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QUALITY ASSURANCE AND STAFF TRAINING

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ABSTRACT

"G.M.P. Trends" is an american magazine publishing extracts of inspection reports : It is an official statement of errors, faults, omissions observed in the US pharmaceutical industry as regard good manufacturing pratices. A comparison between the "G.M.P. Trends" and the ("BPF") "Bonnes Pratiques de Fabrication" (Good manufacturing pratices) points out the errors, defects or omissions observed and thus enable to remodel staff training (1) (2).

Staff training is dealt with different chapters of the "BPF" staff, documents, samples, computerisation and risk generating product. Staff training is regarded as a mean for action: objectives, priority aims, choices and exchanges are to be defined.

We intend to developp an example of answer to staff training needed in the pharmaceutical industry. The aim of this answer is the implementation of the good manufacturing pratices in a system which guarantees quality. This training is carried out within the framework of the directives and recommandations of the W.H.O. and U.N.I.D.O. with as a target the manufacturing of tablets of essential drugs.

INTRODUCTION

GMP Trends is an american magazine publishing bimonthly extracts of reports on inspections carried out in the pharmaceutical industry. It is, at the present time, the only official source of statement of errors, faults, omissions observed in the pharmaceutical industry in the states as regard good manufacturing pratices (GMP). It revals that the reported facts are comparable with those observed elsewhere than in the States. (BPF).

Analysis

A. BEUGNY (3) has studied "GMP Trends" publication during seven years (from september 1978 to january 1986) limiting his study to "Manufacturing Control", that is, control of manufacturing, packaging and analytic control of all pharmaceutical forms excluding sterile forms. 930 infringements, defects, errors, omissions have been recorded. In this paper we have choosen to focus on the sole aspects relating to staff training. As a matter of fact, the recommendations laid down in "Bonnes pratiques de fabrication et production pharmaceutiques" (Good pharmaceutical manufacturing and production pratices" and its english translation "Good pharmaceutical manufacturing pratices" published in 1985 by the "Ministry of Social Affairs" of the French Republic (2) (3) relating to staff consider, in this context, aspects of training, hygiene, procedures and staff. A comparison between "GMP Trends" and the "BPF" reveals the periodicity of defects observed and able to remodel the training contemplated or given.

Recommendations Relating to Staff Training

Staff training is dealt with on several occasions in several chapters.

Role of the Responsible Chemist

"As the matter of example it is specified that the Board of Management of every pharmaceutical establishment, and in partic-

ular, the responsible pharmacist as part of his functions have to achieve the implementation of a staff training scheme" (BPF 2A p 14).

Staff Training

"In order to contribute to the control of the quality of medecines, all persons participating in pharmaceutical activities must be given appropriate initial training" (BPF 2 p9 and 2 p 12). These recommendations provide for adequate measures apt to achieve the adaptation of staff, to check the competence corresponding to the occupied position, to establish a staff training scheme and to attend its implementation as regard initial training, as well as retraining.

"The operations of withdrawing samples make special demand on the recruitement, selection, knowledge, motivation and training of this staff" (BPF 17 p 89).

"The persons extrusted with that study and the operators who will have to use this equipment must have received appropriate training" (BPF 18 p 95).

"For staff and risk generating products "Special training must be given" (BPF 19 p 88).

Among the procedures a written directive provides for "training schemes adapted to functions performed" (BPF 3 A p 11).

Results of the Analysis Focusing on Staff Training

During this study having regard to the criteria expressed to analyse A. BEUGNY's study, it has been noticed that 50% of defects, faults, errors, omissions observed in the staff can be ascribed to the training. The absence of sustainment of the training scheme and the training being ill-adapted to the performed function account for 70,6% of the defects observed in training.

The relative proportions are the following:

- Absence of any training scheme 5,9 %
- Incomplete training scheme 5,9 %
- No special training relating of GMP 17,6 %
- Ill-adapted training 35,3 %
- No sustainment of the training scheme 35,3 %

When the relative importance of defaults, errors, faults, omissions is compared to the importance of the recommandations BPF (GMP) relating to it, it is noticeable that the importance of these recommendations as regard the number of pages is proportionnal to the errors or defaults observed.

EXPERIMENTAL STAGE

Training

Regarded as a mean for action, training has to be defined while there are numerous documents, works, seminars relating to staff training, the procedure of implementation to an undertaking remains personnal.

Indeed the general principles of this approach are described in the BPF under different headings : staff, documents raw materials and amoung others risk generating products, equipment and data processing and more particularly under the heading training to quality (BPF 2 p 12).

"It is essential to introduce appropriate measures to ensure that the staff are adapted to tasks in relation to quality and to verify that everyone has received training and attained a level of competence appropriate to the post they occupy. Every establishment must adopt a staff trainig scheme concerning good manufacturing pratices... This scheme must be implemented and sustained".

Establishing a training scheme entails therefore a preliminary definition of formation, bearing in mind, that it is made by people for people.

Aims

This training scheme entails technics, it is designed for a newly appointed staff (initial training) or to already appointed staff (retraining) and depending on the case, aims will be the following :

- acquirement or updating of knowledge
- improvement or updating of a qualification

These aims imply a perfect control of the operations : for instance, being responsible for a workshop manufacturing solid forms such as tablets is a function which requires a perfect knowledge of the operations. The continuous training of this responsible person will aim to develop his ability, improve the quality of the manufactured products, identify the operations in course (instrumentation of machines, validation of procedures) or to foster new activities (coating, microencapsulation, extrusion).

The anticipation of any evolution of the adaptation of qualification to an evolution may be the essential aim : for instance, the purchase of machines to produce tablets equipped gauge in order to enable the validation of the compression during process and improve the control of the weight of tablets will put into motion an electronic equipment and require a control of the involved physical phenomenon. This phase will call forth alteration of habits and might trigger off conflicted reactions.

In so far as training is regarded as a mean it has to be invested in the mean itself, that is, foster exchanges, communication, relations between the involved personns. One might even say that a marketing approach is required to gather people around an aim, to motivate manpower and, in this context, the

"quality circle" can be regarded as an important element for succes. It has to be borne in mind that the development of any person is a factor of success.

The definition of aims and of an approach will entail choices; each undertaking defines its training policy according to its resources but, in our view the person responsible for quality is the one who must play the most important role in the setting up of a training scheme.

Methods

One can have recourse to an internal department or to service external to the indertaking. For instance, in France the Institute of Training of the Pharmaceutical Industry (IFIP) (6) organises group-training and supplies undertaking with video-programms on technological topics such as packaging. The experience shows that an internal training has to face the classical hisdvance of the firm : disturbance of phone-calls and information requests. It is therefore more suitable, unless required by a technological training, to avoid the traditional rooms and be away from solli-citations which disturb reflexion. One must aspire to active participation and continuous evaluation of training = communication is therefore essential,

RESULTS

Within the scope of assistance of developping countries the U.N.I.D.O. organised in collaboration with the French Government and in cooperation with the University of Lille a traininig period in pharmaceutical technologies for 21 participants from 12 african countries.

Our purpose was te develop an example of answers to training needs for pharmacists and technicians in the pharmaceutical industry. A training scheme has to define the goal to reach, the means given, the priorities considered and the planned schedule.

*Goal : The training period aims at actualizing and improving knowledge and the experience of trainees in accordance with the BPF (GMP). The participants were all involved is the production of drugs.

*Means : Tablets is a widespread form of medecine, its manufacturing does not require any equipment difficult to handle and the good manufacturing pratices can therefore perfectly be applied to it.

*Schedule : Three weeks of theoretical and practical training followed by a week of practical work through visits to industrial places.

*Priorities : Conception and manufacturing of drug in the scope of oral solid forms (tablets) with a methodology of formulation and a system quality system.

Motivations

The third conference on pharmaceutical industry organised by the U.N.I.D.O. is invited to implement the conclusions and recommendations of the two last conferences, in particular, in the area of international cooperation where it is important to promote access to information, practical knowledge relating to the pharmaceutical industry and to foster their exchanges between developped and developping countries ... at the level of national decision-makers as well as the level of undertakings (4).

The text of the WHO (World Health Organisation) relating to the good manufacturing pratices adopted in 1975, is general but can be implemented. The scope of application of the programm encompasses aspects of initial estimation, guarantee of quality and inspection measures, the guarantee of quality depends on the drug or on the environment required for its manufacture. The report 722 of the expert committee on the use of basic drugs advises to set up installations for the manufacturing, at the beginning, of simple pharmaceutical forms, before taking the decision to later, manufacture locally, raw materials.

The study carried out by these international organisations concerns the method and means enabling to elaborate and control a policy in the pharmaceutical field.

Purposes

We have a double purpose :

Intensive Retraining of Technicians who have Acquired a Personnal Experience.

Indeed, it has to be borne in mind that it specifications of quality as well as, technologies used, become more complex, it is easily shown that even a small investment makes valid results. The directive of the W.H.O. relating to the selection of pharmaceutical forms specify that "in a number of cases a choice of preparation existe particularly as regard solid forms. Tablets being generally cheaper than capsules".

It becomes then obvious that the implementation of the good manufacturing practices leads to reconsider the problem of production: training must be adopted to the functions and tasks and in paralled the advantages provided by the system have to be stressed (cf methods).

Training centred on tablets manufacturing includes 3 stages :

*Allow participants to position themselves on the environment of medicine, from its conception up to its manufacturing by taking into account economic, statutory technical and scientifical aspects. (9)

*Allow participants to acquire a strategy of analysis and method directly applicable, more precisely a methodology of formulation of tablets. The choice of equipment must be stressed (determining the size of the batch), of auxiliary substances (restricting oneself to the essential ones : binding substance, desintegrant, lubricant) with a minimum of technics without

forgetting the necessary validations. The constant search for a better correspondance between the appraisal of needs (hardness, disagregation, dissolution) and a logical and economical management; doubled with a rational approach : a technology optimising the production appear essential (OPT).

*Give the participants an overall view on the quality system as it is understood, implemented and expressed by the development of norms (ISO) and their national counterparts.

*Give them a new outlook on the role, responsibility and behaviour of people. The quality assurance involves traditional aspects of management but also a creation of a team-spirit and common reflexion expressed by pratical teaching : case-studies, games, debates. (10)

*A booklet = "Information on Pharmaceutical Technologies" containing directives and recommendation for the tableting of substances of essential drugs (survey of the methods granulation, compression and typical equipment) has been published by the programm of action for essential drugs (WHO Geneva) and another booklet is available : "Master Formulae of tablets of essential drugs" which contains the manufacturing formulas of 12 essential drugs in tablets together with manufacturing - sketches, method of manufacturing and validations.

*The training seminar takes place with theorical are practical teaching with case-studies, solution and debates.

Technical Influence of Auxiliary Substances Used in the Processing Drugs

This influence has to be taken into account. Indeed whereas the problem of the industrial processing of vegetal drugs is often a traditional one in developing countries, the choice of the usable auxiliary substances is shown little concern.

In so far as stability and liberation of the active drug are not subjected to any modification a substitution of auxiliary

substances can be effected for local substances easily available (for instance a starch of manioc can replace corn or wheat).

It is obvious that the development of training actions as regard the quality must rationally the linked to national health policies.

CONCLUSION

The global appraisal of quality is a factor of economy and not a commercial gimmick. It is to be made public that quality requires a cooperation of all the studied factors : method of work, study of materials and equipment, motivation of the staff, intervention of specific criteria (hardness of tablets).

The goal is excellence manufacturing, how can it be achieved ? By explaining the wheelwork that makes the system work, by analysing logically the problems set and by determining relations "cause/effect" : the method (OPT) optimising of production technology is perfectly suitable for the pharmaceutical industry.

The way choosen by the authors is quality assurance in the scope of the pharmaceutical industry centred on the tablets manufacturing.

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APPENDICE: GLOSSARY

Medicines

There are many expressions like products, pharmaceuticals, drugs pharmaceutical products, medicinal product, to designate medicines. But the most important is to bear in mind that the active matter (drug product) is not the final medicine. The only definition which fits with quality assurance is the following :

A medicine is the SUM TOTAL, placed at the disposal of the user, i.e. the patient ; this sum total has the following components :

a) dosage form (drug product which has been processed to the point where it is now in a form which may be administered in individual doses) ;

b) the primary package, in direct contact with the dosage form ;

c) the labels;

d) the printed secondary package ;

e) the leaflet of notice (information to the users).

In somes cases - hospital dosage form - some above components are missing : however for quality assurance problems, the definition still remains : the "sum total given to the user".

In any cases, medicines are dangerous products, if used unapropriately. This is the reason why an official licence is needed for their production, distribution and sale and samples officially taken by inspectors of Ministry of Health for random checks.

Quality

International Standard Organizaion (ISO) defines quality as : "The totality of features and characteristics of a product, process or service, that bear on its ability to satisty stated on implied needs".

Quality of a medicine is the sum total of all factors contributing directly or indirectly to its security, its efficiency and its acceptability. However, the more practical and useful definition for quality assurance of medicinal product in the following :

The designation "Quality", applied to a drug product requires that it :

- contain the quantity of each active ingredient claimed on its label, within the applicable limits of its specifications ;

contain the same quantity of active ingredient frome one dosage unit to the next ;

Be free from extraneous susbtances ;

Maintain its potency, therapeutic availability, and appearance until used;

Upon administration release the active ingredient for full biological availability.

Pharmaceutical Industry

Pharmaceutical industry refers to pharmaceutical establishments in which medicines are manufactured, packaged, stored, controlled and released for sale. Generally, they are subject to formal ministerial authorization for opening and are regularly inspected by the Pharmaceutical Inspectors of the Ministry of Health.

System

A system is a regulated pattern of interacting activities and techniques which are united to form an organised whole.

The main characteristics of a system are :

Totality ; componed of elements, but different from the sum of them.

Interaction ; from a positive or negative action from A to B, arises a reaction from B to A, either positive or negative. This retroactive loop can lead to unforeseen effects, called "perverse effects".

Industrial systems involve people ; therefore, are due to nature of human being, perverse effects arise. Perverse effects are unexpected effects, very often the contrary of what was in view.

Complexity ; information, circulating inside is so abundant than time, method and intelligence are needed to unravel the maze.

Organization ; essential to the system, it could be described by organization chart and programme.

Quality Assurance System and Quality Control Activity

In the pharmaceutical industry, objectives of quality assurance (Q.A.) are achieved, when products and processes to obtain them, have been defined to be placed in such a system which leads to the intented level of quality.

The quality Assurance System deals with future, i.e. products which will be produced tomorrow.

Quality Control (Q.C.) is a sub-system, an activity which works in the present and immediate past by releasing products for use. Quality Control is part of the Good Manufacturing Practice (GMP).