

(Pentalgin Table №.10 (Ukraine) in the city of Rivne at the minimum wage) to 3.75 (Solpadein active tabl №.12, Odessa, for a minimum pension). The most readily available preparations of the Ukrainian production were Codeterp tablets №.10 (10x1) and Pentalgin Table. №.10 the highest CAS that were defined by the average pension in Ukraine is 2.44 and 0.89, respectively in Odessa [6,7].

**Conclusions.** With the method of assignment of the price accessibility of codeine containing drugs in different regions of Ukraine, conducted price analysis out for research drugstores in oblast centers of Rivne, Odesa and Kharkiv oblasts availability. In general, according to the results of the study, it was found that codeine-containing drugs are available to the population at a price: the calculated CAS. The most readily available preparations of the Ukrainian production were Codeterp tablets №.10 (10x1) and Pentalgin Table. №.10 the highest CAS in Odessa.

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## THE INVESTIGATION OF THE EFFICACY OF THE COOLING ELEMENT IN THE MODE OF "COLD CHAIN"

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**Introduction.** The pharmaceutical market of remedies is actively developing in the direction of biotechnologies, due to the increase of using the targeted therapy in contrast to the conventional therapy, the increase of demand for monoclonal antibodies, the prescription of orphan medicines, vaccines and biosimilars [5].

Especial attention is focussed by medical immunobiological preparations (MIBPs) which are used for the immunoprophylaxis and the immunotherapy, and require the special storage conditions, videlicet the organization of storage, transportation and the usage with the help of the "cold chain". Therefore, pharmaceutical enterprises are taking additional measures to ensure the quality of their products from the beginning of the manufacture to the distribution of their products. A significant part of the MIBPs requires the storage conditions of a fairly narrow temperature interval from +2 °C to +8 °C, and the temperature of +5 °C is optimal. Certain vaccines can be stored and transported at a temperature from -80 °C to +2 °C [4].

In Ukraine the requirements of the creation of a cold chain and abidance by the terms of storage and transportation of MIBP are regulated by certain regulatory documents [1, 2]. But definite complexities, such as the absence of common standard testing methodologies for insulated containers, refrigeration rooms, refrigerating equipment, carrier vehicles and temperature control devices, as also the lack of standard requirements for a temperature control system in the cold chain, require MIBP manufacturers to apply a scientific approach during the development of the "cold chain" in order to ensure the quality of their remedies [3].

The cooling elements, which are packed together with MIBP, take on an indispensable the role in providing and maintaining the established temperature regimes. Therefore, the efficacy of the cooling element has a direct critical influence on the preservation of the quality of medical remedies.

**The aim of the study.** Experimentally investigate the efficacy of the cooling element at the stage of development of the logistic "cold chain" for warehousing and transportation of vaccines for the veterinary use.

**Methods of research.** The object of research was the experimental samples of the cooling element of the own manufacture. The efficacy of the cooling element was determined experimentally by the criterion of maintaining the temperature during the development of a scheme for packaging of finished products of vaccines for veterinary using for the purpose of further storage and transportation of finished remedies in the "cold chain" mode.

**Main results.** The manufactured cooling element was prepacked in polymeric container of the type of HDPE Durable Plastic Ice Packs type SAP CMC Inside Liquid For Cold Chain Transportation supplier, China, intended for the maintaining a product temperature from + 2 °C to + 8 °C.

For modeling the storage conditions of the vaccine the standard thermoboxes made of foamed plastic with the internal dimensions (W × V × D) 585 mm × 300 mm × 260 mm were used, in which the products are sold.

Before the start of the experiment, the thermoboxes were kept for 24 hours in the refrigerating room of the enterprise at a temperature from + 2 °C to + 8 °C in the open state, and the cooling elements were frozen at a temperature of minus 20 °C.

Were studied two packaging designs to the group tare packs of vaccines with cooling elements.

The scheme of placement №1 (a). In thermoboxes were packed three rows of boxes with the remedy (lyophilized vaccine in a R10 bottle, in a carton package), and the free volume over the boxes with the vaccine was filled with the cooling elements

in two layers. The top and bottom of the cooling elements were insulated with corrugated card sheets at the appropriate box sizes (585 mm × 260 mm). Afterwards the temperature detectors were placed in the thermoboxes (Fig.1), then the boxes were closed tightly.

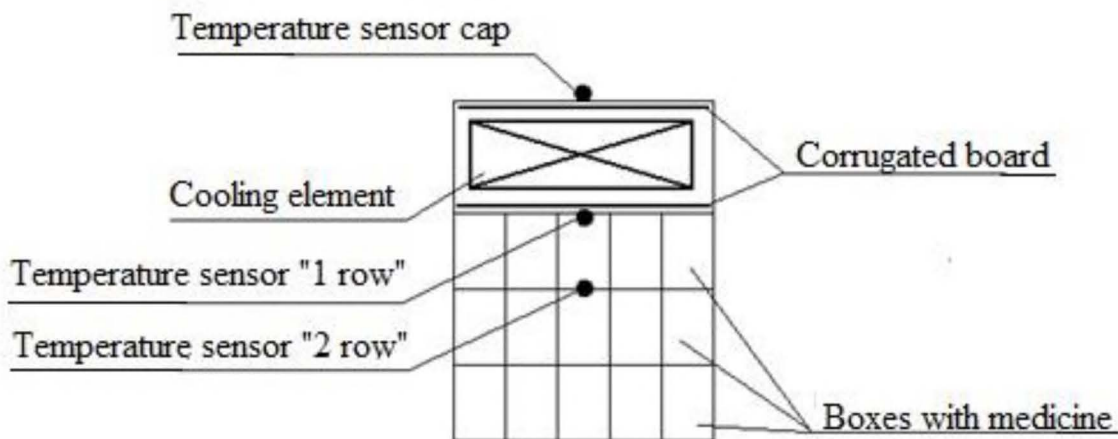


Fig. 1. Packaging of remedies with the cooling elements, placed in one layer.

The scheme of placement №2 (b). Into the thermoboxes were packed three rows of boxes with the remedy (lyophilized vaccine in a R10 bottle, in a carton package). Cooling elements were placed in two layers between the rows of packages of the remedies. From the top and bottom cooling elements were insulated with corrugated card sheets at the appropriate box sizes, to avoid a direct contact with the secondary package of vaccines. Afterwards the temperature detectors were placed in the thermoboxes (Fig.2), then the boxes were closed tightly.

Packed off boxes with finished products were placed in the conditions of the test temperature at the "cold chain" mode at  $5 \pm 3 \text{ }^\circ\text{C}$  in the refrigerating room of the enterprise, the exposure time was 72 hours (test code 1a, 1b), and at 2 modes of stress tests: the ambient temperature of  $20\text{-}25 \text{ }^\circ\text{C}$  in the premises of the finished product storage, the time of exposure was 48 hours (test code 2a, 2b), and the ambient temperature was  $37 \pm 0,5 \text{ }^\circ\text{C}$  in the thermal room of the enterprise, the time of exposure was 24 hours (test code 3a, 3b).

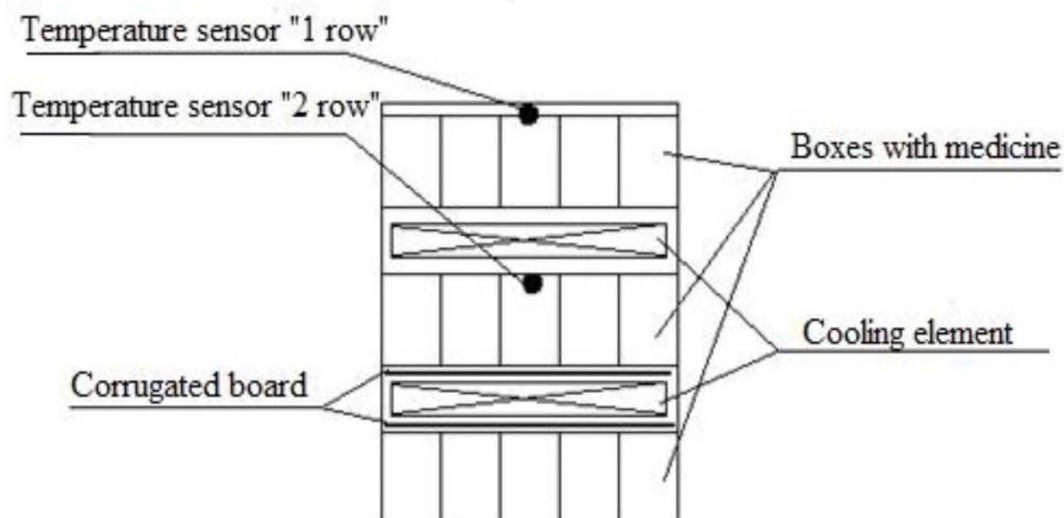


Fig. 2. Packaging of the remedies with cooling elements, placed in two layers.

After storing at the test conditions the temperature values for the researching period were taken from the temperature sensors with the help of the USB-carrier and were analyzed. The results of the researches are presented in the Table 1.

Table 1

Results of the research of temperature values in package of group tares depending on the design of the exposition

Code of the experiment	Number of boxes, pc.	Ambient temperature, °C	Exposure time, h.	Temperature range in the package of the group tare during the exposure, °C		Conclusions
				«1 row»	«2 row»	
1a	6	5±3°C	72	«1 row»	from 1,6 to 5,9	withstands
				«2 row»	from 2,1 to 6,2	withstands
1b	8	5±3°C	72	«1 row»	from 2,0 to 6,7	withstands
				«2 row»	from 2,1 to 6,3	withstands
2a	7	20-25°C	48	«1 row»	from 3,2 to 7,1	withstands
				«2 row»	from 3,3 to 11,3	<i>does not withstand</i>
2b	8	20-25°C	48	«1 row»	from 2,3 to 8,0	withstands
				«2 row»	from 2,3 to 7,4	withstands
3a	6	37±0,5°C	24	«1 row»	from 3,0 to 8,0	withstands
				«2 row»	from 3,1 to 14,6	<i>does not withstand</i>
3b	8	37±0,5°C	24	«1 row»	from 3,3 to 8,0	withstands
				«2 row»	from 3,2 to 10,8	<i>does not withstand</i>

All in all, the placement of cooling elements in accordance with scheme number 1 provides the required storage temperature (not higher than 8 ° C) only at the uninterrupted duty of the "cold chain". In case of the possible locations of tare packages with the remedies at ambient temperature in indoor or summer weather, such as waiting before loading in vehicles or transit movements, scheme 1 of the accommodation of cooling elements does not provide the "cold chain" mode inside the thermobox. The packages of the finished remedies in the thermoboxes are placed densely, thus there is no convection of air and intense heat exchange. In the conditions of the absence of convection heat exchange is carried out mainly through the direct contact "box - cooling element" and "box - the wall of the box."

It is confirmed that the placement of cooling elements according to scheme №2 provides the required storage temperature (not above 8 ° C) both in "cold chain" mode as well as 48 hours at outdoor ambient temperature of 20-25 ° C. In the conditions of placement in accordance to scheme 2, an equal distribution of temperature in the thermoboxes is achieved and a direct contact of each package with a cooling element is provided through a thin layer of corrugated card.

But according to the printouts from the temperature sensors, at the 44th hour the temperature rises almost to the extreme and is 8 ° C. Also, if the group tare package is at a sufficiently high ambient temperature, the cooling elements will inhibit the growth of temperature inside the thermocontainer, but do not provide the declared storage conditions of remedies that is critical for such medicinal forms as

vaccines.

### **Conclusions.**

1. Cooling elements, which are packed together with vaccines, play an important role in providing and maintaining the established temperature regimes. The efficacy of the cooling element as the provision of the necessary temperature regime of the remedy at fluctuations of the ambient temperature has a direct critical influence on the preservation of the quality of medicinal remedies.

2. It is necessary to place the cooling elements in the thermoboxes in such way which can assure the direct contact of each package of the remedy with a cooling element.

3. The scheme of the layout of the secondary package of the remedies and cooling elements, which provides convection and proper heat exchange by contact even on the one side of the package of the remedy, allows to store and transport vaccine in the "cold chain" mode for 3 days with the maintaining of declared temperature conditions.

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## **DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF ORODISPERSE FILM WITH ANTIMICROBIAL ACTION**

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**Introduction.** In recent decades, active research has begun in the field of the development of films for dentistry. The composition, technology and standardization