Brief Communication

DESIGNING A MODEL OF DRUG QUALITY ASSURANCE FOR IRAN

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ABSTRACT

Objective: To take up the project for designing a Drug Quality Assurance Model (GMP) for Iran.

Methodology: It is a descriptive and comparative study. GMP models from USA, EU, Australia and Iran, and WHO, ICH and PIC/S were selected for the comparative study. Internet sites and scientific journals were used for data collection. The comparative study determined the primary proposed model. Then, based on Delphi technique, the primary model was evaluated by experts and eventually the final model was designed, for application in Iran.

Results: The comparative study and feedbacks of experts determined the final proposed model for pharmaceutical quality assurance (GMP) for Iran, which consisted of two parts. The first part included thirteen chapters consisting sixty-two major titles. The second part consisted of sixteen annexes.

Conclusion: Establishment of standards of the final model of GMP in the drug industry could lead to the improvement of quality of national manufactured drugs, hence, promoting the population health levels.

KEY WORDS: Drug, Quality Assurance, GMP.

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INTRODUCTION

Drug Industry is currently the second largest global industrial sector by market value.[1] Often 20–50% of the recurrent government health budget in developing countries is used to procure drugs.[2] In several developing countries, there is a great concern that the prevalence of low quality drugs is high.[3] In addition, the manufacturing of substandard medicines remains a global concern.[4] In the drug industry, quality more accurately reflects adherence to the rules as Good Manufacturing Practice (GMP).[5] GMPs are a set of manufacturing protocols designed to ensure that every batch of a pharmaceutical product meets the very high quality standards required for a drug.[6] The drugs must be manufactured in accordance with GMP, the internationally accepted standard for the production of medicinal products.[7] In an increasing number of countries, manufacturers are required to follow GMP guidelines.[8] Therefore, the authors decided to make a comparative study of drug quality assurance systems of USA, EU, Australia and also WHO, ICH and PIC/S to design a model for Iran.

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METHODOLOGY

This is a descriptive, cross sectional and comparative study carried out in two phases. The first phase was study of selected GMP

Table-I: Comparison of six selected GMP models according to their structures including number of parts, chapters, annexes, major titles and words.

GMP models	*Parts*	*Chapters*	*Annexes*	*Major Titles*	*Words(without annexes)*
USA	2	11	0	60	13914
EU	2	9	19	43	13492
Australia	1	17	0	42	16895
WHO	2	9	17	43	13492
ICH	1	19	0	86	18177
PIC/S	2	9	18	43	13492

models. The criteria such as history of applied GMP model, to be leader and initiative for other countries and degree of institutionalization of drug quality assurance in the health system was adopted for selecting the country. According to mentioned criteria, USA, EU and Australia were selected. Indeed, in order to expand the field of study and use of international experiences, it was decided to study the GMP models of WHO, ICH and PIC/S. After selection and review of models, basic principles of GMP models were determined. These models were compared on two basis. (I) first was about the structures of models including number of parts, chapters, annexes, major titles and words of models (structural base) and (II) second was about the illustrations of requirements (contextual base). Table-I shows the comparison between six selected models based on their structures. Comparative study of contexts of models was carried out in two stages. In the first stage, the chapters of models and in the second stage the annexes were studied. Table-II shows comparison of selected models. At the end of comparative study, a model of GMP for Iran was formed which had 13 chapters and 18 annexes.

In the second phase, by using Delphi technique, opinion was sought from professionals for the suggested model. In the first step, twelve pharmaceutical companies were selected and from each company a manager (from quality assurance unit, production, etc.) was chosen for opinion about the suggestive model. The selected companies were followings: Darupakhsh, Elhavi, Loghman, Caspian Tamin, Faravardehaye Daruee Iran, Kimidaru, Iran Hormon, Zahravi, Pars Minoo, Exir, Sobhan Daru and Sina Daru. In the second step of Delphi technique, pharmaceutical experts and inspectors of ministry were selected for completing the questionnaires. In two steps, hundred percent of questionnaires were completed and returned. After primary analysis with SPSS software, the acceptance criterion of 75% was determined. The chapters and annexes that had acceptance rate below 75% were deleted. All suggested chapters were accepted, but two suggested annexes and three major titles were rejected. Table-III shows the final suggestive model of GMP for Iran.

Historical background of selected Models:

USA: In 1906 the original Food and Drugs Act was passed by Congress.[9] In 1938 the Federal Food, Drug, and Cosmetic Act of 1938[14] and in 1962 the Kefauver-Harris Drug Amendments are passed.[10,11] The principles of GMP of USA (cGMP) are in "21 Code of Federal Regulations Parts 210 and 211".[12]

EU: The first edition of the European GMP was published in 1989. In 2005 re-structuring of GMP guide was carried out. The current guide includes 9 chapters and 18 annexes.[13]

Australia: The Australian Code of Good Manufacturing Practice was first published in 1969. It was revised four times over the following years, before the latest version was published in 2002.[14-16]

WHO: The first WHO draft text on GMP was prepared in 1967. Later, the text was revised four times. The latest version of the GMP was published in 2003 and is more similar to EU model.[17]

ICH: ICH was created in 1990. The main focus of the ICH process is the preparation of

Table-II: Contextual comparison of selected six GMP models based on main concepts.

Main Concepts	*USA*	*EU*	*WHO*	*Australia*	*ICH*	*PIC/S*
1. Quality Management	Subpart A: General Provisions	1. Quality Management 2. Self Inspection	1.Quality assurance 2.Good manufacturing practices for pharmaceutical products (GMP) 8.Self-inspection and quality audits	1.Quality Management 2. Self Inspection	2.Quality Management	1.Quality Management 2. Self Inspection
2. Personnel	Subpart B: Personnel	2.Personnel	9.Personnel 10.Training 11.Personal hygiene	2.Personnel	3.Personnel	2. Personnel
3. Premises and facilities	Subpart C: Buildings and facilities	3.Premises and Equipments	3.Sanitation and hygiene 12.Premises	3.Premises and Equipments	4.Buildings facilities	3.Premises and Equipments
4. Equipment	Subpart J: Records and reports	3.Premises and Equipments	13.Equipment	3.Premises and Equipments	5. Process Equipments	3.Premises and Equipments
5. Documentation and records	Subpart E: Control of components and drug product containers and closures	4. Documentation and records	4.Qualification and validation 15.Documentation	4. Documentation and records	6. Documentation and record	4.Documentation and records
6. Materials Management	Subpart F: Production and process controls	----	14.Materials	----	7. Materials Management	----
7. Production and In process control	Subpart F: Production and process controls	5. Production	16.Good practices in production	5. Production	8. Production and In process control	5. Production
8. Packaging and labeling	Subpart G: Packaging and labeling control	---	---	---	9. Packaging Identification labelingof APIs and Intermediates	----
9. Storage and distribution	Subpart H: Holding and distribution	---	---	---	10. Storage and distribution	---
10. Laboratory Controls	Subpart I: Laboratory Controls	6. Quality Control	17.Good practices in quality control	6. Quality Control	11. Laboratory Controls	6. Quality Control
11. Rejection and Re-use of materials	Subpart K: Returned and salvaged drug products	---	---	---	14. Rejection and Re-use of materials	---
12. Complaints and recalls	---	8.Complaints and Product recalls	5.Complaints 6.Product recalls	8.Complaints and Product recalls	15.Complaints and recalls	8.Complaints and Product recalls
13. Contract manufacture and analysis	---	7. Contract manufacture and analysis	7.Contract production and analysis	7. Contract manufacture and analysis	16. Contract manufacture (Including laboratories)	7. Contract manufacture and analysis

Table-III: Schematic view of final suggested quality assurance (GMP) model for Iran.

GMP	
Chapters	*Annexes*
1. Quality management	1. Manufacture of sterile medicinal products
2. Personnel	2. Manufacture of biological medicinal product for human use
3. Premises and Facilities	3. Manufacture of Radiopharmaceuticals
4.Equipment	4. Manufacture of Veterinary medicinal products other than immunological veterinary medicinal products
5. Documentation	5. Manufacture of & Records immunological veterinary
6. Materials Management	6. Manfacture of Medicinal Gases
7. Production and in process control	7. Manufacture of herbal medicinal products
8. Packaging and labeling	8. Sampling of starting and packaging materials
9. Stroge and distribution	9. Manufacture of liquids, creams and ointments
10. Laboratory control	10.Manufacture of pressurised metered dose aerosol preparations for inhalation
11. Rejection and re-use of materials	11. Computerized system
12. Complaints and recalls	12. Manfacture of investigational medicinal
13. Contract manufacture and analysis	13. Manufacture of Medicinal products derived from human blood or plasma
	14. Qualification and validation
	15. Certification by a qualified person and batch release
	16. Reference and retention samples

harmonized guidelines that can be adopted in the three ICH regions.[18] In 2000, ICH published a relatively complete GMP guide consisting of ICH regions opinions.[18,19]

PIC/S: PIC/S is the abbreviation and logo used to describe both the Pharmaceutical Inspection Convention (PIC) and the Pharmaceutical Inspection Co-operation Scheme (PIC Scheme) operating together in parallel. PIC/S became operational in November 1995.[20] The last version of its GMP is published in 2006.[20]

Iran: The first medical law in Iran was approved in 1955 as "Medical, Drug, Food and Drink Regulations". In 1957 and later in 1987, the regulations were revised and some changes were made. In 1988, "Regulations of Drug Manufacture and Importation" was approved.[21] In 2004, a draft under the title of Good Manufacturing Practice (GMP) of Pharmaceutical Products for Human and Veterinary Use, was published by the Drug Regulatory Authority of Health Ministry.[22] In the preface of draft it is stated that the book has been published as a draft to receive readers suggestions and after completion of draft, the first edition of it will be published. It should be noted that after passing three years of the draft publishing, there is no declared official standard reference (the first edition of GMP) to pharmaceutical companies in Iran.

DISCUSSION

A considerable part of health budget in developing countries is used to procure drugs.[1] Surely, in order to preventing of wasting of such important sources in health system, there should be a great attention to quality of medicines.[2] Only about 20% of countries have well developed and operational medicines regulation.[4] It has shown that the poor quality medicines could result in treatment failure and resistance.[23-25] O'Brien and coworkers[26] in a reported outbreak of 88 paediatric deaths caused by diethylene glycol poisoning and Langerman[6] in a report of 5 deaths from China in 2006 caused by the drug Armillarisin A, stated that the similar disaster will continue to occur until countries establish regulations that ensure the quality and safety of pharmaceutical products.Ovretveit[27] believes that one of the four ways to improve quality is to use methods designed specifically to improve quality. GMP provides clear defined standards for employees.[28] Implementation of GMP in a

pharmaceutical company can enhance the competitive factors of company worldwide so it is a basic requirement [7,29,30] has an important role in organizational success and excellence[31,32] and is one of the basic principles of quality assurance in developed countries.[33,34] Several countries have attempted to establish the GMP in their health systems.[8,19] In drug industry, GMP implementation has been manifested its important role in various productions as OTC[35], cosmetics,[36] dietary supplements and ingredients,[37] exipients,[38] biopharmaceuticals,[39] herbal medicines,[40,41] vaccines,[42] nanomedicines,[43] gene therapy[44] and traditional medicines.[45] Based on the needs to improve and maintain the quality of medicines in Iran, GMP standards need to be implemented. Our suggested model of GMP is an attempt in achieving this objective.

CONCLUSION

Establishment of standards of the final model of GMP in the drug industry of Iran can lead to the improvement of quality of local manufactured drugs and promoting the population health levels by following mechanisms[46]: communicating the culture of quality assurance in drug industry and presenting the practical strategies for improving the quality of medicines; availability of high quality medicines to public and prevention of potential risks caused by consumption of low quality medicines; fostering the movement toward "The Fourth Cultural, Economical and Social Development Plan (2005-2009) of Islamic Republic of Iran", specially articles 87, 88 part A and article 94 of chapter 7 (Health promotion and Life improvement).[47]

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