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Issues of Safe Use of a New Herbicide Preparation Based on Nikosulfuron

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Abstract. The article presents the results of complex hygienic and toxicological studies: toxicological assessment of the herbicide, hygienic standards in environmental objects and regulations for safe use.
Keywords: toxicity, herbicide, standard, regulation, water, air, soil, environment.

RELEVANCE

One of the means of increasing the efficiency of agricultural production is the chemical method of controlling weeds, diseases, pests of cultivated plants, which contributes to a significant reduction in losses in agriculture. The costs of its use quickly pay off due to increased yields, increased shelf life of plant products, and improved appearance of agricultural products.

Pesticides are classified by chemical composition, objects of application, as well as by the nature of action and methods of penetration into the body. Having high efficiency, the use of pesticides is associated with high risks of environmental pollution and danger to humans and beneficial flora and fauna. Such properties of pesticides as high toxicity, persistence in the environment, ability to be transported through food chains, migrate to adjacent environments (water bodies, soil, air), accumulate in products and, with constant use, cause the emergence of resistant forms of harmful organisms, require justification and strict regulation of their use in agriculture. The basis for the regulation of the use of pesticides is a quantitative assessment of their danger to humans and natural systems. The assessment of the danger of pesticides for humans and warm-blooded animals is carried out according to toxicological and hygienic criteria, taking into account such indicators as average lethal doses when administered into the stomach and applied to the skin, average lethal concentration in the air, characterizing respectively the oral, skin-resorptive and inhalation toxicity of the substance, the coefficient of functional cumulation, the stability of the pesticide in the soil (the time of decomposition into non-toxic components), as well as the presence of specific effects: teratogenic, embryotoxic, etc. These toxicological and hygienic criteria in turn form the basis for the development of hygienic standards: the permissible daily dose of a substance for humans and the maximum permissible content of pesticides in agricultural products and environmental objects.

The current stage of the country's development puts forward new tasks for agriculture - large, complex, responsible tasks, among which is the task of providing effective pesticides. In various branches of agriculture, the elimination of crop losses from pests, diseases and weeds is an urgent task. The current development of agriculture requires the search for and application of radial methods and means of destroying and suppressing weeds. In this regard, the chemical method allows you to get rid of weeds in the shortest possible time with the least labor costs. For this purpose, herbicides are used in agriculture [7]. Fighting weeds with traditional methods takes a lot of time and effort, especially if you do not have a small vegetable garden with several beds, but a large plot or even a farm. In this case, you cannot do without herbicides, with which you can quickly and easily get rid of vegetation or individual types of weeds. Herbicides are of two types: continuous (destroy all plants in general) and selective (aimed at combating certain types of weeds) action. However, much depends on the concentration of the active substance - if you do not follow the instructions, you can harm crops or not achieve the desired result. Herbicides can affect different types of plants: trees, shrubs (arboricides); aquatic plants (algaecides); other vegetation (herbicides). If it is necessary to completely get rid of plants (for example, after harvesting or before sowing, near industrial facilities, etc.), herbicides of continuous action are used, which have a systemic effect on them. In this case, not only the above-ground part is destroyed, but also the roots. If you need to get rid of unsprouted seeds, a powerful root system, the best option would be a soil herbicide, which is added to the soil. But preventive treatment is not always possible, and in the process of growing crops, weed seeds still get into the beds. To quickly get rid of them, without allowing them to harm the plantings, a substance of targeted action is used. This can be either a systemic herbicide or a contact herbicide (damages only the above-ground part of the plant). In any case, it should be a selective option. However, a continuous one can also be used, provided that only weeds are sprayed [6].

Volume and methods of the study. The work used hygienic toxicological and statistical methods. The studies were carried out in accordance with the "Methodology of complex and accelerated standardization of pesticides in environmental objects" [5], the degree of danger was determined in accordance with SanPiN RUz No. 0067-24 "Hygienic classification by toxicity and hazard" [1]. The toxicity of the drug was studied in accordance with GOST 32644-2014 "Test methods for the effects of chemical products on the human body (Acute oral toxicity - method for determining the class of acute toxicity)" [2]; GOST 32436-2020 "Test methods for the impact of chemical products on the human body (tests for assessing acute irritant effects on the skin)" [3]; GOST 32373-2020 "Test methods for the impact of chemical products on the human body (Basic requirements for conducting tests to assess acute toxicity upon dermal administration)" [4].

We have studied a new herbicide based on nicosulfuron. Oktava is a selective post-emergence herbicide of systemic action, recommended for use on corn and cereals, against annual and perennial cereals, annual and perennial dicotyledonous weeds, with a consumption rate of 0.8 - 1.0 l / ha. Active ingredient - nicosulfuron + florasulam. Aggregate state - viscous oily liquid, from light gray to yellow, with a weak specific odor. pH of 1% solution - 4.5 ± 1.5. Density - 0.970 ± 0.2 g / cm3. Flash point - in a closed crucible 92 ° C. Preparative form - oily liquid, from light gray to yellow, with a weak specific odor.

RESEARCH RESULTS.

Acute toxicity. Experimental studies to establish the hazard class of the drug were conducted on laboratory animals - white rats. The experiment involved 42 animals of both sexes, weighing 140 - 170 g, which were divided into 7 groups of 6 individuals each. The animals were administered the drug enterally in doses of 1000.0 - 2000.0 - 3000.0 - 4000.0 - 5000.0 - 6000.0 - 7000.0 mg / kg. The obtained results made it possible to establish the median lethal dose (LD50) for rats at the level of - 4375.0 mg / kg, LD16 - 2225.0 mg / kg, LD84 - 6450.0 mg / kg. Similar studies were conducted on white mice, the median lethal dose (LD50) was established at the level of - 4125.0 mg / kg. Signs of intoxication were identical in all types of laboratory animals and were expressed in decreased activity, huddling of animals in the corner of the cage. Analyzing the obtained data, it can be concluded that the drug, according to the parameters of acute toxicity, belongs to low-hazard substances (SanPiN No. 0067-24) [1]. The irritating effect of the drug on the skin was studied on experimental animals - white rats. The drug was applied to the skin of experimental animals in its native form. The skin reaction was recorded at the end of a 4-hour exposure, as well as 1 and 16 hours after a single exposure. After removing the application and washing off the drug, quickly passing hyperemia of the experimental areas was observed. The observed signs of irritation disappeared 24 hours after the beginning of the experiment. Conclusion: the drug has a weak irritating effect on the skin. The irritating effect of the preparation on the mucous membranes of the eyes was studied by introducing 2 drops of the preparation into the conjunctival sac of the rabbit's eye, the second eye served as a control. Observations were carried out dynamically after 1-4 hours, 1, 3, 5 days. Immediately after the introduction of the preparation, frequent blinking and restlessness of the animals were observed. After 1 hour, moderate hyperemia and slight lacrimation were observed. After 3 hours from the beginning of the experiment, slight suppuration of the experimental eye was added to the existing signs of irritation. After 24 hours from the beginning of the experiment, narrowing of the palpebral fissure was noted against the background of signs of conjunctivitis. On the 2nd day of the experiment, a decrease in signs of irritation and slight suppuration were noted. Signs of irritation completely disappeared on the 3rd day of the experiment. Conclusion: the preparation has a moderate irritating effect on the mucous membranes of the eyes of experimental animals.

Cumulative properties. The ability of the preparation to accumulate in the body of experimental animals was studied on white rats for 3 months. The animals were divided into 2 groups: Group 1 - control; Group 2 - experimental, where the animals received the preparation intragastrically at a dose of 1/10 LD50. The effect of the preparation at a dose of 1/10 LD50 led to a change in some integral biochemical parameters of the animals' blood. Statistically significant increases in alkaline phosphatase activity were noted 30 days after the beginning of the experiment and amounted to 237.5 U / l against 171.3 U / l in the control. An increase in the indicator was noted throughout the entire baiting period and by the end of the experiment it was increased by 33.5%. A 30-day recovery period was sufficient to normalize the studied indicator. As a result of the biological effect of the preparation on the body of experimental animals, changes in aminotransferase activity were observed. Intragastric administration of the herbicide at a dose of 1/10 LD50 resulted in an increase in alanine aminotransferase activity starting from the 30th day of the experiment and was

significantly increased until the end of the inoculation period. Thus, 60 days after inoculation, the indicator was increased by 75.2%. After the recovery period, the studied indicator was restored ($P < 0.01$). Similar changes were observed when studying aspartaminotransferase in the blood serum of experimental animals. Changes in the studied biochemical parameters of the blood of experimental animals and the absence of their death throughout the experimental period allow us to conclude that the herbicide (Octava) has a functional cumulation.

Chronic toxicity. As a result of studying the toxicity of the drug in a chronic experiment, the threshold and maximum ineffective doses were established at the level of 10.0 and 1.0 mg/kg. Based on changes in biochemical parameters of the blood (activity of ALT, AST, alkaline phosphatase), the permissible daily dose for humans (PDI) was calculated and scientifically substantiated at the level of 1.2 mg/person/day.

Standardization of the drug in environmental objects and food products. Water. When studying the stability of a substance in water, it is best to use a direct analytical method for determining it in water. However, studies are carried out in most cases with low concentrations of the substance under study, which cannot always be determined by conventional analytical methods. In such cases, the use of methods that provide indirect indications of the degree of stability of the substance in water is of great importance. One of the indirect methods, widely used in the practice of hygienic standardization, is the study of the stability of a substance by studying the intensity of odor, color or taste. Some biological tests are also used as indirect methods, which in some cases allow detecting a decrease in the toxicity of preparations in water or the appearance of new toxic products as a result of the destruction of the substance under study. Such tests include the development and death of daphnia. The stability of the herbicide "Octava" was studied by indirect methods by observing changes in odor intensity. The initial concentrations for the experiment were the concentrations of the preparation: 0.04 mg / l; 0.4 mg / l and 4.0 mg / l. The studies were carried out in 3-liter vessels for 30 days. The results of the studies showed that the preparation in low concentrations (0.04 mg / l) decomposes within the first day. The preparation in a concentration of 0.4 mg / l - within 5 days. The concentration of the preparation of 4.0 mg / l - on the 7th day of the experiment. The transformation of the herbicide "Octava" in water was also judged by the survival of daphnia. The results of the studies showed that the maximum concentration of the drug of 4.0 mg / l caused the death of daphnia during the first day of the experiment. Concentrations of the drug of 0.04 mg / l and 0.4 mg / l did not affect the development and death of daphnia. When the drug gets into water, it gives it a slight specific odor. The odor was determined qualitatively and quantitatively by the intensity of points. The effect of the drug on the organoleptic properties of water was studied with concentrations of the drug from 0.17 to 8.0 mg / l. The data obtained during the experiments showed that the odor threshold (intensity of 1 point) is at the level of 0.4 mg / l, the practical threshold (the odor intensity is 2 points) is at the level of 0.81 mg / l. When comparing the odor intensity indicators of the drug in water, according to various methods, we can conclude that they are at the same level, which indicates the reliability of the studies. In threshold concentrations by odor (0.4 mg/l), the preparation had no effect on transparency, color, or foaming. However, in this concentration, the preparation forms a barely noticeable film on the water surface. The preparation in a concentration of 0.04 mg/l did not have film-forming properties. Oktava in a concentration of 0.04 mg/l did

not affect the sanitary regime of water in reservoirs (did not affect biochemical oxygen consumption or nitrification processes). According to the sanitary-toxicological experiment, the threshold concentration of the preparation was recommended at 1.2 mg/l by calculation. Thus, based on the conducted comprehensive studies, taking into account the data of the sanitary-toxicological experiment, the recommended MAC of the preparation in water of reservoirs is -0.04 mg/l (limiting organoleptic sign of harmfulness).

Air. Taking into account the data on the toxicity of the preparation, stability in environmental objects, physicochemical properties, the MAC of the preparation in the air of the working area has been scientifically substantiated and calculated at the level of - 3.0 mg/m3, the MAC of the preparation in the atmospheric air at the level of - 0.2 mg/m3.

Food products of plant origin. Guided by generally accepted hygienic approaches to substantiating the permissible levels of the preparation in agricultural products, taking into account the average daily consumption rates of the product, the MRL of the preparation in corn is recommended at 0.008 mg/kg ≈ 0.01 mg/kg.

Soil. The calculation of the APC of the preparation in the soil was carried out on the basis of the "Methodology" [5] taking into account the MRL of the preparation in food products. The approximate permissible concentration of the preparation in the soil is recommended at the level of - 0.39 mg/kg. The complex of conducted hygienic and toxicological studies allows us to draw a conclusion about the possibility of using the new herbicide "Octava" in agricultural practice in Uzbekistan in compliance with the developed hygienic regulations for use (sanitary protection zone (SPZ) - 100 meters, time of return to work - 5 days).

CONCLUSION. The herbicide preparation based on nicosulfuron (Octava) is a low-hazard compound; it has a weak irritant effect on the skin, cumulative properties of a functional nature.

The developed hygienic standards and regulations for the safe use of the preparation will contribute to the safe use of the herbicide in agricultural practice.

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