EFFECT OF THE MATERIAL OF PRIMARY PACKAGING CONTAINERS ON PROVIDING VISUAL INSPECTION OF PHARMACEUTICAL PRODUCTS

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ABSTRACT

Introduction: Nowadays, all over the world the requirements for drug quality have become more and more strict and its evaluation is one of the most important tasks. Usually, input quality control of medicines and other groups of goods is carried out organoleptically (mainly visually) by authorized people from pharmaceutical establishments. Primary packaging is one of the most critical components in this process, because it strongly influences the possibility of visual control of goods and, of course, it should be transparent.

The aim of this article was to analyze primary packaging of some drugs and the possibility of their identification and quality evaluation.

Materials and Methods: Objects of this study were primary packages of 65 randomly chosen drugs produced by some leading manufacturers in different dosage forms. Inspection analysis of the quality of the researched medicinal products was provided in 8 steps: checking of the accompanying documents, checking the quantity of the goods, organoleptic control of packaging, checking of labeling, checking of barcodes, checking of completeness, visual control of a product, accompanying documentation for the intake of the goods.

Results and Conclusion: All investigated drugs passed the first 6 stages of inspection analysis positively. 46 samples out of 65 (or 71%) could not be visually controlled (stage 7) and their appearance was impossible to check because of the non-transparency of the containers. When separated into different forms, the distribution is the following: 53% of studied tablet drugs, 88% of eye drops and 100% of suppositories cannot be evaluated visually.

Keywords: *visual inspection, drugs, packaging materials, primary packaging, quality*

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INTRODUCTION

The range of pharmaceutical products on the Ukrainian market is formed by both domestic and imported drugs. Nowadays, consumer requirements for drug quality are significantly increasing. Due to economical imbalance substantial reduction in the production volume has occured. Meanwhile, the market is full of low-quality, substandard and counterfeit goods. According to the data of the Organi-

zation for Economic Co-operation and Development (OECD) the international trade of counterfeit goods reaches $200 billion per year (1). A significant decline in the living standards has affected their entry into the domestic market. Most buyers cannot afford expensive brand drugs, which is why counterfeit drugs is directed to them. As a consequence, in developing countries they can take up to 35% of the pharmaceutical market (2).

Use of such products is associated with a significant risk for the life and health of the consumers. Counterfeit drugs are the major cause of morbidity, mortality, and loss of confidence in the healthcare system (3). According to data (4), most of the counterfeit reports are related to antibiotics, antiprotozoals, hormones, and steroids. Therefore, the challenge of supplying the domestic market with high-quality drugs is very urgent now.

Manufacturers have to develop more and more advanced methods to prevent counterfeiting of their own goods. These means can be divided into two main groups: visible and hidden ones. The first group involves advanced barcodes, holograms, three-dimensional images, special inks, watermarks (5–8). The second group includes radio-frequency identification (RFID) tags, UV-sensitive hidden paints, biometric fingerprints, etc. (8–12). It's important for all of these means to be able to control the goods and their authenticity during the entire supply chain and finally in pharmacies.

The quality level of the products is a relative characteristic based on a comparison of actual indicators of the product quality with standard ones.

Nowadays, all over the world consumer requirements for drug quality have become much stricter and its determination and methods of its expression are some of the most important tasks of our time (13).

The quantitative characteristics of the products are characterized by quality parameters. It's possible to define either single or comprehensive indexes. Comprehensive evaluation characterizes the overall quality level of the tested product and allows the drawing of conclusions about the conformity of its properties to the consumer needs and the requirements of normative documents (14,15).

Legal regulation of the drug control procedures in Ukraine is provided by President Decrees and legal acts of the Ministries, which adopt National strategies, concepts and programs (16–22). Currently, there are four supplements to the State Pharmacopoeia of Ukraine (in 2004, 2008, 2009, 2011), among which the 1st supplement which establishes the requirements for drugs containers (23).

At present, quality control of medicinal products is carried out under order № 677 of the Ministry of Public Health of Ukraine dated 29.09.2014 "On approval of the rules for quality control of medicinal products in wholesale and retail trade" (22).

Input quality control of medicines in retail and wholesale trade is carried out organoleptically (mainly visually) by authorized people from pharmaceutical establishments having a license for providing business activities in the wholesale and retail trade of medicines. The visual method is based on the use of information obtained by the senses – sight, hearing, smell and touch.

The organoleptic method has certain advantages. First, it does not require special instruments, devices, and complex equipment. Second, it provides fast indicating and is always used first, even sometimes eliminating the need for measuring methods especially when taste, flavors, smells, colors, consistence of perfumes and cosmetics are tested. Its main disadvantage is subjectivity. In order to reduce it one uses quantitative methods to evaluate some quality parameters (24).

At the reception of goods an authorized person checks:

- compliance of the drugs to shipping documents regarding quantity, dosage, batch numbers, expire dates, registration status, name, dosage form, manufacturer. Each batch of a drug must be accompanied with copies of the batch quality certificate which is given by the manufacturer (for imported medicines - by the foreign manufacturer together with a stamped conclusion about the quality of the imported drug given in Ukraine);
- labeling of the secondary and primary packaging, presence of a leaflet for the drug specifying instructions for its use, appearance and integrity of the secondary packaging, uniformity, ab-

sence of damages, quality of the packaging materials. If necessary, drugs are tested after opening the package, for their size, shape, color, homogeneity, quantity of units in the package, presence or absence of impurities.

If the result from the input control is positive, an authorized person gives permission for the distribution of the drug batches obtained.

In case of any doubt about the quality of the medicines during the performance of a visual inspection, an authorized person takes samples from the suspicious drugs and sends them to the Territorial Inspectorate for Drug Quality and Safety Control to provide full laboratory examination. Until obtaining the conclusion about the quality of the suspicious batches they are kept within a quarantined area (premise), separately from other products.

Based on the above-mentioned, it can be concluded that the inspection analysis lies in the evaluation of shipping documents, labeling, and appearance of secondary and sometimes primary packaging, but the organoleptic analysis of certain drugs is made only when required. This suggests that quality evaluation of drug forms may be skipped.

Therefore, most publications about the falsification of medicines are focused on assessing the quality of the secondary packaging materials and labeling (25–27).

In practice, only a few studies were conducted and several papers about the effects of the primary packaging materials on the organoleptic properties of drugs during input control were published (28,29).

Thus, there is a need for a comprehensive inspection analysis to determine the quality of medicines produced in Ukraine and abroad.

Sale of medicines and medical devices is not possible without their pre-packaging.

Primary packaging is one of the most important components and functions of the drug production process. It protects them from the environment and ensures the preservation of the properties during the entire "life cycle" of a drug - from manufacturing to consumption by a patient.

The packaging consists of a container, a product placed therein, a closure and labeling.

The main requirements to primary packaging are conventionally divided into:

1. Design.

Primary packaging should be designed to:

- protect a drug from adverse environmental conditions;
- protect against mechanical impacts;
- be tight and stable;
- protect against microbial contamination;
- provide metered or separated withdrawing of a drug;
- have first opening control;
- have good appearance and convenience in use;
- be safe.

2. Requirements of the materials.

Packaging materials used for the packing of medicinal products must be authorized for use by the Ministry of Public Health of Ukraine, and also comply with specified requirements, not affect the stability and pharmacological properties of drugs, not contain carcinogenic and toxic components, heavy metals, arsenic and other harmful impurities in quantities exceeding the standard norms, as well as dyes that are not permitted to use; should be free of any foreign smell and microbial contamination above the established norms. The packaging of sterile medical products should be composed of materials resistant to pre-sterilization, withstand sterilization methods specified by the manufacturing process and must not contain mechanical impurities.

3. The specific requirements for packaging are determined mainly by the chemical composition of a drug and its production process.

Containers for packaging of medicines containing hygroscopic, volatile and oxidizing agents should provide moisture, vapor and gas barrier within the relevant indicators of normative documents; for drugs of fatty base - should have low fat (oil) penetrability; for light sensitive drugs - should be opaque. For injection solutions, eye drops, on the contrary, packaging should be transparent to make inclusion control possible.

4. General requirements for packaging (30):

- clarity of the texts printed on a packaging;
- availability of instructions for use;
- attractive color design;
- availability of the first opening control;
- safety of use;

- absence of sharp corners and edges.

The additional requirements to primary packaging for pharmaceuticals are regulated by normative documentation including:

- composition of the packaging material indicating, in particular, qualitative composition of the different parts of a package, as well as non-plastic parts;
- description of a closing element (composition and test methods) including, if necessary, description of a waterproof and airtight seal;
- method of package opening and, if necessary, devices ensuring safety;
- container information (multidose or monodose) and measuring devices;
- description of the closing element which prevents opening of a container by children.

Considering all of the above-mentioned information, the aim of this article was to study influence of primary packaging materials on the identification of medicines and the evaluation of their quality.

OBJECTS AND METHODS OF RESEARCH

Objects of this study were the primary packages of randomly chosen drugs produced by some of the leading manufacturers in different forms. The subject of the study was the possibility of identification of this drugs and the evaluation of their quality indicators.

Inspection analysis of the quality level of the researched medicinal products was provided in the following steps (Fig. 1).

Stage 1. Checking of the accompanying documents for incoming goods.

The documentary analysis has the aim to evaluate the commodity characteristics of the goods based on the information in the accompanying shipping documents. Checking the completeness of the accompanying documents (invoices, waybills, tax waybills, batch (lot) quality certificates, list of medicinal products and other documents confirming the amount and the quality of incoming goods) as well as the correctness of their drawing up. The authenticity and correctness of the filled out documents are evaluated by the presence of the required data, signatures, stamps of the supplying company, its name and address. In addition, cross-verification of the main characteristics of the goods specified in various documents (invoices, batch and conformity certificates) and labeling is provided.

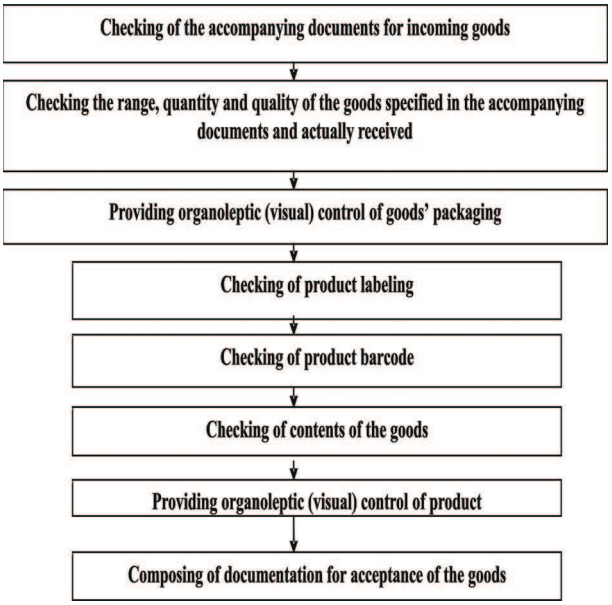

Fig. 1. Stages of quality level evaluation of the researched medicinal products.

Stage 2. Checking the range, quantity and quality of the goods specified in the accompanying documents and the ones actually received.

The assortment analysis of goods has the aim to verify their conformity to name, article, trademark specified in the labeling and the accompanying documents.

Checking the goods by their quantity is carried out by comparing those specified in the orders, accompanying shipping documents of the supplier and the ones actually received.

The quantity of products is counted in the units specified in the supply contracts.

Quality control is provided by comparing the quality of the incoming goods, their completeness, packaging and labeling with the requirements of the standards, as well as the contract terms and the data of supplier's accompanying shipping documents confirming quality of these products (e.g., drug batch certificates).

Stage 3. Providing organoleptic (visual) control of the product packaging.

Packaging protects a product from the external environment. Its integrity and state influence the quantity, quality and safety of the goods.

Packaging control includes a number of measures to check integrity, quality of primary and secondary packaging, and their compliance with the physical and chemical properties of the drugs.

Checking the integrity and quality of secondary packaging begins from a detection of unusual sounds such as broken glass and others. Then attention is paid to size, shape (top, sides and bottom, possible deformations and damages as a result of mechanical stress), conformity to storage conditions (elevated temperature, humidity, etc.), quality of the material from which the packaging is made and its print design (distinct markings, color characteristics, possible change of colors). The presence or absence of defects is checked: local discoloration, dirt, dents, cracks, damage, leakage of contents, signs of forgery or unauthorized opening, presence or absence of protective signs or seals, sometimes visible only under special lighting (e.g., UV), etc.

Primary packaging is checked for integrity of the container, presence of seals, first opening control, labeling.

Stage 4. Checking of product labeling.

Labeling is intended to identify products as well as to provide information about the manufacturer, qualitative and quantitative characteristics of a product. Special requirements are applied to labeling: distinct and well-defined text and images, visibility, compliance with the consumer properties of the goods, authenticity (the information given on a label must correspond to the quantity and quality of the goods), manufacturer's name, country of origin and others.

During the checking process the information on the labeling is analyzed and it must be identical to that specified in the accompanying shipping documents.

When checking the labeling of medicinal products, attention should be paid to matching the drug batch number on the primary, secondary packaging and the one in the accompanying shipping documents. It's necessary to ensure that the manufacturing of this drug batch has not been discontinued.

The labeling on the secondary packaging of a finished medicinal product includes: country of the manufacturer, manufacturer's name, their trademark and address, name of the finished medicinal product in Ukrainian and/or Russian and/or English and/or Latin, form of the medicine, quantity of the finished product, concentration (activity or dose), qualitative and quantitative composition of the ingredients, way of administration, batch number, expiration date, registration number, storage conditions, barcode.

Labeling on ampoules, syringe tubes and pipettes includes the name of the finished product, concentration or activity, quantity of the drug, batch number, expiration date. The following should be indicated on a tube: the name of the drug, dose (or concentration or activity of the drug), batch number, expiration date, the proprietor of the registration certificate.

Labeling of drugs with Braille font: according to the Order of the Ministry of Public Health of Ukraine № 722 dated 25.08.2010 "About approval of the labeling of medicinal products with Braille font", which was enforced on 26.11.2010, requirements for drug labeling were introduced considering the Directive of the European Parliament and Council of Europe N 2004/27/EC from 31.03.2004.

Braille marking is applied to the secondary packaging of medicinal products and should be presented in Ukrainian and by the applicant's request in Russian or another language.

Braille marking includes:

- name of the drug (for drugs in one form and dose as well as for herbal preparations this is enough);
- dose of the active substance (if a drug is produced in multiple doses);
- form (if a drug is produced in multiple forms).

Stage 5. Checking the product barcode.

When analyzing barcodes of goods it's necessary to check:

1. Number of barcodes. Often, only one barcode type is applied to the packaging such as European Article Numbering (EAN) or Universal Product Code (UPC). Use of two barcode types is acceptable if a manufacturer is registered in two associations. In this case, they

should be printed on opposite sides of the package.

2. Location of the barcode. The location of a barcode on a package (or a product) must conform to the requirements of the national standards.

Generally, it's recommended to place the barcode mark on the back side of a package (product) in the lower right corner. It's allowed to place it in the lower right quadrant of any other side of a packaging. General Specifications GS1 show strict requirements: the minimum distance of a barcode (including a stabilization zone) from any edge of a package (product) must be not less than 8 mm and not more than 102 mm.

The standard orientation of a barcode is horizontal: the digits printed below the barcode should be oriented in the same direction as the text or graphic design of the packaging.

When a barcode is located on a curved surface, the angle between the tangents to the curved surfaces, one of which passes through the midpoint of a barcode and another one – through the outer edge of barcode limiting zone, should not exceed 30°.

A barcode should not be placed onto other labeling elements (text, images, perforations).

3. Check of the digits and their correctness is determined by scanner or by calculation. A failure may indicate a technical error when typing a barcode or a falsification of a product.
4. Dimensions of the barcode. Codes recommended for application onto the packaging of medicines are divided by their size in small, normal and large ones. The most commonly used standard size is 10 mm in height, 27 mm or 36 mm in length.
5. Color of barcode marks. A barcode should be black, blue, green or dark brown. Shades of red and yellow colors for bars are not allowed as they cannot be read by a scanner. Background color should be white but it can also be yellow or beige.
6. Print quality of the barcode. Bars should be uniform in color and contrast, without blurs or lighter spots inside.
7. Compliance with the code list registered in the EAN association. The first two or three digits of a barcode should correspond to an EAN number assigned to the country. The origin and identification of a product manufactured in a certain country should be checked. Non-compliance of these digits is a sign of product falsification.

Stage 6. Checking of the contents of the goods.

Checking for completeness means to verify the compliance of a set of the products to the list of individual components specified in the operating manuals or related documents.

The term completeness includes the combination of elements forming a single product unit with certain consumer properties of the goods, and these elements are used as a whole but not separately.

When checking the completeness of the finished medical product, presence or absence of instructions (leaflets), dispensers and other devices for the use of this drug are verified.

Stage 7. Providing organoleptic (visual) control of a product.

General organoleptic characteristics are as follows: appearance, taste, smell, consistency. Appearance is the comprehensive parameter including shape, color, state of a surface. Appearance is not only easy to check but also one of the most important criteria for a comprehensive evaluation of product quality. It is the first stage of product identification by manufacturers, sellers and buyers. Organoleptic control of medicine forms is carried out using the parameter in monographs "Appearance" or "Description" (9,31,32).

Requirements for tablets.

The evaluation of tablet quality begins with a check of their appearance (organoleptic properties) which is affected by the following factors during production: compressing conditions, adhesion and cohesion properties of the mass to be compressed, its moisture content, particle size distribution, surface and precision of the press tools, method of coating, etc.

The following defects should be absent on tablets: protrusions (projections on the surface or adhering powder particles); hollows (craters, crumbled parts of tablets); dirt or dust; marbling (non-uni-

form color, local color changes); chips (different layers in the tablets, reduced thickness); agglutination (sticking of tablets together or their binding to damaged surfaces); crumbling; deformations (non-round shape); scratches; coating defects (non-uniform coating surface, varying thickness, shift of the core from center).

Tablets should have a round or other shape with flat or biconvex surfaces, unbroken edges; the surface should be smooth and uniform in color unless otherwise indicated in the reference documentation (32).

Requirements for suppositories.

Depending on the structure and characteristics of the body cavities suppositories may have various geometric shapes and sizes. They are divided into rectal, vaginal suppositories and sticks. Rectal suppositories are administered into the rectum, vaginal ones – into the vagina, and sticks – into urinary and other canals (cervix, ear canal, fistulas and wounds). All suppositories, especially rectal and urethral ones, should have sufficient hardness allowing them to overcome the resistance of tissues and sphincters; otherwise they would become deformed and their use becomes impossible.

Suppositories should have a proper uniform shape, smooth consistency and sufficient hardness, which provides ease of use, their color and smell should correspond to the properties of the ingredients. Uniform consistency is checked visually for absence of foreign materials or coarse surfaces. Presence of air bubbles or funnel-shaped hollows are acceptable.

Requirements for eye drops and injection solutions.

Eye drops and injection solutions should not contain mechanical impurities visible with a naked eye. They should be transparent, sterile, isotonic and stable, suspension drops may form a precipitate which should be re-suspended easily by agitation forming a stable suspension. To control visible particles, 60 ampoules from a batch are randomly chosen. Presence of visible mechanical impurities is allowed in no more than one item (31).

Stage 8. Preparing the documentation for the reception of the goods.

Based on the results from the inspection analysis, commission members prepare corresponding documents about the reception of the goods by quantity, quality and completeness. These acts are compiled separately by each supplier and for each batch of goods received according the accompanying shipping documents.

To provide a study of quality indicators of some medicines to conform them to the requirements of the inspection analysis, we took randomly 65 samples of drugs produced by different manufacturers in various forms. These drugs are presented in the Table 1. Their compliance with the established organoleptic characteristics was determined by the procedures specified in current reference documents, pharmacopoeian monographs and others.

Table 1. Test samples of medicines

Sample number	Form	Primary packaging	Name of the product and the manufacturer
		Sandoz, Lek, Poland, Austria, Romania, Slovenia	
1	tablets	non-transparent blister pack	Rami Sandoz 5 mg, 10 mg, 25 mg (Lek S.A., Poland)
2	tablets	non-transparent blister pack	Azithro Sandoz®, 250 mg, 500 mg, (Sandoz, Romania)
3	tablets	non-transparent blister pack	Cefuroxim Sandoz®, 250 mg, 500 mg, (Sandoz, GmBH)
4	tablets	transparent blister pack	Nakom 25 mg / 250 mg (Lek Pharmaceutical Company, Slovenia)
5	tablets	transparent blister pack	Dicinon 250 mg (Lek Pharmaceutical Company, Slovenia)

6	tablets	transparent blister pack	Ospamox DT®, 1000 mg, (Sandoz GmBH, Austria)
7	tablets	transparent blister pack	Ospamox®, 500 mg, 1000 mg (Sandoz GmBH, Austria)
8	tablets	transparent blister pack	Persen (Lek Pharmaceutical Company, Slovenia)
		Alcon-Couvreur, Belgium	
9	eye drops	white polymeric non-transparent vial	Tobrex 0.3 %, 5 ml
10	eye drops	white polymeric non-transparent vial	Quinax 0.015 %, 15 ml
11	eye drops	white polymeric non-transparent vial	Betoptic S 0.25 %, 5 ml
12	eye drops	white polymeric non-transparent vial	Azopt 1 %, 5 ml
13	eye drops	polymeric non-trans-parent dropper-vial	Maxitrol 5 ml
14	eye drops	polymeric transparent dropper-vial	Maxidex 0.1%, 5 ml
15	eye drops	polymeric transparent vial	Mydriacyl 1 % , 15 ml
		Krka Novo-Mesto, Slovenia	
16	tablets	non-transparent blister pack	Ampril 2.5 mg, 5 mg, 10 mg
17	tablets	non-transparent blister pack	Amlessa 4 mg / 5 mg, 4 mg /10 mg, 8 mg / 5 mg, 8 mg / 10 mg
18	tablets	non-transparent blister pack	Bisoprolol 5 mg, 10 mg
19	tablets	non-transparent blister pack	Roxera 10 mg, 20 mg
20	tablets	non-transparent blister pack	Atoris 10 mg, 20 mg, 30 mg, 40 mg
21	tablets	non-transparent blister pack	Koriol 12.5 mg, 25 mg, 3.125 mg, 6,25 mg
22	tablets	non-transparent blister pack	Nolpasa 20 mg, 40 mg

Continuation of the Table 1.

23	tablets	non-transparent blister pack	Enap 2.5 mg, 5 mg, 10 mg, 20 mg
24	tablets	non-transparent blister pack	Enap H 10 mg
25	tablets	non-transparent blister pack	Enap HL 10 mg, 20 mg
26	tablets	transparent blister pack	Vasylil 10 mg, 20 mg
27	tablets	transparent blister pack	Valsakor 80 mg, 160 mg, 320 mg
28	tablets	transparent blister pack	Valsakor HD 160 mg / 25 mg, 320 mg / 25 mg
29	tablets	transparent blister pack	Lorista 50 mg, 100 mg

30	tablets	transparent blister pack	Lorista H 50 mg / 2.5 mg
31	tablets	transparent blister pack	Lorista HD 100 mg /25 mg
32	tablets	transparent blister pack	Cyprinol 250 mg, 500 mg, 750 mg
		Berlin-Chemie / Menarini Pharma Gmbh (representative, Germany)	
33	tablets	non-transparent blister pack	Lekramen 10 mg, 20 mg
34	tablets	non-transparent blister pack	Berlipril 5 mg, 10 mg, 20 mg
35	tablets	non-transparent blister pack	L-thyroxine 75, L-thyroxine 50, L-thyroxine 125, L-thyroxine 100, L-thyroxine 150
36	tablets	non-transparent blister pack	Mezym-forte 10000, 20000
37	tablets	non-transparent blister pack	Dicloberl 50 mg
38	tablets	non-transparent blister pack	Berlithion 300 mg
39	tablets	transparent blister pack	Corvitol 50 mg, 100 mg
40	tablets	transparent blister pack	Trifas 10 mg, Trifas–COR 5 mg
41	tablets	transparent blister pack	Nebilet 5 mg
42	tablets	transparent blister pack	Falimint 25 mg
43	tablets	transparent blister pack	Siofor 500 mg, 850 mg, 1000 mg
		Pharmak, Ukraine	
44	eye drops	white polymeric non-transparent vial	Vial 0.05 % 10 ml
45	eye drops	white polymeric non-transparent vial	Vial light 0.5 % 10 ml

Continuation of the Table 1.

46	eye/ear drops	white polymeric non-transparent vial	Cypropharm 10 ml
47	eye drops	white polymeric non-transparent vial	Ophthymol 5 ml, 10 ml
48	eye drops	white polymeric non-transparent vial	Dexamethazone-Biopharma 0.1% 5 ml, 10 ml (Biopharma Ltd., Ukraine)
		Lekchim-Kharkov, Ukraine	
49	rectal suppositories	non-transparent blister pack with PVC-film	Prostatilen-zinc 30 mg/100 mg/100 mg №10
50	rectal suppositories	non-transparent blister pack with PVC-film	Bethiolum 15 mg/200 mg №10
51	rectal suppositories	non-transparent blister pack with PVC-film	No-H-sha 40 mg №10
52	rectal suppositories	non-transparent blister pack with PVC-film	Anaesthezol №5

53	rectal suppositories	non-transparent blister pack with PVC-film	Prostatilen 30 mg №10
54	rectal suppositories	non-transparent blister pack with PVC-film	Hippophaes oleum 350 mg №10
55	vaginal suppositories	non-transparent blister pack with PVC-film	Klioron 16 mg №10
56	rectal/vaginal suppositories	non-transparent blister pack with PVC-film	Tamistol 15 mg №5
		Nizhpharm Ltd., Russian Federation	
57	rectal suppositories	non-transparent blister pack with PVC-film	Papaverin 20 mg №10
58	vaginal suppositories	non-transparent blister pack with PVC-film	Livarole 400 mg №5
59	vaginal suppositories	non-transparent blister pack with PVC-film	Hexicon 16 mg №10
60	rectal suppositories	non-transparent blister pack with PVC-film	Hippophaes oleum 500 mg №10
61	rectal suppositories	non-transparent blister pack with PVC-film	Vitaprostum 50 mg №10
62	vaginal suppositories	non-transparent blister pack with PVC-film	Benatex 18.9 mg №10
63	vaginal suppositories	non-transparent blister pack with PVC-film	Depanthol 100 mg / 16 mg №10
64	rectal suppositories	non-transparent blister pack with PVC-film	Cefeconum D 250 mg, 100 mg, №10
65	rectal suppositories	non-transparent blister pack with PVC-film	Glycerol 2110 mg, 1240 mg №10

RESULTS AND DISCUSSION

Results of inspection analysis of medicinal products studied in the paper are presented in the Table 2.

According to the data in the Table 2 we can conclude that all samples passed the first 6 stages of inspection analysis successfully.

Table 2. Results of the inspection analysis of the studied samples

Number of stage	Parameter to be tested	Results
1	Accompanying documents for the incoming goods	Conforms to the requirements
2	Range, quantity and quality of the goods specified in the accompanying documents and the ones actually received	Conforms to the requirements
3	Organoleptic (visual) control of the product packaging	Conforms to the requirements
4	Product labeling	Conforms to the requirements
5	Product barcode	Conforms to the requirements
6	Contents of the goods	Conforms to the requirements
7	Organoleptic (visual) control of the drugs	Samples (4-8, 14-15, 26-32, 39-43) satisfy the requirements. Samples (1 - 3, 9 - 13, 16- 25, 33 - 38, 44 - 65) cannot be visually evaluated for quality of the formulation.

The possibility of visual control of the medicines (stage 7) depends, first of all, on the properties of the primary packaging containers, namely, their transparency. As it can be seen from our results, 46 samples out of 65 (or 71%) cannot be visually identified and their appearance is impossible to check because of the opacity of the containers. When it comes to different forms 53% of studied tablet drugs, 88% of the eye drops and 100% of the suppositories cannot be evaluated visually. Analyzing drugs from different manufacturers we found that Sandoz and Lek produce 3 brand names (tablets) in non-transparent blister packs out of the 8 ones researched, Alcon-Couvreur (eye drops) – 5 out of 7, Krka Novo-Mesto (tablets) – 10 out of 17, Berlin-Chemie (tablets) – 6 out of 11, Pharmak, Ukraine (eye drops) – all 5 of them, Lekchim-Kharkov, Ukraine (suppositories) – all 8 of them, Nizhpharm, Russia ((suppositories) – all 9.

This means that we are not able to properly evaluate such drugs while placed into primary packaging. Even the containers of most of the eye drops were made from opaque plastic, whereas according to the GMP requirements they should be as transparent as possible.

CONCLUSIONS

Based on the inspection analysis of the accompanying documentation, quantity, packaging, labeling, barcodes and completeness of randomly selected 65 drug samples produced by different manufacturers in tablet, drop and suppository forms, we can conclude that all of them complied with the requirements of the normative documentation at the first 6 stages of inspection. However, it was impossible to evaluate 71% of the studied samples by the parameter "Appearance" because of the non-transparence of their primary containers. The results of the research will play an important role in the development of advanced kinds of packaging which can allow proper identification and evaluation of drug quality in various forms.

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