UDC 614.777; 664.001.25 (07)
DOI: 10.21668/health.risk/2018.4.14.eng

Read online

GENETICALLY MODIFIED FOOD PRODUCTS: DEVELOPMENT OF SAFETY ASSEESSMENT SYSTEM IN RUSSIA

N.V. Tyshko, E.O. Sadykova

Federal Research Center for Nutrition, Biotechnology and Food Safety, 2/14 Ust'inskiy lane, Moscow, 109240, Russian Federation

The paper gives an overview of basic approaches to assessing safety of genetically modified organisms (GMOs) that are used in food products manufacturing. It contains data on overall volumes of GMOs production in the world and outlines basic trends in development of GMOs safety assessment in the Russian Federation.

In Russia a system for GMOs safety assessment was first created on the basis of domestic experience accumulated via medical and biological research on protein products of microbiological synthesis taking into account all the approaches that existed in the world. A combined algorithm was substantiated; the algorithm includes examinations of GMOs properties and obligatory examinations in vivo: toxicological ones performed via a chronic experiment on rats; allergic ones performed via a modeling experiment on rats; immunologic and genotoxic ones performed via experiments on mice. The system was developed further as, first of all, there was a search for biomarkers that allow to make toxicological research more sensitive; secondly, reproductive functions and offspring development were studied. Experts confirmed that parameters of apoptosis activity could be used as biomarkers; reproductive functions and offspring development were studied over several generations; the most sensitive parameters of rats' reproductive functions were determined under modeled toxic exposure; experts examined an influence exerted on reproductive functions by the seasonal factor and studied prenatal and postnatal development of offspring. New requirements to conducting medical and biological assessment of GMOs were formulated. Starting from 2011, reproductive toxicity of GMOs has been an obligatory part in the state certification of new GM products.

Requirements to safety assessment of GMOs with combined features have been developed on the basis of domestic and international experience; these requirements correspond to regulation principles for GMOs application in food products.

Key words: *genetically modified organisms, food products, safety assessment, biological markers.*

Scientific developments in molecular biology and genetic engineering have allowed to create new selection techniques based on targeted modifications of plants genomes. From 1996 to 2016 areas where genetically modified crops are being grown have increased worldwide by more than 100 times and have achieved a total square equal to 185.1 million ha [1, p. 2]; 28 various plants have GM analogues and overall number of existing GM lines is 495, 462 out of them being agricultural crops (Table 1) [2]. Basic GM cultures are soya with its crops being grown on 91.4 million ha (49 % from the total square of GMO crops and 78 % from the total area where soya crops are grown); corn grown on 60.6 million ha (33 % and 33 % respectively); cotton, 22.3 million ha (12 % and 64% respectively); rape, 8.6 million ha (5 % and 24% respectively) [1, p. 90].

Food and forage manufactured from genetically modified vegetable organisms have appeared on the market and it has led to a necessity to develop approaches to complex assessment of such products, first of all, safety assessment. A procedure for assessing safety of GM food was first introduced in 90ties last century; apart from analyzing properties of a donor-organism and a recipient-organism, a technique for genetic modification, and characteristics of a newly obtained organism, it assessed safety of a new protein expressed on the basis of recombinant DNA and equivalence of GMO chemical structure and its traditional analogue

Nadezhda V. Tyshko – Candidate of Medical Sciences, Head of the Laboratory for Safety Assessment of Biological Technologies and New Food Sources (e-mail: tnv@ion.ru; tel.: +7 (495) 698-53-64; ORCID: https://orcid.org/0000-0002-8532-5327).

Elvira O. Sadykova – Candidate of Biological Sciences, Senior Researcher at the Laboratory for Safety Assessment of Biological Technologies and New Food Sources (e-mail: seo@ion.ru; tel.: +7 (495) 698-53-64; ORCID: https://orcid.org/0000-0001-5446-5653).

Table 1

Plants and cultures with GM analogues (as per July 2017)

No.	Culture	Number of GM lines	Number of lines with combined features obtained via hybridization
Agricultural plants			
1	Aubergine	1	–
2	Beans	1	–
3	Melon	2	–
4	Marrow	2	–
5	Potato	47	–
6	Corn	233	187, out of them 63 (2x), 67 (3x), 41 (4x), 12 (5x), 4 (6x)
7	Flax	1	–
8	Papaya	4	–
9	Wheat	1	–
10	Rape	43	24, out of them 12 (2x), 2 (3x)
11	Rice	7	–
12	Sugar beet	3	–
13	Sugar cane	4	–
14	Sweet pepper	1	–
15	Plum	1	–
16	Soya	36	11, out of them 9 (2x), 1 (3x), 1 (4x)
17	Tomato	11	–
18	Cotton	58	23, out of them 12 (2x), 7 (3x), 4 (4x)
19	Chicory	3	–
20	Apple	3	–
Other plants			
21	Cloves	19	–
22	Lucerne	5	2 (2x)
23	Petunia	1	–
24	Bent	1	
25	Rose	2	–
26	Tobacco	2	–
27	Poplar	2	–
28	Gum tree	1	–

No.	Culture	Number of GM lines	Number of lines with combined features obtained via hybridization
Agricultural plants			
1	Aubergine	1	–
2	Beans	1	–
3	Melon	2	–
4	Marrow	2	–
5	Potato	47	–
6	Corn	233	187, out of them 63 (2x), 67 (3x), 41 (4x), 12 (5x), 4 (6x)
7	Flax	1	–
8	Papaya	4	–
9	Wheat	1	–
10	Rape	43	24, out of them 12 (2x), 2 (3x)
11	Rice	7	–

12	Sugar beet	3	–
13	Sugar cane	4	–
14	Sweet pepper	1	–
15	Plum	1	–
16	Soya	36	11, out of them 9 (2x), 1 (3x), 1 (4x)
17	Tomato	11	–
18	Cotton	58	23, out of them 12 (2x), 7 (3x), 4 (4x)
19	Chicory	3	–
20	Apple	3	–
Other plants			
21	Cloves	19	–
22	Lucerne	5	2 (2x)
23	Petunia	1	–
24	Bent	1	
25	Rose	2	–
26	Tobacco	2	–
27	Poplar	2	–
28	Gum tree	1	–

as per basic macro- and micro-nutrients, minor substances, anti-nutrients, natural and anthropogenic contaminants, and characterized technological parameters of GM vegetable raw materials [3, p. 30–39; 4, p. 10–13; 5, p. 6–9; 6, p. 4–11] as well. This approach to GMO assessment underlies national systems that nowadays exist in different countries all over the world.

A Russian system for GMO safety assessment was first created in 1995–1996. The system was developed on the basis of domestic experience in medical and biological research performed on protein products of microbiological synthesis [7, p. 59–70], as well as taking into account existing international approaches [3, p. 30–39; 4, p. 10–13; 5, p. 6–9;6, p. 4–11]. It was a combined algorithm that, apart from the above mentioned examinations of GMO properties, included an obligatory set of examinations *in vivo:* toxicological ones performed as a chronic experiment on rats; allergic ones performed as a model experiment on rats; immunological and genotoxic ones performed as experiments on mice (MG 2.3.2.970–00, 2000)[1]. Starting from safety assessments performed for the first GM lines that were subject to state registration the system has been recognized on the international level and has been qualified as the strictest one among similar systems applied for assessing GMO safety. Experience in GMO examinations accumulated in Russia over 1999–2005 confirmed that the approach was quite efficient; however, development of toxicological examinations methodology as well as a stable trend for a growth in squares of GM agricultural crops and GM lines and plants with GM analogues that appeared at that time made it necessary to develop the system for safety assessment further and in an advance mode.

There are some promising lines of development for the GMO safety assessment; first of all, it is searching for biological markers that allow to increase sensitivity of toxicological examinations; secondly, examination of reproductive functions and offspring development. Accomplished examinations confirmed that it was possible to apply parameters of apoptosis activity as biomarkers [8, p. 35;9, p. 997; 10, p. 194; 11, p. 213; 12, p.172;13, p. 203], and reproductive functions and offspring development in subsequent generations

[1] MG 2.3.2.970-00. medical and biological assessment of food products obtained from genetically modified sources: Methodical Guidelines [web-source] // KODEKS: an electronic fund of legal and reference documentation. – URL: http://docs.cntd.ru/document/1200006955 (date of visit July 05, 2018).

were studied as well, and it allowed to determine the most sensitive parameters of rats' reproductive function under model toxic exposure and to study influence exerted by seasonality factor on the reproductive function, prenatal and postnatal development of offspring [14, p. 45–47; 15, p. 24; 16, p. 259; 17, p. 334–339;18, p. 73;19, p. 36–42]. Eventually, new requirements to medical and biological GMO assessment were formulated and fixed in the methodical guidelines 2.3.2.2306–07[2]. Starting from 2011, assessment of GMP reproductive toxicity has been obligatory within state registration procedures for new GM lines.

According to an existing non-official classification, nowadays vegetable GMOs include the first generation cultures, as well as cultures belonging to the second, third, and subsequent ones. GM cultures of the first generation distributed on the world food market and created in 1994–2004 have better agronomic properties such as resistance to pesticides, pests, viruses, fungal infections, and new consumer properties. In the early 2000s it was assumed [20, p. 849–851] the GM cultures of the second and subsequent generations, apart from improved agronomic properties, would have longer shelf life, greater nutrient value and better taste; they would be free of allergens and able to produce immune preparations and medications; their blooming and fruiting periods would be changed as well as shapes and quantities of their fruits; their photosynthesis would be more efficient; they would produce nutrients with greater assimilation etc. However, most GM cultures belonging to the second generation are similar in their properties to those of the first one and the only difference between them is that the former were produced with more sophisticated and developed techniques for plants genomes transformation; such techniques allow to avoid application of marker genes associated with resistance to antibiotics or regulatory transcription elements (promoters and terminators). Besides, a considerable number of GM cultures belonging to the second generation are so called "hybridization stacks" (or GM stacks) obtained via conventional crossing of two or more GMO lines that are characterized with a combination of features inherent to parent GM lines. Therefore, this non-official classification to great extent deals with a period when GMO were created. In spite of being widely used, it is rather provisional and doesn't allow to unambiguously classify GM objects as per their specific properties.

Occurrence of GMO with combined features and a growth in their output worldwide (Table 1) made it necessary to create new approaches to safety assessment and state registration of such GMO in the Russian Federation (in 2015 corps of such GMO were grown on 58.5 million ha which accounted for 33 % of all the areas where GM cultures were grown, and in 2016 it was 75.4 million ha or 41% of the overall areas with GM crops) [1, p. 94; 21, p. 34]. Analysis of the world experience accumulated in the sphere proves it is necessary to differentiate a set of examinations depending on a technique which was applied to obtain GMO with combined features; the first technique, or Transformation stack, means a new gene (or genes) is introduced into a genome of an already existing and previously registered GMO with a genetic engineering technique; the second one, or Molecular stack, means that a genome belonging to a donor plant is transformed by genetic engineering with a vector or multiple vectors that contain two or more genes responsible for new properties; the third one, or Breeding stack, means that two already existing GMO are used as two parents forms to obtain a hybrid with conventional selection. Lines which are obtained with transformation or molecular stack are considered to be new GMO and are subject to complete registration

[2] Surveillance over manufacturing and distribution of GMO-containing food products: A collection of methodical guidelines. Part 2 [web-source]. – M., 2008. –URL:http://files.stroyinf.ru/Data2/1/4293785/4293785688.htm (date of visit July 05, 2018).

procedures [22, p. 1; 23, p. 2]. To regulate hybrid GMO application is the most difficult issue as it is impossible to identify such products as PCR-analysis results reveal two (and more) GMO lines in such a way as if there is a mixture of them. Lines obtained via hybridization are treated in different way in various jurisdictions; they are considered to be a conventional selection product in the USA, Canada, Australia, and New Zealand and are not subject to a state registration provided that the initial GM lines have already been registered [24, p. 45]; but each new GMO obtained with already registered parents GM lines should be registered again in the EU countries, however, as long as safety is concerned, registration only deals with possible effects produced by interaction between two proteins (genes) that provide occurrence of new properties.

It is should be taken into account, that when a GMO with combined features obtained via hybridization of three or more parent lines (GMO of higher order) is registered, it means that all possible combinations created due to genetic segregation of such GMO (splitting of features in F1 and higher generations according to Mendel law) should be considered automatically registered. For example, if we register a GMO obtained via hybridization of six parent lines, we should also register all 63 possible hybrids that belong to F1 generation and contain recombinant DNA. A similar approach is applied in the European Union, Argentina, Brazil, the Philippines, Paraguay, Uruguay, and Japan [25, p. 8; 26; 27].

Basing on the analysis of domestic and international experience, experts have developed requirements to assessing safety of GMO with combined features; these requirements should correspond to principles of control over GMO application as food products generalized in MG 2.3.2.3388-16[3]. The requirements are very close to a system for GMO safety assessment existing in Russia, the only basic difference concerns only GMO with combined features obtained via hybridization: in case initial GM lines have already undergone state registration on the Customs Union territory, a simplified set of examinations can be applied. Safety assessment in such cases should include expert analysis and estimation of data submitted by an applicant as well as initial GM lines submitted/obtained at a registration stage; expert assessment of techniques for GMO detection, identification, and quantification; confirmation whether Parameters of GMO safety and quality (contents of toxic elements, mycotoxins, radionuclides, pesticides, etc.) conform to requirements fixed by the Customs Union Technical Regulations (TP TC 021/2011 "On food products safety" and/or corresponding Technical Regulations that fix obligatory requirements to specific food products)[4]. Experts should also analyze data on compositional equivalence of initial GM lines and their conventional analogues (macro- and micronutrients contents), results of toxicological, allergic and other research, as well as results of post-registration monitoring accomplished in countries where GMO with combined features have been registered earlier.

When developing approaches to assessing safety of GMO with combined features obtained via hybridization, experts were guided by two preconditions: first, advisability of requirements (they should be based on analysis of scientific literature, approaches to GMO safety assessment existing both in Russia and abroad, accumulated scientific base [28, p. 2–14; 29, p. 1845–1849; 30, p. 71–73; 31, p. 104–107]); second, possibilities to make sure these requirements are met (since GMO obtained with hybridization can be identified only basing on inspection of documents as results of PCR analysis performed on such GMO reveal only occurrence of parent GM lines in a sample as if it contains a mixture of them, and a manufac-

[3] MG 2.3.2.3388-16. Medical and biological assessment of safety of vegetable GMO with combined features: Methodical guidelines [web-source] // KODEKS: an electronic fund of legal and reference documentation. – URL: http://docs.cntd.ru/document/456042958 (date of visit July 05, 2018).

[4] CU TR 021/2011. On food products safety: The Customs Union Technical Regulations [web-source] // KODEKS: an electronic fund of legal and reference documentation. – URL: http://docs.cntd.ru/document/902320560 (date of visit July 05, 2018).

turer can always register separate lines and not a combined development). GM soya belonging to MON87701×MON89788 line is the only example of GMO with combined features that can be unambiguously determined with PCR technique; it is due to MON87701 line being commercially distributed only when it is combined with another line. Obviously, in a situation when there are the strictest requirements to confirming safety of GMO with combined features and with parent lines already been examined and registered on the Customs Union territory, most such GMO will remain beyond regulation. The suggested approach creates conditions that are utmost favorable for a manufacturer to enter legal frameworks and can provide a possibility to control GMO with combined features. Naturally, such approach can be applied only to GMO with their parent lines being profoundly examined and allowed for use as food products.

To sum up, an issue of GMO regulation is a complicated one and it requires maximum possible interaction between controlling authorities and manufacturers, creation of an open and transparent system that will allow to meet requirements fixed in the Federal Law No.358-FZ issued on July 03, 2016[5] and an assignment by the RF President No. Pr-1178 issued on June 22, 2016[6] on providing monitoring over impacts exerted by GMO people and the environment.

Funding. The work has been accomplished due to support by a grant provided by the Russian scientific fund No. 16-16-00124

Conflict of interests. The authors state there is no any conflict of interests.

References

1. Global Status of Commercialized Biotech/GM Crops: 2016. *ISAAA Brief*. No. 52. ISAAA: Ithaca, NY, 2016, 125 p. Available at: https://www.isaaa.org/resources/publications/briefs/52/download/isaaa-brief-52-2016.pdf (10.07.2017).

2. GM Approval Database. *ISAAA Editorial Policy.* Available at: http://www.isaaa.org/gmapprovaldatabase/ (10.07.2017).

3. Strategies for assessing the safety of foods produced by biotechnology. Report of a Joint FAO/WHO Consultation. Geneva, World Health Organization, 1991. Available at: http://apps.who.int/iris/bitstream/handle/10665/41465/9241561459-eng.pdf?sequence=1&isAllowed=y (10.07.2017).

4. Safety evaluation of foods derived by modern biotechnology: concepts and principles. Paris, Organization for Economic Co-operation and Development (OECD), 1993, 77 p. https://www.oecd.org/science/biotrack/41036698.pdf (10.07.2017).

5. Application of the principles of substantial equivalence to the safety evaluation of foods or food components from plants derived by modern biotechnology. Report of a WHO Workshop. Geneva, World Health Organization, WHO/FNU/FOS/95.1. WHO, 1995. Available at: http://apps.who.int/iris/bitstream/10665/58909/1/WHO_FNU_FOS_95.1.pdf (10.07.2017).

6. Biotechnology and food safety. Report of a joint FAO/WHO consultation. Rome, FAO, 1996. Available at: http://www.fao.org/ag/agn/food/pdf/biotechnology.pdf (10.07.2017).

7. Mediko-biologicheskie issledovaniya uglevodorodnykh drozhzhei (1964–1970 gg.) [Biomedical studies of hydrocarbon yeast (1964–1970)]. In: A.A. Pokrovskoii ed. Moscow, Nauka Publ., 1972, 145 p. (in Russian).

8. Tyshko N.V., Selyaskin K.E., Tutel'yan V.A. Opredelenie naibolee chuvstvitel'nykh metodov dlya otsenki aktivnosti apoptoza v organakh krys na modeli toksicheskogo vozdeistviya tetrakhlormetana [Determination of the most sensitive methods for assessing the activity of apoptosis in rat organs on the model of toxic effects of carbon tetrachloride]. *Mezhdunarodnyi zhurnal eksperimental'nogo obrazovaniya*, 2015, no. 2–1, pp. 34–36 (in Russian).

[5] On making amendments into certain legal acts of the Russian Federation concerning improvement of state regulation in the sphere of genetic engineering: The Federal Law issued on July 03, 2016 No. 358-FZ [web-source] // KonsultantPlus. – URL: http://www.consultant.ru/document/cons_doc_LAW_200732/ (date of visit October 01, 2018).

[6] A list of assignments as per results of "the Direct Line with Vladimir Putin": The assignment by the RF President sated June 22, 2016 No. Pr-1178. [web-source] // GARANT.RU. – URL: http://www.garant.ru/products/ipo/prime/doc/71874466/ (date of visit October 01, 2018).

9. Tyshko N.V., Selyaskin K.E., Tutel'yan V.A. Detection of rat internal organs apoptosis activity based on model of ccl4 toxic effects. *Fundamental'nye issledovaniya*, 2014, no. 10 (pert 5), pp. 993–998 (in Russian).

10. Tyshko N.V., Selyaskin K.E., Tutel'yan V.A. Ispol'zovanie pokazatelei aktivnosti apoptoza v kachestve sistemnykh biomarkerov pri otsenke bezopasnosti GMO (stat'ya) [Using indicators of apoptosis activity as systemic biomarkers in assessing the safety of GMOs (article)]. *Transgennye rasteniya: tekhnologii sozdaniya, biologicheskie svoistva, primenenie, biobezopasnost': Materialy V Vserossiiskogo simpoziuma*. Moscow, 2014, pp. 192–195 (in Russian).

11. Tyshko N.V., Selyaskin K.E., Tutel'yan V.A. Pokazateli aktivnosti apoptoza v kachestve chuvstvitel'nykh biomarkerov pri otsenke bezopasnosti pishchevoi produktsii, poluchennoi s ispol'zovaniem sovremennykh biotekhnologii [Indicators of apoptosis activity as a sensitive biomarker in assessing the safety of food products obtained using modern biotechnology]. *Sovremennye tekhnologii produktov pitaniya: Materialy mezhdunarodnoi nauchno-prakticheskoi konferentsii*. Kursk, 2014, pp. 210–213 (in Russian).

12. Shestakova S.I., Zhminchenko V.M., Pashorina V.A., Sadykova E.O., Timonin A.N., Tyshko N.V. Izmenenie aktivnosti apoptoza v organakh krys linii Vistar na raznykh etapakh ontogeneticheskogo razvitiya [Changes in the activity of apoptosis in the organs of Wistar rats at different stages of ontogenetic development]. *Voprosy pitaniya*, 2015, vol. 84 (prilozhenie), no. 3, pp. 172–174 (in Russian).

13. Sadykova E.O., Tyshko N.V., Khismatullina Z.R. Ispol'zovanie pokazatelei apoptoza v kachestve biomarkerov vozdeistviya ekotoksikantov [Using apoptosis indicators as biomarkers of exposure to ecotoxicants]. *Materialy shkoly molodykh uchenykh «Osnovy zdorovogo pitaniya i puti profilaktiki alimentarno-zavisimykh zabolevanii»*. Moscow, 2016, pp. 201–205 (in Russian).

14. Utembaeva N.T., Pashorina V.A., Selyaskin K.E., Tyshko N.V. Methodical approaches to studying influence of seasonal factor on rat reproductive function in experiments on alimentary influence. *Voprosy pitaniya*, 2009, vol. 78, no. 1, pp. 43–48 (in Russian).

15. Tyshko N.V., Zhminchenko V.M., Pashorina V.A., Saprykin V.P., Selyaskin K.E., Utembaeva N.T., Tutel'yan V.A. Assessment of the impact of GMO of plant origin on rat progeny development in 3 generations. *Voprosy pitaniya*, 2011, vol. 80, no. 1, pp. 14–28 (in Russian).

16. Zhminchenko V.M., Pashorina V.A., Selyaskin K.E., Tyshko N.V. Otsenka reproduktivnoi toksichnosti v mediko-biologicheskikh issledovaniyakh biotekhnologicheskoi produktsii: osobennosti postanovki eksperimenta [Assessment of reproductive toxicity in biomedical research of biotechnological products: features of the experiment]. *Voprosy pitaniya*, 2014, vol. 83, no. 3, pp. 258–259 (in Russian).

17. Tyshko N.V., Zhminchenko V.M., Selyaskin K.E., Pashorina V.A., Utembaeva N.T., Tutelyan V.A. Assessment of the impact of genetically modified LibertyLink® maize on reproductive function and progeny development of Wistar rats in three generations. *Toxicology Reports*, 2014, vol. 1, pp. 330–340. DOI: 10.1016/j.toxrep.2014.05.013

18. Tyshko N.V., Zhminchenko V.M., Pashorina V.A., Saprykin V.P., Selyaskin K.E., Utembaeva N.T., Tutel'yan V.A. Evaluation of the effect of genetically modified plants on rat progeny development. *Gigiena i sanitariya*, 2011, no. 6, pp.73–77.

19. *Tyshko N.V., Selyaskin K.E., Mel'nik E.A., Pashorina V.A., Zhminchenko V.M.* The separate and combined effects of calcium pantothenate deficiency and cadmium intoxication on rat reproductive function. *Voprosy pitaniya*, 2012, vol. 81, no. 1, pp. 33–43 (in Russian).

20. Vasil I.K. The science and politics of plant biotechnology – a personal perspective. *Nature biotechnology*, 2003, vol. 21, no. 8, pp. 849–851.

21. Parisi C., Tillie P., Rodríguez-Cerezo E. The global pipeline of GM crops out to 2020. *Nature Biotechnology*, 2016, vol. 34, no. 1, pp. 31–36. DOI:10.1038/nbt.3449.

22. Guidance Document of the Scientific Panel on Genetically Modified Organisms for the risk assessment of genetically modified plants containing stacked transformation events. *EFSA Journal*, 2007, vol. 512, pp. 1–5.

23. Commission Implementing Regulation (EU) No 503/2013 of 3 April 2013 on applications for authorisation of genetically modified food and feed in accordance with Regulation (EC) No 1829/2003 of the European Parliament and of the Council and amending Commission Regula-

tions (EC) No 641/2004 and (EC) No 1981/2006. Available at: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:157:0001:0048:EN:PDF (10.07.2017).

24. Proposed Rule: Premarket Notice Concerning Bioengineered Foods. Federal Register, 66. US Food and Drug Administration. Washington, FDA, 2001, pp. 4706–4738.

25. Panel on Genetically Modified Organisms (GMO); Scientific Opinion on Guidance for risk assessment of food and feed from genetically modified plants. *EFSA J. EFSA*, 2011, vol. 2150, pp. 1–37.

26. European Food Safety Authority (EFSA). Available at: http://www.efsa.europa.eu/ (10.07.2017).

27. Organisation for Economic Co-operation and Development (OECD). Available at: http://www.oecd.org/ (10.07.2017).

28. Kramer C., Brune P., McDonald J., Nesbitt M., Sauve A., Storck-Weyhermueller S. Evolution of risk assessment strategies for food and feed uses of stacked GM events. *Plant Biotechnol. J.*, 2016, pp. 1–15. Available at: https://www.onlinelibrary.wiley.com/doi/full/10.1111/pbi.12551 (10.07.2017).

29. Weber N., Halpin C., Hannah L.C., Jez J.M., Kough J., Parrott W. Editor's choice: crop genome plasticity and its relevance to food and feed safety of genetically engineered breeding stacks. *Plant Physiol*, 2012, vol. 160, pp. 1842–1853.

30. De Schrijver A., Devos Y., Van den Bulckea M., Cadot P., De Loose M., Reheul D., Sneyers M. Risk assessment of GM stacked events obtained from crosses between GM events. *Trends Food Sci. Technol*., 2007, vol. 18, pp. 101–109. DOI:10.1111/pbi.12551

31. Kok E., Pedersen J., Onori R., Sowa S., Schauzu M., De Schrijver A., Teeri T. Plants with stacked genetically modified events: to assess or not to assess? *Trends Biotechnol*., 2014, vol. 32, pp. 70–73. DOI: 10.1016/j.tibtech.2013.12.001

Tyshko N.V., Sadykova E.O. Genetically modified food products: development of safety asseessment system in Russia. Health Risk Analysis, 2018, no. 4, pp. 119–126. DOI: 10.21668/health.risk/2018.4.14.eng

Received: 16.09.2018
Accepted: 18.12.2018
Published: 30.12.2018