SHORT COMMUNICATION

A STUDY ON THE PACKAGING INFORMATION OF ESSENTIAL DRUG PRODUCTS USED AT UNION AND THANA HEALTH COMPLEX LEVEL IN BANGLADESH

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ABSTRACT

The samples of secondary packaging items (cartons, labels and package inserts) of 45 essential drug products used at Union health and family welfare center and Thana health complex level, that included 23 solid (tablet and capsule), 34 liquid (syrup, suspension, and injectables) and 4 semisolid (ointment and cream) preparations either manufactured in Bangladesh or imported by local distributing agencies, were thoroughly examined from April 30, 2005 to March 31, 2006 on the basis of 32 parameters which are usually regarded important for the labeling of any pharmaceutical preparation including essential drug products. Many of the products were available simultaneously as solid, liquid and topical (total 74 different) dosage forms and all dosage forms have been considered in this study. The secondary packaging items of a total of 58 pharmaceutical companies for 45 generics of essential drug products have been collected, sorted/arranged and meticulously studied, and packaging parameters were accumulated for analysis. It has been observed that many of the important packaging information were either completely missing or not properly described. This study was aimed at examining the extent of the packaging information provided in the secondary packaging items.

Keywords: Packaging information, essential drug, carton, insert, label, tablet, syrup.

INTRODUCTION

Public opinion sometimes considers packaging to be superfluous (WHO 2002) but the concept of packaging comes from our very nature that save the substances from contamination by dust, fiber, microorganisms and also from environmental factors such as moisture, temperature, UV ray of the sun etc. Drugs are life saving chemical substances and they can not be dispensed as such. They are also very much prone to contamination by dust, fiber, microorganisms and also to environmental factors. So packaging is needed to preserve the integrity of the product and its selection depends on product's physical and chemical characteristics, its protective needs and its marketing requirements. Packaging therefore can be defined as an economical means of providing, presentation, protection, identification/information, containment, convenience and compliance for a product during storage, carriage, display and use until such time as the product is used or administered. This total time scale must be within the shelf life of the product. A package consists of (i) the container in which the product is placed, (ii) the closure which seals the container, (iii) the carton or outer, which gives secondary protection against mechanical and other environmental hazards, and also serves for the display of written information, (iv) the box in which multiples of the product are packed. Packs are classifies into two classes, (i) the primary pack– consists of those packaging components which form the part of the pack directly containing the product. The main functions of the primary pack are to contain and to restrict any chemical, climatic and biological or occasionally mechanical hazards which may cause or lead to product deterioration, and (ii) The secondary pack- the packaging external to the primary pack is known as the secondary packaging. It mainly provides the additional physical protection and patient information (Corce *et al.*, 1986; Dean1988; Dean, 1988; Bentley, 1992; Giles and Pecina 1985; Khan1990; BP, 1988; Harburn 1990; and Gennaro 1990). Essential medicines are those that satisfy the health care needs of the majority of the population. They should be available at all times in adequate amounts and in the appropriate dosage forms, and at a price that individuals and the community can afford (BDNF, 2001 and WHO, 2005). World Health Organization (WHO, 2002) in its 36th report on 'WHO expert committee on specifications for pharmaceutical preparations' (Annex 9-Guidelines on packaging for pharmaceutical products) proposes some parameters that must be printed on the secondary packaging items. These are, for example, (a) the name of

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the product, (b) a list of the active ingredients showing the amount of each present and a statement of net contents, e.g. number of dosage units, mass or volume, (c) the batch number assigned by the manufacturer, (d) the expiry date in an uncoded form, (e) any special storage conditions or handling precautions that may be necessary, (f) the directions for use, and any warnings and precautions that may be necessary, (g) the name and address of the manufacturer or the company or person responsible for placing the product on the market. These are the generalized parameters and can only be advisory but the precise information that should be printed on the secondary packaging items must be specified by respective national legislation (WHO, 1987).

Currently, a large number of essential drug products of different manufacturers are available in the local market in various brand names. The health care providers (physicians, pharmacists, nurses and community health workers) as well as the end users (patients) largely rely on the information provided by the manufacturers on the labeling of these products. Does the labeling of these products bear all the necessary information and instructions? Are the information and instructions well presented and clearly displayed? In deed, this is a critical question for safe and effective therapy. Bangladesh is a developing country with poorly organized health care system. The drugs are rarely dispensed to the patients by a qualified physicians, pharmacists, nurses and health workers. Therefore, importance of proper labeling is much more needed here and this is especially true for essential products that are used at Union and Thana level where qualified doctors, pharmacists and nurses are not sufficient/available for providing health care services. To the best of our knowledge no work has so far been performed in Bangladesh on instructions/packaging information provided by manufacturers for proper use of essential drugs. In this background, the present work was performed to investigate whether or not the manufacturers provide all the necessary information and instructions in the labeling of essential drug products available in the local market of Bangladesh.

MATERIALS AND METHODS

The labeling samples used in this research work included labels, inner cartoons and package inserts of the essential drug preparations available in the local market (Rajshahi district including metropolitan area). The samples were collected from different retail pharmacies of villages and small towns as well as from different hospitals, clinics and retail medicine shops of Rajshahi city from April 30, 2005 to March 31, 2006. We collected the labeling samples of following 45 brands of essential drug products (BDNF, 2001): (A) List of 12 drugs for use by the village level health workers (Union health and family welfare center level)-(1) aspirin tablet, (2) chloroquine phosphate tablet/syrup, (3) aluminium hydroxide gel tablet/ suspension, (4) piperazine tablet/elixir, (5) glucose electrolyte powder (ORS), (6) phenoxymethyl penicillin (Penicillin V) tablet/syrup, (7) ampicillin capsule/ syrup/injection, (8) ergometrine/Methylergo-metrine maleate tablet/injection, (9) ferrous sulphate tablet/syrup, (10) ephedrine, (11) vitamin A 200000 units capsule/ 100000units injection, (12) chloramphenicol eye-ear/ointment/drops (Total 22 different dosage forms); (B) List of additional 33 drugs for primary health care up to the Thana health complex level-(13) Paracetamol tablet/elixir, (14) pethidine hydrochloride injection, (15) sulphadoxin with pyrimethamine, (16) levamisole tablet/ elixir, (17) chloropheniramine tablet/elixir, injection (18) lidocaine 1%, (19) isoniazid with thiacetazone tablet, (20) streptomycin sulphate injection, (21) metronidazole tablet/elixir/injection, (22) atropine sulphate injection, (23) hyoscine-n-butyl bromide tablet/injection, (24) chlorohexidine-chloroxylenol solution/cream, (25) procaine penicillin injection, (26) tetracycline-oxytetra-cycline capsule/injection/ointment, (27) Phenobarbitone tablet/injection, (28) diazepam tablet/injection, (29) chloropromazine tablet/injection/syrup, (30) I.V. saline of various strengths (0.9%, 0.25%, 0.18%) with 4% dextrose-0.9% saline without dextrose, (31) dextrose in water (5%, 25%, 50%) (32) redistilled water (pyrogen free) ampoules, (33) cholera fluid, (34) oxytocin, (35) furesemide tablet/injection, (36) prednisolone tablet, (37) propranolol tablet/injection, (38) aminophylline injection/tablet (39) co-trimoxazole tablet/suspension, (40) homatropine, (41) DT-SPT-Polio-tetanol, (42) diphtheria anti toxin, (43) vitamin B complex tablet/multivitamin drops, (44) salicylic acid and benzoic acid ointment and (45) benzyl benzoate saponated (A total of 52 different dosage forms). As mentioned earlier, a single product occurred as more than one dosage forms. Therefore a total of 74 different dosage forms have been consulted.

The secondary packaging items of a total of 58 different pharmaceutical industries (that have been coded as PI1, PI2……..PIn etc.) were collected. A total of 193 secondary packaging materials for all products have been accumulated. The samples were collected randomly so as to include all categories of national and multinational pharmaceutical industries. All the collected samples were coded properly and then packaging information of essential drug products were accumulated for analysis. Following 32 points were selected for conducting the present study: 1) Trade name, 2) Generic name, 3) Name of the manufacturer, 4) Address of the manufacturer, 5) Composition, 6) Mechanism of action (Pharmacology), 7) Indication, 8) Contraindication, 9) Side effect, 10) Instruction for use, 11) Storage condition/Pharmaceutical precaution, 12) Warning, 13) Manufacturing date, 14)

Expiry date, 15) Batch No./Lot No., 16) Manufacturing Licence No., 17) Product Licence No. (DAR no.), 18) Price, 19) Overdose, 20) Interaction, 21) Instruction for pediatric/geriatric/adult dose, 22) Use in pregnancy and lactation, 23) Sterility statement, 24) Dosage form (delivery system), 25) Preservative (in case of liquid/injection), 26) Time of rejection after opening, 27) Supply of the label or insert, 28) Dose to be administered, 29) How supplied (packaging quantity), 30) Volume of the product, 31) Legibility of the inserts, 32) Bilinguality. All the samples were thoroughly checked against these parameters, and the findings were recorded and presented in a tabular form.

RESULTS AND DISCUSSION

We worked with 45 essential drug products out of which 23 were solids (tablet and capsules), 33 were liquids (syrup, suspension, and parenterals) and 4 were semisolids (ointments and creams). We arranged the data in a reverse way for easy understanding. At first we presented the data of percent occurrences of packaging parameters of essential drug products in table 1 and then only those parameters that did not occur for 100% or products with incomplete and missing parameters are presented in table 2.

Table 1 show that many of the important packaging parameters did not occur for 100%, that means they are missing. It indicates that packaging information of many essential drug products available in the local market had serious drawbacks about which the practicing (industrial and hospital) pharmacists and regulatory authority should take necessary actions. It was observed that many pharmaceutical companies in the supplied inserts wrote “More details are available on request” but almost all

Table 1: Percent occurrences of packaging parameters of essential drug products.

S. No.	Regulatory & general Parameters	% occurrences
1	Trade name	100
2	Generic name	100
3	Name of the manufacturer	100
4	Full mailing address of the manufacturer	7
5	Manufacturing date	100
6	Expiry date	100
7	Batch No./Lot No	100
8	Manufacturing Licence No.	100
9	Product Licence No. (DAR no.)	100
10	Price	100
11	Sterility statement	100
12	Supply of the label or insert	88
13	How supplied (packaging quantity)	100
14	Volume of the product	100
15	Legibility of the inserts	93
16	Bilinguality	63
17	Dosage form (delivery system)	100
Clinical parameters		
1	Composition	100
2	Mechanism of action (Pharmacology)	83
3	Indication	100
4	Contraindication	86
5	Adverse/Side effect	83
6	Instruction for use	100
7	Storage condition/Pharmaceutical precaution	100
8	Warning	76
9	Overdose	31
10	Drug interaction	43
11	Instruction for pediatric/geriatric dose	?
12	Use in pregnancy and lactation	48
13	Preservative (in case of ophthalmic/injection)	?
14	Time of rejection after opening	?
15	Dose to be administered	100

n indicates number of pharmaceutical companies examined and availability of related information

pharmaceutical companies did not give their full mailing address. How a person (either a physician or a patient), therefore, can request a specific pharmaceutical company? Most of the pharmaceutical companies, for example, wrote "The XYZ pharmaceutical Ltd., Dhaka Bangladesh". In our present study we found that out of 58, only one manufacturer (pharmaceutical company) wrote the full mailing address.

It is observed from the results that labeling of most essential drug products available in the local market had grave pitfalls. Not even a single product covered all the 32 parameters used to study the present work. Some important information, which is considered very important in the labeling of essential drug products, was either missing or improperly described. Only a few manufacturer made in their labeling a statement about preservative used, sterility statement, instruction for pediatric/geriatric use, rejection time after opening while these information are very important for safe and effective use of essential drug preparations (Carter, 1987). Side effect, contraindication and storage condition/ pharmaceutical precaution were also not mentioned in the labeling of a great percentage of products. Full address of the manufacturer was not available in the labeling of any product, while it is indispensable for communication with the manufacturer if necessary. Other information like ML No., DAR No., price, sterility etc. was also missing in the labeling of some products.

The labeling of an essential drug product must provide physicians or other users with all the information needed to assure the safe and proper use of the therapeutic agent. It must contain a full and balanced presentation of the positive as well as the negative aspects of the drug product.

Kenagy and Stein (2001) discussed the medical errors associated with naming, labeling and packaging of pharmaceuticals. They observed that sound-alike and look-alike drug names and packages can lead pharmacists and nurses to unintended interchanges of drugs that can result in patient injury or death. They opined that human factors such as simplicity, standardization, differentiation, lack of duplication and unambiguous communication etc. have often been ignored in drug naming, labeling and packaging. "Trade dress" is the concept that underlies labeling and packaging issues for the drug industry and drug companies are reluctant to change trade dress and brand names. During examining the revised information of drug package inserts Okuyama *et al*. (2005) found that an informational delay or lack occasionally occurred and variations among pharmaceutical companies were observed. Among pharmaceutical companies, many of the clinically important information such as warnings, contraindications, adverse effects and drug interactions varied over a range of 37%. Outi Nieminen *et al.* (2005) studied the differences in product information of biopharmaceuticals in the EU and the USA and found that products of EU contained more detailed instructions to the prescribers, specially safety information such as contraindication and warnings was more conservative

Table 2: The information of labeling parameters (both regulatory and general and clinical) that did not occur for 100% in case of a single product (Vitamin B complex)

ED43	Full address	AE	BL	CI	DI	Pharmacology	Overdose	Pregnancy	Supply of label	legibility	Precaution/ Warning
PIL1	-	+	?	+	+	+	+	+	+	+	+
PIL2	-	-	+	-	-	-	-	-	-	+	-
PIL3	-	-	+	-	-	+	-	-	+	+	-
PIL4	-	+	+	-	-	+	-	-	+	+	-
PIL5	-	+	+	+	+	+	-	-	+	+	+
PIL6	-	+	+	-	+	+	-	-	+	+	-
PIL7	-	+	+	+	+	+	-	-	+	+	+
PIL8	+	-	+	-	-	-	-	-	-	+	-
PIL9	-	-	+		-	-	-	-	-	+	-
PIL10	-	-	+		-	-	-	-	-	+	-
PIL11	-	-	+		-	-	-	-	-	+	-
PIL12	-	+	?	+	+	+	-	+	+	+	+

ED43-essential drug no.43, AE-adverse effects, BL-bilinguality, CI-contraindication, DI-drug interaction.
+ indicates presence of the related information; - indicates absence of the related information
? indicates partial presence of the related information

while USA products gave a detailed description of the efficacy and safety result of the pivotal clinical trials. Saito *et al.* (2005) in their study on pharmacokinetic drug interaction of statins and reflection of such interaction in package inserts found that some important data such as change in AUC (area under the curve), instructions for dosage adjustments are provided only in a few cases and they conclude that all pharmacokinetic drug interactions including relevant quantitative data for potential effectors and details on mechanisms of interaction need to be given in package inserts to ensure safe and proper use of the drugs concerned because inclusion of such information in the package inserts serves as an extremely valuable aid for health care providers. Clayton has drawn attention to the frequent need for special instructions to ensure that patients take medicines in a manner that produces maximum therapeutic effect (Clayton, 1972). But the present study revealed that the secondary packaging item of essential drug products available in Bangladesh lacks much important information. Recently Marzban *et al*. conducted a research work on the Labeling pattern of ophthalmic products available in Bangladesh and inferred that many of the important packaging information are not available from the supplied labels, inserts and inner cartoons of the eye preparations available in the local market (Marzban *et al.*, 1998). Bangladesh has attained almost self-sufficiency in the pharmaceutical sector and in the current decade turned to be a medicine exporting country. There are about 210 pharmaceutical companies in the country engaged in producing quality allopathic medicines. In 1982 the annual market for Pharmaceuticals was Tk. 243 crores but in 2000 it increased to 1800 crores. Now, about 95% of the medicines are manufactured in Bangladesh by national pharmaceutical industries. Moreover, Bangladesh is now a medicine exporting country. The manufacturers are now trying to export their pharmaceutical products in 62 countries of the world and established pharmaceutical plants in Nepal, Pakistan and Vietnam. The multidisciplinary professional education of the pharmacists also ensured the quality of pharmaceutical products. ACI, Beximco, Square and some other leading pharmaceutical industries are certified by ISO 9000 for their unique quality systems meaning that they are now able to do pharmaceutical business in the international arena. Some raw materials for medicine are also manufactured in our country. Along side that; auxiliary or linkage industries (packaging {paper, plastic, bottles, caps, tubes, and ampoules}, printing etc.) are also developed. On the other hand traditional medical care systems such as Unani, Ayurvedi and Homeopathy also play a major role in providing medical care to the peoples (Amran, 2003; Amran, 2003 and Amran, 2003). With such an excellent background, the lack of clinically important information such as adverse effects, contraindications, overdose, warnings/precautions, drug interaction, use in pregnancy and lactations, name of preservative used and time of rejection after opening etc. on the secondary packaging items is very unfortunate and unwanted. The exact and proper information on the secondary packaging materials are also necessary to

Table 3: The information of labeling parameters that did not occur for 100% in case of a single product (Metronidazole, ED21)

ED21	Full address	AE	BL	CI	DI	Pharmacology	Overdose	Pregnancy/Lactation	Supply of label	legibility	Precaution/ Warning
PIL13	-	+	+	+	-	+	-	-	+	+	+
PIL14	-	+	+	+	+	+	-	-	+	+	+
PIL15	-	+	?	+	-	+	-	-	+	+	+
PIL16	-	+	?	+	+	+	-	-	+	+	+
PIL17	-	+	+	+	-	+	-	+	+	+	+
PIL18	-	+	?	+	-	+	-	-	+	+	+
PIL19	-	+	?	+	+	+	-	+	+	+	+
PIL20	+	+	?	+	+	+	-	+	+	+	+
PIL21	-	+	+	+	+	+	-	-	+	+	+
PIL22	-	+	?	+	-	+	-	-	+	+	+
PIL23	-	+	+	-	-	-	-	-	+	+	+
PIL24	-	+	+	-	-	+	-	-	+	+	+
PIl25	-	-	+	-	-	-	-	-	-	+	-
PIL26	-	+	+	+	+	+	-	+	+	+	-

ED21-essential drug no.21, AE-adverse effects, BL-bilinguality, CI-contraindication, DI-drug interaction
+ indicates presence of the related information; - indicates absence of the related information
? indicates partial presence of the related information

combat counterfeiting of medicinal products because counterfeiting may, sometimes, occur by mislabeling, mispackaging or change of the original package and deletion of expiry dates from the bottles or vials of pharmaceutical products (Amran, 2005). So, the manufacturers of pharmaceutical products should be more careful in designing the secondary packaging items of essential drug products. The directorate of drugs administration of Bangladesh also should formulate strict rules regarding labeling of pharmaceutical products including essential drug products and also monitor strictly whether the manufacturers abide by the laws. Health professionals like nurses, pharmacists and doctors can play a pivotal role in counseling the patients on proper use of the essential drug products and also by giving necessary suggestions to the manufacturers and the concerned drug authorities in developing proper labeling system for essential drug products.

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