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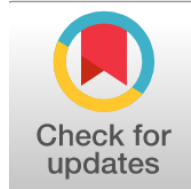
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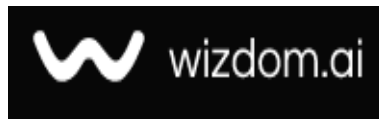
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## **Ecological - hygienic aspects and safety parameters of the use of the Zaragen insecticide in agriculture**

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### **Abstract**

This article states major results of multifaceted, comprehensive hygienic and toxicological studies, Zaragen can be recommended for use in agriculture on cotton, tomato and potato crops as an insecticide with mandatory compliance with the recommended consumption rates, hygienic standards and regulations, safety rules for the use of pesticidal preparations.

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## Introduction

The problem of chemical plant protection products attracts growing attention not only of workers in agricultural, chemical and medical sciences, but also of the general public. The problem of protecting public health in connection with the widespread use of pesticides worries hygienists in many countries of the world [2,4]. First of all, this is a general hygiene, large-scale, complex and multifaceted problem. To protect cultivated plants from numerous pests and diseases, as well as weeds, a significant range of chemicals is used. All these substances in the aggregate and each separately are intended for the destruction of harmful organisms [5,7]. Many pesticides are very persistent; they retain their toxic properties under natural conditions for a long time [7, 9]. It should be specially noted that pesticides are more and more involved in the cycle of substances in nature and, therefore, become a regular, and not an accidental factor in environmental pollution. [3.14]. The constant increase in the assortment and quantity of applied pesticides, the expansion of the scope of their use in various fields of the national economy, leads to an increase in the possible ways of getting them into food. From the point of view of possible contamination of food products, water ponds with pesticides is a great danger. [6.10]. Pesticides can fall on plants with streams of atmospheric air, with precipitation. [1.14]. Pesticides through contaminated water, food, atmospheric air can enter the human body. Some of them possess toxic, concerto genic, embryo toxics and other actions for the human body. That is why the research of toxic, carcinogenic, mutagenic and other negative properties of pesticides is of paramount importance.

The main issue in preventing pollution of the environment and protecting public health is the search for low-toxic and low-resistance pesticide preparations.

As a result of such searches, created a new, perspective drug Zaragen k.s

To address the issue of its widespread use in agriculture, there is a need to develop hygienic standards and regulations for safe use in agriculture.

## The purpose of the study:

before us was set the goal to assess the danger of Zaragen c.s. into the environment and develop hygienic norms and regulations that guarantee safety for food consumers, to prevent atmospheric air, air from the working zone, water of reservoirs and soil from contaminating this preparation.

## Material and methods:

The object of the study was a new insecticide Zaragen k.s., manufactured by "ZARATRUST" LLC Uzbekistan. Zaragen c.s. - a systemic insecticide with a unique mechanism even to insensitive pests. It is highly effective against a wide range of pests of cotton, tomatoes and potatoes.

Active ingredient: chlorantraniprol; preparative form - suspension concentrate (c.s.).

The maximum permissible concentration of Zaragen in atmospheric air, air of the working zone, the maximum permissible level in foodstuffs and the estimated permissible concentration of insecticide in the soil were established using the calculation method. The determination of the residual amounts of Zaragen in the environment was carried out according to the guidelines 4.1.3005-12 "Determination of the residual amounts of chlorantraniliprol in cabbage, lettuce, raisins in high performance liquid chromatography." [12,13].

The determination of Zaragen in the air of the working area and flushing from the skin was carried out according to the guidelines 4.1.2460-09. [13].

## Results and discussion:

### Acute toxicity study results

Determination of the parameters of acute toxicity of the drug during intragastric exposure was performed on white rats. For the experiment, 60 experimental rats of both sexes were used. The experimental animals were divided into 3 groups, one group of them was the control. The animals were taken in the experiment, which were administered intragastrically Zaragen, in doses from 1000 mg/kg to 6000 mg/kg. After statistical processing, the average lethal dose of the drug for white rats was set at 4750 mg/kg (tab)

**Table 1 Establishment of LD50 (medium lethal dose)**

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Dose mg / kg X3	Mortality	X	y	B	XB	XB 2	YB	XYB
1000	0	1	3,04	1,0	1,0	1,0	3,04	3,04
2000	Y3	2	3,72	5,2	5,2	10,4	9,67	19,34
3000	0	3	4,48	4,5	13,5	40,5	20,6	60,48
4000	10	4	5,0	5,0	20,0	50,0	25,0	200,0
5000	30	5 (8)	5,84	3,9	31,2	249,6	22,3	18,14
6000	50	6 (11)	6,96	1,2	13,2	145,2	8,35	91,85
18,2	84,1	526,7	89,2	557				

**Table 1.**

**The clinical picture of poisoning:** animals became agitated, followed by depression, breathing became difficult, profuse salivation, involuntary urination, lack of appetite, experimental animals were disheveled, unkempt.

Based on the foregoing, we can conclude that the drug in terms of acute toxicity belongs to hazard class IV (low toxic chemical compound) [15].

## Studies of the effect of the drug on the skin and mucous membranes of the eyes

### Action on the skin

The effect of the drug on the skin was studied in white rats. The shaved skin in the abdomen (2x2) was applied in its native form. After a 4-hour exposure, the drug was washed off and the experimental sites were monitored. As a result of studies, it was found that the drug caused slight irritation of the skin, expressed in slight redness in the experimental areas of the skin, there was a slight swelling. By the end of the working day, the signs of irritation decreased and completely disappeared after 24 hours from the start of the experiment. Thus, we can conclude that the drug has a weak irritating effect on the skin.

### Action on the eyes .

During the research of the irritating effect on the mucous membranes of the eyes, the drug was applied once in the conjunctival sac of the eye of rats in the amount of 1-2 drops. The second eye served as a control. 10 minutes after the experimental animals were introduced into the eye, irritation of the mucous membrane of the eye was observed, which was manifested by frequent blinking, anxiety, lacrimation, and redness of the conjunctiva. 4 hours after the introduction of the drug, inflammation of the cornea and edema were noted. On the 2nd day of the experiment, there was a sharp decrease in signs of irritation, which completely disappeared on the 3rd day of the experiment. Thus, the drug "Zaragen" has a slightly irritating effect on the mucous membranes of the eyes.

### The study of the cumulative properties of the drug

The cumulative ability of the drug was studied by the method of "subchronic" Lim toxicity under conditions of repeated administration to white rats. The cumulative properties were judged by the criterion of death and the behavior of animals. It was established that the drug does not have material cumulation, because no death of animals was observed throughout the experiment. However, according to the manifestation of some signs of intoxication, it can be concluded that the drug has cumulative functional properties.

## Results

**As a result of studying the chronic toxicity of the drug** using mathematical modeling, the threshold and maximum effective doses of Zaragen were set at 5.0 and 0.5 mg/kg body weight, respectively. Based on the data obtained, the allowable daily dose of the drug for humans at the level of 0.6 mg/kg person/day was calculated and scientifically substantiated.

### Long-term effects of the drug

**Oncogenicity:** In 18-month experiment in mice, it was found that the drug was not oncogenic for male and female mice, NOAEL was 7000 ppm (equivalent to 935 mg/kg/day) for males and 1155 mg/kg/day for females.

**Teratogenicity and embryo toxicity:** in the experiment on rats, the effect of the substance on body weight,

weight gain, food intake of any dose was not found. There was no effect on external, visceral and skeletal malformations at any dose. NOAEL for the mother and fetus was set at 1000 mg/kg W/day.

Reproductive toxicity and gonodotoxicity in experiments on 2 generations of rats established NOAEL for systemic toxicity for parents at the level of 20,000 ppm.

**Mutagenicity:** the drug was evaluated in bacterial in vitro and in vivo experiments to study genetic toxicity. A negative result was noted in all experiments, which indicates the absence of mutagenic effects of the drug Zaragen.

## **Establishment of the maximum permissible concentration (MPC) of Zaragen in the water of water bodies**

As a result of the use of pesticidal preparations in agriculture, there is the possibility of contamination of nearby water bodies and an adverse effect on the organoleptic properties of water and the sanitary regime of water in water bodies. The study of the drug on the organoleptic properties of water made it possible to establish that the drug has the ability to give water a weak specific odor and a slight aftertaste. The threshold concentration by smell is set at 0.33 mg/L. A comparison of the threshold and maximum inactive concentrations according to all harmful criteria (organoleptic, sanitary-toxicological) allowed recommending MPC (maximum permissible concentration) in water of reservoirs at the level of 0.2 mg/l, the limiting sign of harmfulness is organoleptic.

## **Establishment of the maximum permissible concentration (MPC) of Zaragen in the air of the working zone and atmospheric air**

Based on the results of a sanitary-hygienic research and data on the toxicity of the drug, it is recommended and scientifically substantiated by calculation: the MPC of the drug in the air of the working area at the level of 3.0 mg/m<sup>3</sup> in atmospheric air is 0.2 mg/m<sup>3</sup>.

## **Justification of the maximum permissible levels of the drug**

### **(MPL) in foods**

Based on the results of sanitary-hygienic studies and the methodological approach to rationing pesticidal preparations in food products, the maximum permissible levels (MPL) are recommended and scientifically substantiated: in cottonseed oil - "not allowed", in tomatoes - 0.05 mg/kg, in potatoes - 0.1 mg/kg.

## **Justification of the approximate permissible concentration (APC) of**

### **Zaragen in the soil**

Approximately permissible concentrations of the drug in the soil were calculated according to the "methodology of integrated and accelerated rationing of pesticides in environmental objects" [11]. Taking into account the toxicological parameters of the drug, it is calculated and scientifically justified that the estimated permissible concentration of Zaragen in the soil is 0.1 mg/kg

Based on the conducted complex of sanitary - hygienic and toxicological studies and expert examination of the documentation submitted by the company, it was established:

- Zaragen insecticide of systemic action with a unique mechanism of action, even insensitive to pests of crops;
- the drug for acute toxicity belongs to the IV group of danger (low toxic chemical plant protection products) of pesticidal compounds (13);
- Zaragen insecticide has a weak irritant effect on the skin and mucous membranes of the eyes;
- the drug has cumulative properties of a functional nature;
- Zaragen does not have oncogenic, embryo toxic, mutagenic effects;

- Allowed harmless human daily dose (ADD) of the drug is 0.6 mg/person/day, the maximum permissible concentration (MPC) in the air of the working area is 3.0 mg/m<sup>3</sup>, in atmospheric air - 0.2 mg/m<sup>3</sup>, the maximum permissible level (MPL) in potatoes - 0.1 mg/kg, in tomatoes - 0.05 mg/kg, in cottonseed oil "not allowed", the approximate permissible concentration (APC) in the soil is set at 0.1 mg/kg.

## **Conclusions**

Based on the results of multifaceted, comprehensive hygienic and toxicological studies, Zaragen can be recommended for use in agriculture on cotton, tomato and potato crops as an insecticide with mandatory

compliance with the recommended consumption rates, hygienic standards and regulations, safety rules for the use of pesticidal preparations.

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