

УДОСКОНАЛЕННЯ СИСТЕМИ МОНІТОРИНГУ У НАВКОЛИШНЬОМУ СЕРЕДОВИЩІ ПЕСТИЦИДІВ, ЯКІ ВПЛИВАЮТЬ НА ЩИТОПОДІБНУ ЗАЛОЗУ

Антоненко А.М., Вавріневич О.П., Омельчук С.Т., Шпак Б.І., Коршун М.М.

IMPROVEMENT OF THE MONITORING SYSTEM IN THE ENVIRONMENT OF PESTICIDES AFFECTING THYROID GLAND

¹ANTONENKO A.M.,

¹VAVRINEVYCH O.P.,

²OMELCHUK S.T.,

³SHPAK B.I.,

¹KORSHUN M.M.,

¹Bohomolets National
Medical University, Kyiv,
Ukraine

²Hygiene and Ecology
Institute Bohomolets of
National Medical University,
Kyiv, Ukraine

³«Syngenta» LLC,
Kyiv, Ukraine

Pesticides are among the chemicals most studied in terms of adverse effects on the thyroid gland (DDT, amitrol, carbamate and dithiocarbamate class compounds, including manzoceb metabolite ethylenethiourea etc.) [1, 2]. It has been found that the effect of background concentrations of the tested compounds does not have a negative effect on the thyroid gland, while the effect on higher levels, professional or accidental, can lead to changes in thyroid gland [1, 3].

However, to date, agriculture in most countries, especially developing ones, is heavily reliant on pesticide application, which prevents or reduces losses from pests and thus increases yields and product quality, even in terms

of external attractiveness, which is often important for consumers [4, 5]. From this point of view, pesticides are an economical, labor-saving and effective mean for the control of pests, diseases and weeds in agriculture [5].

Same time pathology of the endocrine system takes one of the leading places in the structure of the general morbidity of the population of Ukraine and the world. Among endocrine diseases in Ukraine, the main place takes pathology of the thyroid gland (about 44%, in the endemic western regions – 70%).

Despite their popularity and widespread use, pesticides pose a serious risk to human health: farmers (professional contingents) when mixing and applying pesticides or working in cultivated

УДОСКОНАЛЕННЯ СИСТЕМИ МОНІТОРИНГУ
У ДОВКІЛЛІ ПЕСТИЦИДІВ, ЯКІ ВПЛИВАЮТЬ
НА ЩИТОПОДІБНУ ЗАЛОЗУ

¹Антоненко А.М., ¹Вавріневич О.П.,
²Омельчук С.Т., ³Шпак Б.І., ¹Коршун М.М.,

¹Національний медичний університет
ім. О.О. Богомольця, м. Київ, Україна

²Інститут гігієни та екології Національного
медичного університету ім. О.О. Богомольця,
м. Київ, Україна

³ООО «Сингента», м. Київ, Україна

Пестициди належать до хімічних речовин, найбільш досліджених у плані негативного впливу на щитоподібну залозу. Однак сільське господарство більшості країн, особливо тих, що розвиваються, значно залежить від застосування пестицидів, що дозволяє запобігти або зменшити втрати від шкідників і таким чином підвищити врожайність та якість продукції, навіть з точки зору зовнішньої привабливості, що часто є важливим для споживачів.

Мета – гігієнічне обґрунтування критеріїв відбору пестицидів, які впливають на щитоподібну залозу для їх моніторингу у довкіллі.

Матеріали і методи досліджень. Нами використано методи лабораторного та натурного гігієнічного експериментів, фізико-хімічні (хроматографічні), органолептичні, фізичні методи, методи математичного моделювання та статистичного аналізу.

Результати та обговорення. При вирішенні питання про необхідність проведення моніторингу в Україні для пестициду, який впливає на

щитоподібну залозу, оцінюють кожен із запропонованих показників у балах та знаходять їхню загальну суму. Якщо препарати на основі досліджуваної сполуки застосовують на різних культурах або у різних ґрунтово-кліматичних умовах, то для оцінки беруть найбільше значення періоду напівруйнування. Після додавання усіх отриманих балів необхідність проведення моніторингу оцінюють таким чином: якщо загальна сума становить 11-16 балів, проведення моніторингу необов'язково; 17-27 балів – моніторинг проводити бажано; 28-38 балів – моніторинг проводити обов'язково; 39-44 бали – використання пестициду необхідно заборонити.

Висновок. Таким чином, нами було удосконалено систему моніторингу пестицидів, які можуть впливати на функціонування щитоподібної залози, а саме: було запропоновано бальну оцінку критеріїв відбору для проведення моніторингових досліджень, а також додаткові (індекс потенційного забруднення ґрунтових та поверхневих вод (LEACH), інтегральний показник небезпечності у разі потрапляння у воду, інтегральний показник небезпечності споживання продуктів (ІПНВП) та специфічні критерії (вплив на щитоподібну залозу як орган-мішень, вираженість тирозинемії, індукованої пестицидом (рівень тирозину у плазмі крові, нмоль/мл).

Ключові слова: пестициди, критерії відбору, клас безпеки, стійкість в об'єктах довкілля, ризик для непрофесійних контингентів, моніторинг.

© Антоненко А.М., Вавріневич О.П., Омельчук С.Т., Шпак Б.І., Коршун М.М. СТАТТЯ, 2019.

fields; for non-professional contingents (bystanders) in the consumption of food and water containing pesticide residues [5].

That is why monitoring the risk of pesticides, which can affect the thyroid gland, when pesticides with water and foodstuffs enter the human body is very important to control the health of the population [6].

Objective. Wesubstantiationthe criteria for selection of pesticides that affect the thyroid gland for their monitoring in the environment.

Materials and methods: The most widely used fungicides and herbicides as the compounds most commonly affecting the functioning of the thyroid gland, and insecticides as the most toxic to warm-blooded animals and humans, have been selected to analyze and identify possible selection criteria for monitoring.

We used methods of laboratory and field hygiene experiments, physico-chemical (chromatographic), organoleptic, physical methods, methods of mathematical modeling and statistical analysis. Statistical processing of the results was performed using the IBM SPSS Statistics Base v. 22 statistical software package. Descriptive statistics were used in the statistical analysis of the obtained data; the comparison of the mean values of the variables was carried out using parametric methods (Student's t-test) with the normal distribution of the features expressed in the interval scale. Differences with a significance level greater than 95% ($p < 0.05$) were considered significant. Compliance with the law of normal distribution of features was tested using the Shapiro-Wilk method.

Results and discussion. A risk assessment for population when consuming food containing pesticide residues is mandatory in the US and European countries [7-10]. In Ukraine, when carrying out state tests of new pesticide formulations, a risk assessment for agricultural producers (professional contingents) is carried out with possible inhalation and dermal penetration of pesticide compounds. There is no assessment of any risk to non-professional contingents in the oral ingestion of pesticide active substances with food and water, risk monitoring for the population

when using contaminated products and water is not carried out.

In Ukraine, monitoring of xenobiotics is currently governed by Article 33 of the Law of Ukraine «On ensuring the sanitary and epidemiological well-being of the population», namely the Procedure for Conducting State Social and Hygienic Monitoring (Decree № 182 of February 22, 2006); Resolution of March 30, 1998 № 391 «On Approval of the Regulation On the State Environmental Monitoring System» (as last amended № 797 dated October 18, 2017); Resolution №758 of September 19, 2018 «On Approval of the Procedure for State Water Monitoring». In 2017 Vavrinevych O.P. and the co-authors developed and substantiated the mechanism of improvement and developed the scheme of functioning of the system of state social-hygienic monitoring of fungicides in environmental objects [11].

The environmental monitoring models that exist in Ukraine today [10, 11] provide for observations of the state of the environment (air, land waters, coastal waters, soil), and the level of its pollution. The implementation of these functions is entrusted to the Ministry of Environment and other central executive organizations, which are the subjects of the state environmental monitoring system, as well as enterprises, institutions and organizations whose activities lead to or may cause environmental denaturation [12]. In addition, a scheme for the functioning of the system of social and hygienic monitoring and prevention of the negative impact of plant protection chemicals on population health has been proposed [12].

However, none of the monitoring systems provides for a risk assessment for non-professional contingents whose organism is predominantly orally administered with drinking water and foodstuffs and pesticides may be released. In addition, they do not contain specific criteria for monitoring of pesticide that affect the thyroid gland, which, as seen above, is extremely relevant to our country today.

The results of the toxicological and hygienic evaluation and study of the mechanisms of action of the investigated pesticides [2] allowed to distinguish in

addition to previously justified toxicological selection criteria for monitoring (hazard class and the allowable daily dose value), two more specific indices: impact on the thyroid gland as target organ and severity of tyrosinemia induced by pesticide (plasma tyrosine level, nmol/ml).

It has been established that in soil and climatic conditions of Ukraine the risk of soil water contamination with all investigated fungicides (isopyrazam, peniopyrad, sedaxan, fluxapiraxad) and most herbicides (acetochlor, dimethachlor, propizochlor, propizolachlor, S-metolachlor, thienecarbazone-methyl, isoxaflutol, mesotrione, glyphosate) is low and maximum possible concentrations in groundwater are low and much lower than permissible. Which is due to low rates of herbicide consumption and a small percentage of active substances in the formulations and indicates the relative safety of human health in the use of water contaminated with compounds [13, 14].

Based on the obtained data, an additional criteria for the assessment of the environmental hazards of the pesticide for monitoring system – the Groundwater and Surface Water Pollution Index (LEACH); indices of the hazard of entry into the human body (integral index of contaminated water consumption hazard (IICWCH) and the integral index of contaminated food consumption hazard (IICFCH) – were proposed.

The analysis of toxicity, mechanisms of action, risk to the environment and the human body of the investigated pesticides affecting the thyroid gland [2, 13-15], allowed to substantiate the scheme of functioning of the monitoring system for monitoring pesticides – risk factors for the development of thyroid disease as a methodic basis of prevention (fig.).

Hygienic monitoring of pesticides that affect the thyroid gland requires, first of all, areas with intensive agriculture, such as Vinnytsia, Cherkasy, Poltava, Kherson, Odesa, Mykolaiv regions. However, in other areas such monitoring is desirable as chemical plant protection products are being actively introduced into Ukrainian agriculture, including privately owned farms

that are mostly unchecked, which complicates the determination of pesticide application volumes [6].

When deciding on the need for monitoring in Ukraine for a pesticide that affects the thyroid gland, each of the proposed indicators have to be evaluated in points (table) and their total value have to be estimated. If formulations based on the test compound are used on different crops or in different soil and climatic conditions, the maximum values of the half-life periods should be taken for the assessment.

After adding all points received, the need for monitoring is evaluated as follows: for a total of 11-16 points – monitoring is

not required; 17-27 points – monitoring is desirable; 28-38 – monitoring is obligatory; 39-44 – pesticide use should be prohibited.

Conclusion. We have improved the monitoring system of pesticide that may affect the functioning of the thyroid gland, namely: it offered a point evaluation of the selection criteria for monitoring studies, proposed additional (the Groundwater and Surface Water Pollution Index (LEACH); indices of the hazard of entry into the human body (integral index of contaminated water consumption hazard (IICWCH) and the integral index of contaminated food consumption hazard (IICFCH)) and specific criteria (effect on thyroid gland as target

organ, severity of pesticide induced tyrosinemia (plasma tyrosine level, nmol/ml).

ЛІТЕРАТУРА

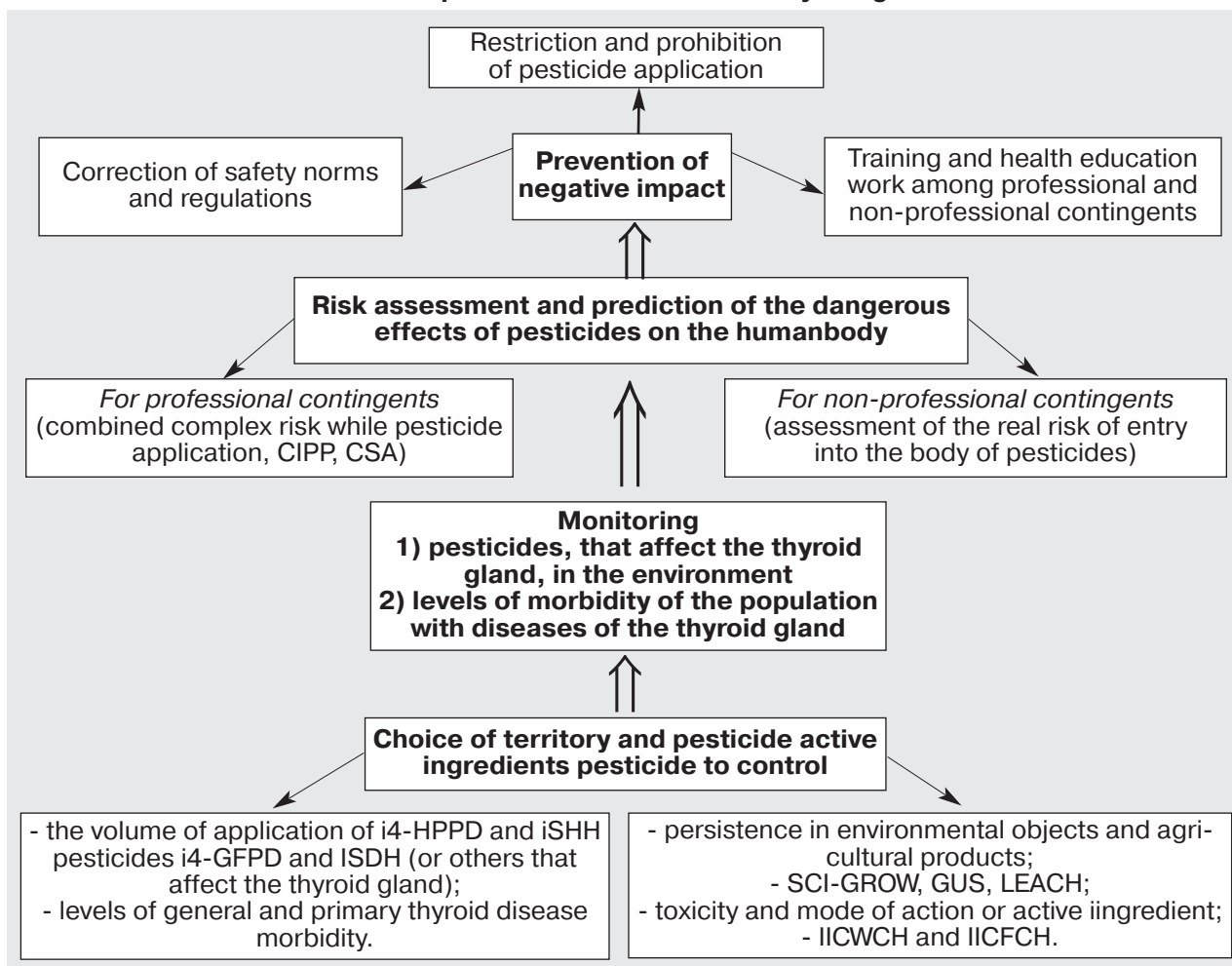
1. Sarne D. Effects of the environment, chemicals and drugs on thyroid function. *Thyroid Disease Manager*. 2010. 54 p. URL:

<https://www.ncbi.nlm.nih.gov/books/NBK285560/>

2. Antonenko A.M., Blagaia A.V., Vavrinevych O.P., Omelchuk S.T., Korshun M.M., Milokhov D.S., Pelio I.M., Bodjar I. Mechanism of action of 4-hydroxyphenylpyruvate dioxygenase inhibitor herbicide on homoterm animals and humans. *Journal of Pre-Clinical and Clinical Research*. 2015. Vol. 9. № 2. P. 148-153.

Figure

Scheme of functioning of the system of hygienic monitoring and prevention of negative effects of pesticides that affect the thyroid gland



Notes:

CIPP – the coefficient of inhalation poisoning possibility;
CSA – the coefficient of selectivity of action;
IICWCH – integral index of contaminated water consumption hazard;
IICFCH – the integral index of contaminated food consumption hazard;

LEACH – the Groundwater and Surface Water Pollution Index;
SCI-GROW – screening of maximum pesticide concentration in groundwater;
GUS – Groundwater Ubiquity Score;
i4-HPPD – 4-hydroxyphenylpyruvate dioxygenase inhibitors;
ISDH – succinate dehydrogenase inhibitors.

IMPROVEMENT OF THE MONITORING SYSTEM
IN THE ENVIRONMENT OF PESTICIDES
AFFECTING THYROIDGLAND

¹Antonenko A.M., ¹Vavrinevych O.P.,

²Omelchuk S.T., ³Shpak B.I.,

¹Korshun M.M.,

¹Bohomolets National Medical University, Kyiv,
Ukraine

²Hygiene and Ecology Institute of Bohomolets
National Medical University, Kyiv, Ukraine

³«Syngenta» LLC, Kyiv, Ukraine

Pesticides are among the chemicals most studied in terms of adverse effects on the thyroid gland. However, agriculture in most countries, especially developing ones, is heavily reliant on pesticide application, which prevents or reduces losses from pests and thus increases yields and product quality, even in terms of external attractiveness, which is often important for consumers.

Objective: The aim of the study is a hygienic substantiation of the selection criteria for monitoring and assessment of the human health risk of pesticides that may affect the thyroid gland.

Materials and methods: We used methods of laboratory and field hygiene experiments, physico-chemical (chromatographic), organoleptic, physical methods, methods of mathematical modeling and statistical analysis.

Results and discussion: When deciding on the need for monitoring in Ukraine for a pesticide

that affects the thyroid gland, each of the proposed indicators have to be evaluated in points and their total value have to be estimated. If formulations based on the test compound are used on different crops or in different soil and climatic conditions, the maximum values of the half-life periods should be taken for the assessment. After adding all points received, the need for monitoring is evaluated as follows: for a total of 11-16 points – monitoring is not required; 17-27 points – monitoring is desirable; 28-38 – monitoring is obligatory; 39-44 – pesticide use should be prohibited.

Conclusion: Thus, we have improved the monitoring system of pesticide that may affect the functioning of the thyroid gland, namely: it offered a point evaluation of the selection criteria for monitoring studies, proposed additional (the Groundwater and Surface Water Pollution Index (LEACH); indices of the hazard of entry into the human body (integral index of contaminated water consumption hazard (IICWCH) and the integral index of contaminated food consumption hazard (IICFCH)) and specific criteria (effect on thyroid gland as target organ, severity of pesticide induced tyrosinemia (plasma tyrosine level, nmol/ml).

Keywords: pesticides, selection criteria, hazard class, environmental persistency, risk for bystanders, monitoring.

3. Brucker-Davis F. Effects of Environmental Synthetic Chemicals on Thyroid Function. *Thyroid*. 2009. Vol. 8. № 9. URL

:<https://www.liebertpub.com/doi/abs/10.1089/thy.1998.8.827>.

4. Soares W.L., Porto M.F.D. Estimating the social cost of

pesticide use: An assessment from acute poisoning in Brazil. *Ecological Economics*. 2009. № 68. P. 2721-2728.

Table

Selection criteria for hygienic monitoring of pesticides that affect the thyroid gland

Criteria	Score in points, depending on the index value			
	1	2	3	4
Toxicological criteria				
Allowable daily dose (ADD), mg/kg	>0,02	0,0051–0,02	0,0021–0,005	0,002
Class of hazard according to State Standards 8.8.1.002-98	4	3	2	1
Impact on the thyroid gland as a target organ	Does not affect	Weak effect in animal experiments	The pronounced effect in animal experiments is likely to be realized in humans	It is proved that it is realized in humans
The severity of pesticide-induced tyrosinemia (plasma tyrosine levels, nmol/ml)	<300	300-1000	1001-1500	>1500
The hazard to environmental objects				
Half-life period (DT ₅₀) in soil, day	<11	11-30	31-120	>120
Half-life period (DT ₅₀) in water, day	<5	5-10	11-30	>30
Half-life period (DT ₅₀) in plants, day	<5	5-14	15-30	>30
the Groundwater and Surface Water Pollution Index (LEACH), units	<0,01	0,01-0,1	0,11-1,0	>1,0
Screening of maximum pesticide concentration in groundwater (SCI-GROW), µg/l	<1,0×10 ⁻³	1,0×10 ⁻³ - 1,0×10 ⁻²	1,1×10 ⁻² - 1,0×10 ⁻¹	>1,0×10 ⁻¹
The hazard to humans				
Integral index of contaminated water consumption hazard (IICWCH), points	4	5-6	7-8	9
Integral index of contaminated food consumption hazard (IICFCH), points	4	5-6	7-8	9

5. Damalas Ch.A., Eleftherohorinos I.G. Pesticide Exposure, Safety Issues, and Risk Assessment Indicators. *International Journal of Environmental Research and Public Health*. 2011. № 8 (5). P. 1402-1419.
6. Antonenko A.M., Vavrinevych O.P., Korshun M.M., Omelchuk S.T. Hygienic assessment of the effects of pesticides application on adult population morbidity with thyroid gland diseases. *Wiadomości Lekarskie*. 2018. T. LXXI. № 2 (cz. II). P. 353-357.
7. US EPA. Overview of Risk Assessment in the Pesticide Program. URL: <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/overview-risk-assessment-pesticide-program> (date of access: 05.09.2019).
8. European Food Safety Authority. Exposure to pesticides data for residents and bystanders, and for environmental risk assessment. URL: <https://data.europa.eu/euodp/data/dataset/exposure-to-pesticides-data-for-residents-and-bystanders-and-for-environmental-risk-assessment> (date of acceptance: 05.09.2019).
9. Regulating Pesticides through Risk Assessment. National Pesticide Information Center. URL: <http://npic.orst.edu/reg/risk.html> (date of access: 05.09.2019).
10. Guidance of EFSA: Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. *European Food Safety Authority (EFSA) Journal*. 2014. № 12 (10). P. 3874-3924.
11. Vavrynevych O.P. Hygienic substantiation of scientific bases of state social-hygienic monitoring at application of fungicides in the agro-prescriptive complex of Ukraine: Author's abstract of doctor of sciences thesis : 14.02.01 / Bogomolets National Medical University. Kyiv, 2017. 42 p.
12. Ecological monitoring of the environment. The official portal of the Ministry of Ecology and Natural Resources of Ukraine. URL: <https://menr.gov.ua/content/ekologichniy-monitoring-dovkillya.html> (date of access: 29.08.2019).

13. Vavrinevych O.P., Antonenko A.M., Omelchuk S.T., Korshun M.M., Bardov V.G. Prediction of soil and ground water contamination with fungicides of different classes according to soil and climate conditions in Ukraine and other European countries. *Georgian Medical News*. 2015. № 5 (242). C. 73-84.
14. Antonenko A.M., Vavrinevych O.P., Omelchuk S.T., Korshun M.M. Comparative hygienic risk assessment of groundwater contamination by herbicides of different chemical classes and hazard prediction for human after consumption of contaminated water. *Journal of Education, Health and Sport. Poland*. 2016. № 9. P. 873-882.
15. Novohatska O.O., Stavnichenko P.V., Kondratiuk M.V., Antonenko A.M., Vavrinevych O.P., Omelchuk S.T., Bardov V.G. Comparative hygienic evaluation of behavior of different pesticides groups in soil, prediction of risk of ground water contamination and its danger for human health in areas with irrigation farming. *Rawal Medical Journal*. 2018. Vol. 43. № 1. P. 129-136.

REFERENCES

1. Sarne D. *Thyroid Disease Manager*. 2010 : 54 p. URL: <https://www.ncbi.nlm.nih.gov/books/NBK285560/>
2. Antonenko A.M., Blagaia A.V., Vavrinevych O.P., Omelchuk S.T., Korshun M.M., Milokhov D.S., Pelio I.M. and Bodjar I. *Journal of Pre-Clinical and Clinical Research*. 2015 ; 9 (2) : 148-153.
3. Brucker-Davis F. *Thyroid*. 2009 ; 8 (9). URL : <https://www.liebertpub.com/doi/abs/10.1089/thy.1998.8.827>.
4. Soares W.L. and Porto M.F.D. *Ecological Economics*. 2009 ; 68 : 2721-2728.
5. Damalas Ch.A. and Eleftherohorinos I.G. *International Journal of Environmental Research and Public Health*. 2011 ; 8 (5) : 1402-1419.
6. Antonenko A.M., Vavrinevych O.P., Korshun M.M. and Omelchuk S.T. *Wiadomości Lekarskie*. 2018 ; LXXI ; № 2 (cz. II) : 353-357.
7. US EPA. Overview of Risk Assessment in the Pesticide Program. URL: <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/overview-risk-assessment-pesticide-program> (date of access: 05.09.2019).
8. European Food Safety Authority. Exposure to Pesticides Data for Residents and Bystanders, and for Environmental Risk Assessment. URL: <https://data.europa.eu/euodp/data/dataset/exposure-to-pesticides-data-for-residents-and-bystanders-and-for-environmental-risk-assessment> (date of acceptance: 05.09.2019).
9. Regulating Pesticides through Risk Assessment. National Pesticide Information Center. URL: <http://npic.orst.edu/reg/risk.html> (date of access: 05.09.2019).
10. Guidance of EFSA: Guidance on the Assessment of Exposure of Operators, Workers, Residents and Bystanders in Risk Assessment for Plant Protection Products. *European Food Safety Authority (EFSA) Journal*. 2014 ; 12 (10) : 3874-3924.
11. Vavrinevych O.P. Hygienic Substantiation of Scientific Bases of State Social-Hygienic Monitoring at Application of Fungicides in the Agro-Prescriptive Complex of Ukraine : Author's Abstract of Doctor of Sciences Thesis / Bogomolets National Medical University. Kyiv, 2017 : 42 p.
12. Ecological Monitoring of the Environment. The Official Portal of the Ministry of Ecology and Natural Resources of Ukraine. URL: <https://menr.gov.ua/content/ekologichniy-monitoring-dovkillya.html>. (date of access: 29.08.2019).
13. Vavrinevych O.P., Antonenko A.M., Omelchuk S.T., Korshun M.M. and Bardov V.G. *Georgian Medical News*. 2015 ; 5 (242) : 73-84.
14. Antonenko A.M., Vavrinevych O.P., Omelchuk S.T. and Korshun M.M. *Journal of Education, Health and Sport*. 2016 ; 6 (9) : 873-882. <http://doi.org/10.5281/zenodo.161844>
15. Novohatska O.O., Stavnichenko P.V., Kondratiuk M.V., Antonenko A.M., Vavrinevych O.P., Omelchuk S.T. and Bardov V.G. *Rawal Medical Journal*. 2018 ; 43 (1) : 129-136. *Надійшла до редакції 18.08.2019*