted by sending the questionnaires to (NPCB) and (NMPB) to get their opinions about the content of the questionnaires.

To distribute questionnaires to Sudanese manufacturers the researcher contacts the Pharmaceutical Manufacturers Association in Sudan. All pharmaceutical manufacturers are members of this Association. The Association representatives suggested seven manufacturers to distribute the questionnaires to because of their market share and number of products distributed in pharmaceutical sectors. The questionnaires were distributed to the seven manufacturers and passed them directly to the Quality Assurance Managers in these factories. All questionnaires were answered with a response rate of 100%.

For answers of questionnaires, a double check system was performed to ensure that the data was credible, transferable,

dependable and confirmable [12]. The key informant's persons revised and approved the answers to the questions. The information gained were organized by categorizing questions into seven main areas, namely the relationship of the regulatory body with manufacturers, GMP local regulations, auditing, registration of pharmaceutical factories and registration of medicines, National Laboratory, pricing, Medicines safety. Certain measures were used to ensure that data is credible, transferable, dependable and confirmable. To enhance the credibility of the study, key informants revised and approved the answers to the questions. The findings and summary of the interview were confirmed by the representative of the secretary general.

All data analysis in this study was analyzed using SPSS version 20.

Results

Manufacturers survey

The relationship of regulatory authority with manufacturers

Table 1 shows that five out of seven of respondents among manufacturers describe relationship of manufacturers with Sudanese regulatory body as weak and two of them have complained to the Sudanese regulatory body and five of them have presented their complain to the authority.

No.	N	Very strong	Strong	Don't know	Weak	Very weak
1	To what extent you describe the degree of relationship with Sudanese regulatory body?	2	0	0	4	1
		Strongly agree	Agree	Don't know	Disagree	Strongly disagree
2	To what extent do you agree that the regulatory body inspection is valuable to performance of manufacturing?	2	4	1	0	0
3	To what extent do you agree that Sudanese GMP certificate is enough evidence of required quality?	2	4	1	0	0
		Yes	No	Don't know	Not applicable	
4	Do you have any complain to the Sudanese regulatory body?	2	4	1	0	
5	Do you present your complain to the regulatory body?	2	5	0	0	
		Delay of medicine release	Unexplained instructions	Inspection results	Others	
6	What is the sort of complain?	2	2	1	2	

Table 1: Relationship between authority and manufacturers.

The Sudanese GMP regulations

The results from the manufacturers as shown in Table 2 Shows that two of them were disagreeing with the GMP regulations, five of them strongly agreed that manufacturers should participate in putting of GMP regulations. Four were strongly desired and desired to share in

putting of GMP regulations. Two were having an opinion that current Sudanese GMP regulations were not effective while five of them announce about difficulty of implementation. The majority of the manufacturers (4 out of seven) convince that about 70% to 80% of the required GMP regulations were implemented.

No.	Scale items	N				
		Strongly agree	Agree	Disagree	Don't know	Strongly disagree
1	To what extent do you agree with the Sudanese GMP regulations?	2	3	2	0	0
2	To what extent do you agree that manufacturers should participate in putting of GMP regulations?	5	1	1	0	0
		Strongly desire	desire	No desire	Don't Know	Not applicable
3	To what extent do you desire to share in putting of GMP regulations?	3	1	1	2	0
		Very effective	Effective	Not effective	Don't know	Not applicable
4	What is the degree of the effectiveness of the current Sudanese GMP regulations?	1	3	2	1	0
		Very easy	Easy	Difficult	Don't know	Not applicable
5	How easy is the implementation of GMP regulations?	0	2	5	0	0
		90%_100%	80%_90%	70%_80%	less than 70%	Don't know
6	How many percentage of implementation of Sudanese GMP regulations in your pharmaceutical factory?	1	1	4	1	0

Table 2: Opinion of manufacturers on GMP regulations.

Majority of the manufacturers as shown in Table 3, strongly agreed and agreed that quality control issues, production issues, storing issues, premises issues, starting materials issues have been adequately

addressed by the Sudanese GMP, while four out of seven were agreed with the Sudanese drug registration guidelines.

No.	Scale items	N				
		Strongly agree	Agree	Don't know	Disagree	Strongly disagree
1	To what extent do you agree that the quality control issues have been adequately addressed by the Sudanese GMP guidelines?	2	4	0	1	0
2	To what extent do you agree that the production issues have been adequately addressed by the Sudanese GMP guidelines?	1	5	1	0	0
3	To what extent do you agree that storing issues have been adequately addressed by the Sudanese GMP guidelines?	3	3	1	0	0
4	To what extent do you agree that the premises issues have been adequately addressed by the Sudanese GMP guidelines?	1	4	2	0	0
5	To what extent do you agree that the starting materials issues have been adequately addressed by the Sudanese GMP guidelines?	2	2	1	2	0
6	To what extent do you agree with the Sudanese drug registration guidelines?	1	3	1	2	0

Table 3: Awareness and Perception of manufacturers on GMP guidelines.

Inspection

As shown in Table 1, six out of seven of the manufacturers strongly agreed and agreed that the regulatory body inspection is valuable for performance of manufacturing. The same number were strongly agreed and agreed that Sudanese GMP certificate is enough evidence of required quality, two of them complained from unexplained instructions and only one complained from results of inspection.

Registration

Table 3 shows that four of manufacturers were strongly agreed and agreed with the Sudanese drug registration guidelines.

The national laboratory

Table 1 show that two of the manufacturers complained from delay of medicines release.

Adequacy of manufacturing facilities

Table 4 shows that five of manufacturers declared that they have adequate number of personnel, based on required profits, production quality and quantity, four of them renew the job description in a define interval. Six of manufacturers give the personnel adequate incentive according to survey results. The same number has an opinion that they have adequate premises for manufacturing processes. Majority of the

No.	Scale items	N				
		Strongly agree	Agree	Don't know	Disagree	Strongly disagree
1	To what extent do you agree that the quality control issues have been adequately addressed by the Sudanese GMP guidelines?	2	4	0	1	0
2	To what extent do you agree that the production issues have been adequately addressed by the Sudanese GMP guidelines?	1	5	1	0	0
3	To what extent do you agree that storing issues have been adequately addressed by the Sudanese GMP guidelines?	3	3	1	0	0
4	To what extent do you agree that the premises issues have been adequately addressed by the Sudanese GMP guidelines?	1	4	2	0	0
5	To what extent do you agree that the starting materials issues have been adequately addressed by the Sudanese GMP guidelines?	2	2	1	2	0
6	To what extent do you agree with the Sudanese drug registration guidelines?	1	3	1	2	0

Table 4: Adequacy of manufacturing facilities.

One of the responsibilities of the Board is to deal with the manufacturers' complaints. There were not more than ten in the last five years mainly focusing on inspection and registration procedures. The NMPB address these complaints through an authorized specialized committee where a time frame is set and all information transpired is documented. There is continuous communication between the regulatory body and manufacturers via email and fax. The head of the inspection team is responsible for the evaluation of the relationship between the regulatory body and manufacturers. His evaluation on the degree of communication effectiveness between them found to be very good.

The Sudanese GMP regulations

The Sudanese GMP regulations basically originated from the World Health Organization Guidelines. Inspectors' and manufacturers' opinions influence the modification of some regulations and priorities of application. The results displayed an acceptance to these regulations among manufacturers. The inspection unit is responsible for the periodical revision of the regulations based on the inspection reports, current global GMP regulations, inspection members' opinions and manufacturers' recommendations. The last revision was done in 2011. The revision report is compared with WHO guidelines and Canadian GMP regulations.

existing equipment as declared by five of manufacturers were working for four to six years. The same percentage did the last calibration for the equipment within three month ago.

Answers of NMPB representatives to questionnaire

The relationship of regulatory authority with manufacturers: Interaction between NMPB and the manufacturers happens through one to three meetings per year, conducted between them and arranged by the NMPB Secretary General to discuss the current situation of GMP implementation, registration and medicines prices.

Although the inspection department assesses the outsourced activity in the pharmaceuticals, there are no definite guidelines for the pharmaceutical outsourcing.

The head of the inspection department is responsible for the evaluation of the manufacturers' perception on GMP regulations depending on audit report results and the degree of GMP compliance. The evaluation should be done every year. Results of the previous one showed a considerable improvement on their perception. The Secretary General is responsible for improving this perception.

Inspection

The head of the inspection department strongly agreed that GMP knowledge is essential for pharmacists. In 2011, a committee from the inspection department evaluated the GMP implementation in Sudan according to the GMP regulations compliance. The main result of the evaluation showed an improvement in the quality of products. Currently an audit form is used by the inspectors. GMP check list based on the WHO guidelines was also included in the form. The audit form has not been changed since 2010. The inspection department has the authority to change the audit form and a committee is in charge of evaluating. The evaluation documents are then kept for future reference. The last evaluation was done in 2012. The inspection department is concerned with the investigation and documentation of the audit report; however the actions taken by the special committee is beyond the control of the department in terms of the deadline for

report submission. The audit reports are confidential, with special codes. The results of the audit were given to the manufacturers to take actions; however, the manufacturers were not happy with the audit report. Audit is carried out regularly based on certain procedures determined by the inspection team which is selected by the NMPB Secretary General.

The head of the inspection department agreed that the local manufacturers highly appreciate the task of the inspection department and give their full cooperation. NMPB has defined the technical requirements for the registration of the pharmaceutical plant. There is a system to ensure that plant hygiene complies with the WHO guidelines and also compared with other global bodies. The NMPB enforces requirements such as the surrounding area and worker hygiene. In 2011, local plant hygiene was evaluated by the registration committee. The result of this evaluation showed an improvement in plant hygiene.

The inspection department is responsible for assessing the qualifications of the personnel working in the manufacturing facility before plant registration. There is regular checking on the key person's qualifications after registration. There are different qualifications for different jobs. The Board offers training courses for personnel in the pharmaceutical factories.

The auditors check the spaces of different sections in the plant to decide whether the processes have adequate premises. There is no standard space limit for every section; this depends on the inspector's view. The plant should fulfill the items mentioned in the check list for the registration.

Registration

NMPB has stated the guidelines for the registration of medicines which was developed by the registration department and approved by a technical committee known as the Registration Committee. It has the authority to revise the guidelines continuously and change them whenever necessary. The main results of the last revision in 2011 resulted in changes in some pharmaceutical product specifications based on the common technical document proposed by the International Conference of Harmonization (ICH). WHO requirements are made as reference for the product specifications.

There is a priority list for medicine registration provided by a special committee from the Board. The last revision for this list was done this year. The main factor influencing medicine selection is the recommendation by doctors and pharmacists. According to the last revision conducted on the fourth of March 2012, there were (293) medicines.

The national laboratory

The National Laboratory is one of the most essential departments in the NMPB. It has all the facilities for doing the tests. There are certain tests for checking the quality of medicine including checking and testing of the starting materials, packaging materials, intermediate materials, final products and recall products.

NMPB medicine pricing

NMPB controls medicine prices and adopts pricing policies depending on prices which can realize availability and affordability. The pricing process is conducted by two main teams: the Costing

Committee which determines the true cost of the product and the pricing team which estimates the retail prices for the general public.

Medicine's safety

NMPB has an advisory committee that is in charge of assessing the adverse effects of medicines. The main measuring points for the safety of medicines include adverse drug reactions and it is assessed and evaluated by an advisory committee. International pharmacopeias and information from marketing authorization holders are the main sources of information regarding safety.

NMPB main regulatory problems

According to the information given by the Secretary General, the main problem is capacity shortage. In addition, I was also told by the head of the inspection department that NMPB could not open branches in the states due to this reason, besides the federalism law of the country. This makes the relation between NMPB and the pharmaceutical sectors in the states solely based on cooperation and technical relation but lacking a supervisory role.

Discussion

The relationship of regulatory authority with manufacturers

The relationship between regulatory bodies and manufacturers is very important for the implementation of GMP in pharmaceutical facilities. Three main indicators were selected to evaluate this relation. The first indicator is the meeting between the two parties; others degree of communication and complaints. The result shows that there is a non-regular meeting which discusses three issues such as GMP, prices and registration; these are in fact the main job scopes of the NMPB. Normally, such free forums are supposed to facilitate direct contact and interaction between manufacturers and the authority, encourage mutual knowledge and speed up transfer of information. The availability of meeting documents help in follow up findings. For the other two indicators the results show a very good degree of communication and the less number of complaints against the NMPB. Hence, it clearly shows that the particular cause of positive perception of the GMP regulations is the strong relation of trust and support between them. But as the majority of the manufacturers were not satisfied with the relationship and describe it as weak relation, NMPB should pay more attention to enhance the efficiency of communication.

The Sudanese GMP regulations

The majority of the manufacturers (5 out of 7) were strongly agreed and agreed with the GMP regulations. This indicates the satisfaction of manufacturers with GMP regulation. Moreover manufacturers had desired to participate in adoption of GMP regulations (4 out of 5). If NMPB give them a chance for that, this would improve GMP compliance especially most of the manufacturers (5 out of 7) strongly agreed with this participation. When (5 out of 7) found difficulty in implementation, this alarm for lack of training personnel or shortage of facilities, ultimately this retarded further GMP application improvement. The majority of manufacturers believe that a high percentage (70% to 80%) of required GMP regulations was implemented. This information was also supported by the audit report.

The result of the GMP regulation perception evaluation in 2012 shows an improvement among manufacturers in terms of positive perception. This is accompanied by progressive enhancement of the GMP compliance as reported in the audit. Continuous revision of the regulations by GMP regulators and manufacturers as showed in the answers has pushed the GMP ball in the right direction. In fact, changes made in some GMP regulations have proven the flexibility of the authority and the gradual application of GMP requirements to give a chance for the manufacturers to implement the possible facilities.

The main factors which influence GMP regulations are the inspection members' ideas, manufacturers' opinions and global GMP regulations, but one question arises: what about the experts in this field? Most likely, the economic situation in the developing countries will not allow a strict application of GMP regulations, and therefore experts can arrange the priorities and strike a balance between authority's enforcement and manufacturers' capability. One of the WHO recommendations for the authority is to facilitate the registration of medicines as one of the tools to compensate for the GMP implementation expenses. This debate between the local authority and manufacturers need a third party that can relieve the pressure of the authority on the manufacturers and at the same time improve GMP compliance; this is exactly what happened in the England where an independent body was established in 1997 [13].

A comparison of GMP regulations between Sudan and Asian countries can help in revising the Sudanese regulations, since they all belong to the group of developing countries. Despite the variation in terms of economic growth, their situation is more similar compared to the Federal Food and drugs administration (FDA) regulations, the rules governing medicinal products in the European Union (EUDRALEX) or Canadian regulations. The way that Sudan handles the WHO regulations support regulators since WHO is a global directing and coordinating authority for health in the world. In addition to that, WHO has an expert committee that is in charge of the pharmaceutical GMP guidelines.

Inspection

Auditors in the NMPB use an audit form that is in accordance with the WHO guidelines. This emphasizes the global view of GMP issues and the adherence of NMPB towards WHO guidelines. Working with the same audit form for more than two years has inhibited the motivation of both the auditors and manufacturers in enhancing the degree of GMP implementation. Therefore, there is a necessity to change the form and this has to be done by an expert committee.

Taking actions based on the audit report may delay the decisions especially since there are no deadlines. The audit reports are confidential except for the relevant manufacturers. By giving manufacturers access to these reports technical information may be disclosed, helping manufacturers to perform a self-inspection system and increase regulatory transparency. The number of audit reports reflects the auditing activity and the number of manufacturers. In 2011, the total number of reports was one hundred. Considering the number of pharmaceutical factories that are currently operating one auditing per one month for each pharmaceutical factory is sufficient. However, complaints are still received from the manufacturers. This implies a need for more communication between auditors and manufacturers. Auditing can provide an opportunity to upgrade the level of GMP application since manufacturers would follow the recommendation made by the regulatory body. A high percentage was taking benefits from the audit performance on improving

manufacturing quality. Therefore, most of the manufacturers were convince with the Sudanese GMP certificate as enough proof of quality. Some of the manufacturers were disagree with the results of the audit as well as complaining from unexplained instructions as displayed in Table 3, this indicate some of the inspectors conclude their job on writing reports without giving technical advice to the manufacturers.

The assessment of personnel documents by the NMPB is not sufficient; there is a need for a field inspection for that purpose to ensure that require qualifications of the personnel are met and applied.

Although the GMP is more of a subjective issue, documentary requirements and guidelines are the fundamental principles for auditing. Therefore, an auditor's views are not sufficient to build the GMP regulatory system.

Medicines registration

NMPB has technical requirements for the registration of pharmaceutical plants. These requirements are in accordance with WHO guidelines such as the requisite of the plant and worker hygiene. The Registration Committee conducted an evaluation in 2011 and asserted the improvement of plant hygiene to a certain required degree.

Matters concerning personnel among the fundamental elements which help to realize the required GMP. The Registration Department of the NMPB has defined certain qualifications for the personnel. Moreover, NMPB also provides training courses for them. Continuous training of the manufacturing workers as well as NMPB personnel will enhance the level of GMP application. These courses should be carefully selected with certain goals.

Equipment's calibration in the production and testing sections is one of the GMP components that are aimed towards accomplishing better efficiency and more consistent performance. Accuracy of the equipment should be frequently and regularly checked by both manufacturers and regulators. The current NMPB inspection on equipment calibration is not adequate to ensure the quality of functioning since it is dependent on documents provided by the manufacturers to an officer. Field inspection by a more competent person before and after registration is more reliable.

It is essential for manufacturers to have enough premises in order to provide enough spaces for different manufacturing processes. NMPB does not have a standard space limit for every section; instead it depends completely on the inspector's view. Hence, guidelines are required to help inspectors and manufacturers to make right decision.

The availability of the registration checklist in the NMPB would help both the authority and manufacturers to make the registration process easier and more efficient. There are two committees that have influence on the guidelines for the registration of medicines. The First one is the guidelines developed by the Registration Committee which later would be revised by a Technical Committee. This will enhance work efficiency, besides overcoming any weaknesses in any of the committees. In addition, although the presence of a committee in charge of the list of the priority medicines registration in NMPB is essential, there should also be an update in information as well as national committee that is in charge of decision making and supervision.

The reason for the dependence on WHO documents as a reference for the products specifications is due to the fact that there is no local document. In fact, the majority of countries have their own documents. Although the committee that selects the priority list for

medicine registration takes the doctors' and pharmacists' recommendations into consideration, there should still be a permanent national committee from the health sectors, and not only from the NMPB. The selection of the committee should rely on the professionalism of the medicine supply and medication therapy. Renewal of the listed items is important to provide update on any alteration in the medication protocols or medicine supply situation. Based on the information given by the NMPB the last revision was done in March 2012. This indicates that the committee is active and operates properly.

The National Laboratory

The National Laboratory safeguards the country from adulterated, substandard or counterfeit medicines. The head of the National Laboratory declared that Sudan has adequate facilities to conduct all the tests for the materials and they also have defined tests for them. This would be a positive sign in shortening the time of the technical processes of medicines in the National Laboratory. The process of medicines release seemed to be slow because some of the manufacturers complain from delay of medicine release as shown in Table 1.

Pricing

Besides its registering and auditing roles, the Sudanese regulatory body plays an important role in pricing. This is where the majority of the medicines policy elements in NMPB are gathered to achieve the same targets.

The pricing process comprises two elements; one is the true cost and the other is the percentage of profits. Two teams were selected to perform these functions. The pricing process depends upon current, real time information. I was informed by the Secretary General of the NMPB that there are continuous meetings held to revise the prices due to the change in economic situation; therefore, updates on the information is essential to make the right decision regarding the prices.

Medicine's safety

The basic measuring point for the safety of medicines is the adverse reaction, and it is the responsibility of the regulatory body to revise the benefit risk ratio for medicines. In the NMPB, an advisory committee first assesses, and evaluates the safety of medicines, and then makes appropriate recommendations. I was informed by the head of the inspection department that sometimes, information on some adverse reactions are received from the doctors, however there is no law encouraging doctors and pharmacists to provide such valuable information.

Although NMPB has the ability to assess the outsourced activities in the pharmaceutical factories, they should nevertheless have guidelines to do so.

The last evaluation of the GMP implementation done by the NMPB in 2011 displayed an improvement in the quality of medicines. This kind of evaluation would help the NMPB to improve the current level of GMP and the means of upgrading the pharmaceutical GMP regulations.

The NMPB uses the service of professionals from outside the NMPB in the technical committees. NMPB has stopped taking additional fees from the pharmaceutical companies. To achieve rapid improvement of

GMP regulatory status, proactive interagency collaboration can assist in providing quick steps in the right direction [14].

Strength and limitation of study

The study couldn't collect testing results data for manufacturers during last year's because it is confidential and not allowed to access in to it. The situation of the GMP regulatory status is quite similar among the developing countries; therefore the results of the study are transferable to other regulatory systems in these countries.

Conclusion

The results asserted the satisfaction of the manufacturers with the current GMP regulations but they were not satisfied with relation with NMPB. Trained auditors are needed to give technical advice to manufacturers. Manufacturers should provide training programs and adequate facilities for the pharmaceutical factories employees to overcome difficulties in implementation. Refer to complaints of manufacturers from delay of medicines release NMPB should provide adequate facilities including personnel and equipment to national laboratory.

Independent experts in the GMP implementation can play a prominent role as an advisory group to the regulatory body and manufacturers as well as preclude any tension that might arise between both parties in applying the regulations and resolve any dispute on the technical priorities. An assessment should also be conducted on the experiences of other countries such as the Arab, African or Asian countries which are closer or more similar to Sudan. The use of audit forms is recommended by the WHO and fortunately it is used in NMPB; nevertheless, it is important to revise and update the form according to changes in the GMP requirements made by the NMPB. It is preferable and advisable for the NMPB to take the requirements and guidelines from the WHO, but it is applicable only when NMPB has developed a documented local guideline and requirements according to the local situation. In the developing countries, this documentation will help both the authority and manufacturers.

The advisory committee for safety of the medicines needs feedback from doctors, pharmacists and even the general public. Therefore, a law is necessary to encourage reporting of the behavior of medicines in the pharmacy shelves or when they have been taken by the patients. There is a need to modify the relation between the NMPB and regulatory authorities of the states since legislation should cover Sudan as a whole, and one of the main roles of the national regulatory authority is to ensure the accessibility of efficacious and safe drugs in the whole country. The use of part time technical evaluators or the collection of fees from the pharmaceutical companies that were practiced previously can affect the consistency of the regulators' decisions and the entire regulatory system. Financial support from the government given to the regulatory authority is compulsory to improve logistical capabilities and provide sufficient qualified staff to perform good regulatory practice. In addition, information exchange between the Sudanese and other authorities could dramatically improve GMP status in Sudan.

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References

1. Patel K, Chotai N (2008) Pharmaceutical GMP: past, present, and future a review. *Die Pharmazie-An IJPS* 63: 251-255.
2. Brunner D (2004) Pharmaceutical Inspection Co-operation Scheme (PIC/S). *J Quality Assurance* 8: 207-211.
3. Basu SB, Gupta AD (2007) Good Manufacturing Practice. In: *The Pharmaceutical Industry*, pp: 1-35.
4. Christian L, Collins L, Maythiwan Kiatgrajai, Agathe Merle, Nayantara Mukherji, et al. (2012) The Problem of Substandard Medicines in Developing Countries, pp: 1-61.
5. Seiter A (2010) A practical approach to pharmaceutical policy. *World Bank Publications*, pp: 1-240.
6. Matsebula T, Goudge J, Lucy G (2005) Regulating the pharmaceutical sector: Coping with low capacity while maintaining regulatory independence. *Health Economics and Financing Programme Working Papers*, London School of Hygiene and Tropical Medicine, London, pp: 1-22.
7. Sandhe KS, Bhambhu VK, et al. (2012) "Drug Regulatory Bodies: Key Role Players in Different Regions." *American Journal of Pharmatech Research*.
8. Elamin E I, M I M Ibrahim, et al. (2010) "Availability of Essential Medicines in Sudan." *Sudanese Journal of Public Health* 5: 33-37.
9. PROFILE C (2010) "Sudan." provider 70: 63-67.
10. Mohamed GK (2007) "The impact of the pharmaceutical regulations on the quality of medicines on the Sudanese market: Importers' perspective." *Sudanese Journal of Public Health* 2: 157-167.
11. Holt D, and Ghobadian A (2009) An empirical study of green supply chain management practices amongst UK manufacturers. *Journal of Manufacturing Technology Management*, 20: 933-956.
12. Cooper DR, Schindler PS and Sun J (2006) *Business research methods 9*: McGraw-hill New York.
13. Norton P (2004) "Regulating the Regulatory State." *Parliamentary Affairs* 57: 785-799.
14. Ravinetto RM, S Cloëz et al. (2009) "Poor-quality medicines in developing countries [reflection and reaction]." *Lancet Infectious Diseases* 9: 267-268.