Final Project Report

1. General Information

1.1. Program and Project information	
Name of the Program:	**PROMIS**
Name of the Project:	**A Bioinformatics Approach to Dairy Cattle Breeding using genomics selection**
The Project acronym:	**BioITGenoSelect**
Total Project budget:	**169.769,96**
Project realization period (from dd/mm/yyyy to dd/mm/yyyy):	Start date:22.07.2020. — End date:21.01.2023.
Project Website[1]:	bioitgenoselect.polj.uns.ac.rs
Reporting period:	**Final Project Report**

1.2. Project participants information	
1.2.1. Principal Investigator (PI) and Lead Science and Research Organization (SRO)	
Name and last name of the PI:	**LjubaŠtrbac**
Academic and/or research title of the PI:	**Assistant professor, PhD**
Lead SRO name:	**University of Novi Sad, Faculty of Agriculture**
Lead SRO authorized person (legal representative) name and last name:	**NedeljkoTica**

1.2.2. Project Partners - Science and Research Organizations (SRO) [2]	
SRO name:	**University of Novi Sad, Faculty of Science**
SRO authorized person (legal representative) name and last name:	**Milica Pavkov Hrvojević**
SRO name:	**University of Novi Sad, Faculty of Technical Science**

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[1] If the project does not have website, enter N/A

[2] Copy this table as needed to provide information for all Partner SROs

SRO authorized person (legal representative) name and last name:	**Srdjan Kolaković**

2. Project Summary

2.1. Project and Progress Summary – Please refer to the project objectives, methodology, achieved results during project implementation and expected impact.

Please present the project`s most significant results in a way that is comprehensible to the general public.

The Project summary can be used by the Science Fund of the Republic of Serbia for promoting and demonstrating the value and impact of the Project.

English (up to 500 words):

The general goal of the project was to improve livestock production through genetic improvement with the application of modern methods in the field of genetics, animal breeding and informatics, which open the way to the development of new tools for more efficient breeding schemes. The main objectives of the project were: formation of a database on pedigrees and production results of dairy cattle, genotyping of animals with the aim of starting the formation of a reference population, development of software tools for easier management of this data, development of statistical models for the evaluation of genomic breeding values and education of breeders and experts in breeding organizations to interpret different sources of information.

First phase of the project was related to equipment procurement for the isolation and quality control of DNA, and the collection of data on the origin and production characteristics of dairy cows (milk yield, milk fat yield, content of milk fat, milk protein yield and content of milk protein). Software tools were developed that were used for normalization of data and automatic preparation for appropriate analyses. The second phase referred to the implementation of quantitative genetic analyses, i.e. calculation of population parameters and prediction of classic breeding values. In the next phase, based on the obtained predictions, cows were selected for genotyping from a total of 7 farms in the territory of AP Vojvodina. Sampling was organized and performed by plucking the hair from the cows' tails. Samples were prepared and sent to the laboratory where genome analysis was performed using 100k SNP chips. After receiving the genotyping result, training was organized at the Biotechnical Faculty in Ljubljana, and after that, the development of models for prediction genomic breeding values was started. In the final phase trainings and lectures were organized for experts in breeding organizations and breeders in order to use the available information more effectively.

A multidisciplinary team of researchers performed the aforementioned tasks, which resulted in the following: a laboratory for molecular genetics at the Faculty of Agriculture in Novi Sad was equipped; a database was formed; software tools were developed; genealogical analyses and prediction of breeding values were carried out; the formation of a reference population was started through the genotyping of 1,600 cows; genomic breeding values were predicted.

The obtained results have multiple impacts on the further development of this branch of animal husbandry. The practical importance is reflected in the fact that modern models have been defined for predicting breeding values of cows that breeders will be able to use when defining breeding programs in their own herds with the aim of increasing milk production. The scientific importance is reflected in the opportunity that members of the research team could use modern methods in the field of genetics and animal breeding, which partly rely on achievements in the field of bioinformatics. Creation of a unique database is a basic prerequisite for an accurate analysis of economically important traits in dairy cattle, using methods that are recognized at the international level.

Serbian (up to 500 words):

Opšti cilj projekta je bio unapređenje stočarske proizvodnje putem genetskog poboljšanja uz primenu savremenih metoda iz oblasti genetike, oplemenjivanja životinja i informatike koje otvaraju put ka razvoju novih alata za efikasnije šeme uzgoja. Glavni ciljevi projekta su bili: formiranje baze podataka o pedigreima i proizvodnim rezultatima mlečnih goveda, genotipizacija životinja sa ciljem da se započne formiranje referentne populacije, razvoj softverskih alata za olakšano upravljanje ovim podacima, razvoj statističkih modela za procenu genomskih oplemenjivačkih vrednosti i edukacija odgajivača i stručnjaka u odgajivačkim organizacijama za tumačenje različitih izvora informacija.

Prva faza projekta se odnosila na nabavku opreme za izolaciju i proveru kvaliteta izolovane DNK, a zatim i na prikupljanje podataka o poreklu i proizvodnim osobinama mlečnih krava (količina mleka, količina mlečne masti, sadržaj mlečne masti, količina mlečnih proteina i sadržaj mlečnih proteina. Razvijani su softverski alati koji su upotrebljeni za normalizaciju podataka i automatsku pripremu za odgovarajuće analize. Druga faza projekta se odnosila na sprovođenje kvantitativno genetskih analiza, odnosno izračunavanje parametara populacije i procena klasičnih oplemenjivačkih vrednosti. U sledećoj fazi su na osnovu dobijenih procena odabrana grla za genotipizaciju sa ukupno 7 farmi na teritoriji AP Vojvodine. Zatim je organizovano uzorkovanje (čupanjem dlake iz repa krava), priprema i slanje uzoraka u laboratoriju gde je izvršena analiza genoma upotrebom 100k SNP čipa. Nakon dobijanja rezultata genotipizacije organizovana je obuka na Biotehničkom fakultetu u Ljubljani i nakon iste pristupilo se razvoju modela za procene genomskih oplemenjivačkih vrednosti. U završnoj fazi realizacije projekta organizovane su obuke i predavanja za stručnjake u odgajivačkim organizacijama i odgajivače kako bi efikasnije koristili dostupne informacije.

Tim istraživača koji je bio multidisciplinarnog karaktera obavljao je navedene zadatke što je rezultiralo sledećim: opremljena je laboratorija za molekularnu genetiku na Poljoprivrednom fakultetu u Novom Sadu; formirana je baza podataka sa podacima o životinjama; razvijeni su softverski alati koji su olakšali pripremu podataka za različite analize; sprovedene su geneološke analize i procene oplemenjivačkih vrednosti na tradicionalni način; započeto je formiranje referentne populacije putem genotipizacije 1.600 krava savremenim metodama iz oblasti genomike; procenjene su genomske oplemenjivačke vrednosti.

Dobijeni razultati imaju višestruki značaj i uticaj na dalji razvoj ove grane stočarstva. Praktični značaj se ogleda u tome što su definisani savremeni modeli za procene priplodnih vrednosti grla koje će odgajivači moći da koriste prilikom definisanja programa parenja u vlastitim stadima sa ciljem povećanja proizvodnje mleka. Naučni značaj koji se ogleda u tome da su članovi istraživačkog tima imali priliku da koriste savremene metode iz oblasti genetike i oplemenjivanja životinja koje se jednim delom oslanjaju i na dostignuća iz oblasti bioinformatike. Izrada jedinstvene baze podataka predstavlja osnovni preduslov za tačnu analizu ekonomsi važnih svojstava u mlečnom govedarstvu i to metodama koje su priznate na međunarodnom nivou.

3. Project Implementation - Final Overview

3.1. Deliverables		
3.1.1. Deliverables - Short description of deliverables achieved during project implementation		
Deliverable ID *		**Deliverable title – insert deliverable name**
1	D2.2	Data normalization software
2	D2	Initial animal database
3	D3.2	Data preparation software
4	D3	Quantitative genetic analysis
5	D4	Reference population
6	D5	Selected animals genotypes
7	D6.2	Genotype conversion software
8	D6	Calculated gEVB
9	D8.1	Project web site
10	D8.3	Published papers in scientific journals
11	D8.5	Full animal database
12	D8.6	e-catalogue
13	D8.8	Breeder training
14	D10.2a	Project report
15	D10.2b	Project report

*Based on major deliverables presented in Table 3.4 in the Project Description (Approved Project Proposal - Project Description, in accordance with the Decision of the Managing Board) and Gantt Chart (Annex 3 of the Contract on the Project financing).

3.1.2. If a deliverable is not reached, please explain - based on deliverables presented in the Project Description document and Gantt Chart (Annex 1 and Annex 3 of the Contract on the Project financing). If all deliverables scheduled during project implementation are reached, enter N/A.
N/A

*Recommended up to 250 words.

3.2. Scientific publications – top three peer reviewed publications

3.2.1. Insert the full reference of the <u>top three</u> accepted or published scientific publications resulted from the project.

	Type of scientific publication*	DOI or ISBN (for books)	Open Access (yes/no)	Full reference title with link of the publication	Publication status**
1	Publication in conference	doi: 10.1109/INFOTEH51037.2021.9400672.	no	Tarjan, I. Šenk, D. Pracner, D. Rajković and Lj. Štrbac, "Possibilities for applying machine learning in dairy cattle breeding," 2021 20th International Symposium INFOTEH-JAHORINA (INFOTEH), 2021, pp. 1-6, https://ieeexplore.ieee.org/document/9400672	published
2	Publication in conference	isbn: 978-90-8686-385-3	no	Šaran, M., Despotov, M., Trivunović, S., Ivković, M., Janković, D., Štrbac, L.J. (2022): Genetic polymorphism of milk proteins in Holstein cattle population from Serbia, The 73rd Annual Meeting of the European Federation of Animal Science, Porto, Portugal 5 - 9 September, 2022. Book of Abstracts, Wageningen Academic Publishers, p. 418, no. 28	published
3	Article in journal	https://doi.org/10.3390/ani13040597	yes	Štrbac L, Pracner D, Šaran M, Janković D, Trivunović S, Ivković M, Tarjan L, Dedović N. Mathematical Modeling and Software Tools for Breeding Value Estimation Based on Phenotypic, Pedigree and Genomic Information of Holstein Friesian Cattle in Serbia. Animals. 2023; 13(4):597.	published

Important note: state only publications that were referenced and accepted during the project realization, or up to submission of the final report.

* Type of scientific publication: article in journal, publication in conference/workshop, book/monograph/anthology, proceeding, research data etc.

** Status can only include "accepted" or "published".

3.3. Open research data					
3.3.1. Insert the full reference with the link to the open data.					
	Title with short description (specify the data in terms of size, structure, format, to whom the dataset is accessible, is it a primary or secondary data, what are the terms of use etc.)	**Link**	**Is the data set openly accessible?**	**Is the data set reusable?**	**If the dataset is linked to a publication, specify the DOI of the publication**
1	Dataset P1 – a collection of pseudonimised data prepared for breeding value processing, including milk yield and farm data, as well as genomic data for 1492 animals and additional pedigree data for about 4742 animals. The data is openly accessible and usable by anyone.	https://bioitgenoselect.polj.uns.ac.rs/genoselect/data-p1	YES	YES	**10.3390/ani13040597**
2	BioItGenoSelectdb - main cattle database of the project. Includes (among others) basic details for 250k animals and their ancesstors, primarly from Vojvodina; data on bulls available for mating; lactation data for active animals and some historic data; linear evalution data; owners and farms data. The data is not publicly available for use, dur to ownership and privacy issues. The data is available to the main breeding organisation. Part of the data are available to authorised breeding organisations. Some of the secundary data is available to the breeders on request.	https://bioitgenoselect.polj.uns.ac.rs/genoselect/	NO	YES	

3.4. Intellectual property rights resulting from the project (if applicable to this project)				
3.4.1. Insert all necessary information regarding intellectual property rights				
Type of IP Rights (patent, trademark, technical solution, industrial design etc)	**Date of the application**	**Official title of the application**	**Has the IPR protection been awarded?**	**If available, official publication number of a protection award**
			YES/NO	
			YES/NO	
			YES/NO	

4. Ethics, Environmental and Social management

4.1. Ethics risks
4.1.1. Please shortly explain if the project team faced any ethical risk during the project lifecycle and describe measures that were undertaken to overcome it.   If there was no risk faced during project implementation, enter N/A.
N/A

*Recommended up to 250 words.

4.2. Environmental and social management
4.2.1. Please describe project impact on environment and society.   In case that your research involved the use of elements that may cause harm to humans, environment, to animals or plants, if your research has negative impact to any vulnerable individuals or groups, if the new or old equipment is not disposed properly, if project implementation includes discharge of wastewater and/or requires environmental protection measures, if existing employees of the SRO(s) are not regularly registered for pension or/and disability insurance, or in case your project has any other environmental and/or social management effect, please shortly describe relevant environmental and/or social management which was undertaken. Otherwise, state N/A.
N/A

*Recommended up to 250 words.

5. Project Sustainability and International Cooperation

5.1. Project sustainability after the project realization and potential cooperation with industry

5.1.1. Please describe how you intend to secure the sustainability after the project end. Are there any new research opportunities that have been opened for the project team members or participating SROs by implementing the project? If yes, please elaborate. Otherwise, state N/A.

The obtained results will serve as a basis for proposals of changes to existing national breeding programs, and the database that was formed during the implementation of the project will continue to be updated for the needs of breeding organizations. The genotyping data obtained from the analysis of the genomes of 1600 cows were only partially investigated during the implementation of this project, and after completion, the genotyping of new cows and the implementation of various analyses will continue. There is a possibility, first of all, in the field of machine learning, the application of which was not a major part of this project.

*Recommended up to 250 words.

5.1.2. Please shortly describe if you have plan for cooperation with partner(s) from the industry after the realization of the project. Otherwise, state N/A.

During the implementation of the project, cooperation was established with farms that breed cows and produce milk, and cooperation will continue in the form of data collection and delivery of evaluation results, which the Faculty of Agriculture in Novi Sad, as a central breeding organization, calculates for the needs of implementing breeding programs.

*Recommended up to 250 words.

5.2. Have you established or have plans for collaborations with international researchers or diaspora researchers within the scope of this project or after its realization? If yes, please specify. Otherwise, state N/A.

Cooperation with the Biotechnical Faculty in Ljubljana was established. There, members of the PROMIS team attended training on the analysis of genomic information. After the implementation of the project, it is planned to apply for bilateral and EU projects with the aim of forming a common database that would be used to calculate the joint predictions of the breeding values of cows in these countries.

*Recommended up to 250 words.

6. Applications for follow-up projects

6.1. a) Have you submitted or plan to submit new project proposal to other funding agencies or to the future calls of the Science Fund of the Republic of Serbia in order to continue your research on the same/similar topic? If yes, please specify.   **b) Have you submitted or plan to submit a project proposal to internationally funded program? If yes, please specify.**
A project proposal was submitted to the Science Fund of the Republic of Serbia as part of the PRIZMA program, which partially continues this research, but emphasizes the introduction of the most modern methods for data processing, such as artificial intelligence. We are planning to submit a project proposal at the EU level with partners from Slovenia, but the corresponding invitation has not yet been announced.

*Recommended up to 250 words.

7. Project Management Information - Final Overview

7.1. Project management information – please describe the overall project management, team performance, collaboration among team members and partner institutions (management of scientific, administrative, and financial tasks, and dissemination and visibility activities).
Project management was a challenge for a number of reasons. The team was multidisciplinary with researchers from three different institutions. Each member of the team worked in accordance with the assigned tasks from the project proposal. However, the biggest problem was communication and the organization of certain field activities, primarily due to the COVID-19 pandemic. Mostly online meetings were held for a significant part of of the project. The team members cooperated with each other solving the set tasks. The realization of activities related to machine learning was difficult because the data did not arrive in the planned period due to extraordinary circumstances. The member of the project team who was in charge of that activity did not manage to implement all activities within the stipulated time, however, cooperation and research will continue to a certain extent even after the implementation of the project. The previous cooperation was improved because the team members became familiar with the activities carried out at all three institutions. Data visibility is provided through the project website, which was created and updated by researchers from SRO1 and SRO2, along with communication with other team members. Each of the researchers was in charge of writing a certain part of the scientific papers, while one (the first author) was in charge of coordinating the activities of other authors, co-authors. Administrative tasks were performed primarily by the manager in cooperation with other members who were in charge of preparing reports in the part related to their activities.

*Recommended up to 250 words.

7.2. Execution of the project

7.2.1. Please provide information on the execution of the project and implementation challenges.

The biggest challenge for the implementation of project activities was coordinating all the activities of researchers from three different institutions during the period when there was a state of emergency due to COVID-19.

*Recommended up to 250 words.

7.2.2. Please describe in what extent and what kind of support did you get from the Lead SRO and partnering SROs during the project implementation. If you have recommendations for improvement with this regard, please specify.

The Institution's support was reflected in the fact that they provided additional staff from accounting (LEAD SRO) and the project implementation department that participated in the preparation of the report. In certain activities related to the preparation of samples for genotyping and data on cows, employees of the Central Breeding Organization were also available. All price differences have been successfully compensated by funds earmarked for the institution.

*Recommended up to 250 words.

7.3. Team capacity development

7.3.1. Please provide information on contribution of the project for the research careers of project team members, including special qualifications and special possibilities / opportunities opened up by the project (especially PhD theses).

During the implementation of the project, data was collected that will be used to write one PhD thesis after the completion of the implementation of the PROMIS project. Also, leadership and participation in the Science Fund project will enable team members to advance to higher positions.
The acquired experience will be a qualification for applying to some other competitions and proposals.

*Recommended up to 250 words.

7.4. Collaboration with the SF
7.4.1. Please describe the overall cooperation and communication with the SF staff during the project realization. If you have recommendations for improvement with this regard, please specify.
Communication was correct via e-mail. Certain deadlines have been extended via mutual agreement.

*Recommended up to 250 words.

8. Promotion, Publicity, and Visibility – Final Overview

8.1. Project promotion, publicity, and visibility		
Type of dissemination and communication activities*	**Link (if available)**	**Type of audience reached**
1 Newspaper interview in the weekend edition of the NOVOSTI newspaper from March 14th 2021	https://www.novosti.rs/ekonomija/vesti/974744/softver-prave-krave-budu-zdrave-projekat-novosadskih-naucnika-unapredjenje-stocarstva-vece-izvozne-sanse	Newspaperreaders and internet viewers.
2 Segment in the TV show "Science for Economy" (ser. "NaukaPrivredi") from June 14th, 2021	https://www.youtube.com/watch?v=tqt6z8MEtdM	TV and internet viewers
3 Interview for TV show for RTSNauka about the PROMIS project	/	TV viewers
4 Workshop on 89th INTERNATIONAL AGRICULTURAL FAIR, May 26th 2022, Novi Sad	/	Breeders and experts in breeding organizations
5 Workshop on Seminar breeding organisations AP Vojvodina, June6-7th 2022, Faculty of Agriculture Novi Sad	/	Breeders and experts in breeding organizations
6 Workshop on Conference - Genomic selection in cattle breeding, September 13 th 2022,Faculty of Agriculture Beograd – Zemun	/	Breeders and experts in breeding organizations

*Organisation of a conference, organisation of a workshop, press release, non-scientific and non-peer reviewed publications (popularised publications), exhibition, flyers, training, social media, website, communication campaign (e.g. radio, TV), participation to a conference, participation to a workshop, participation to an event other than a conference or workshop, video/film, brokerage event, pitch event, trade fair,and other.

9. Final Financial Overview

9.1. Final Financial Overview		
9.1.1. An integral part of this report is Final Financial Report, which form is separately attached in Excel format. Information provided in this report should be in line with the approved budget and approved realised costs.		
Total amount received during project implementation in RSD*	**Project realised cost during project implementation in RSD****	**Unspent funds during project implementation in RSD (deviation)*****
20,032,855.22	**19,724,595.92**	**308,259.30**

*Total amount received for all SROs in total.** Total amount of realised costs for all SROs in total. *** Unspent funds during project implementation should be equal to total amount received during project implementation reduced for project realised costs during project implementation.

9.1.2. Briefly describe financial management of the project during implementation, total amount planned by the approved project budget vs amount spent, deviations and challenges that were encountered related to the financial aspects of the project management. *
Largest part of total amount received for the BioITGenoSelect was spent according to the initially approved project budget, while smaller part was transferred from categories where surpluses occurred (mainly Travel and Conferences, due to cancelations) to the Publications and Equipment. Also, some transfers happened within Equipment and Consumables categories due to the price changes, where some prices increased and other decreased. All transfers were done within the approved Budget modifications by the Science Fund. 2,612.37€ remained unspent, making just 2% of Total Budget.

*Recommended up to 250 words.

Date and signature
Under full moral, material, and criminal responsibility and aware of all legal consequences if not, we declare that information provided in Final Project Report is correct and true.

Name and last name of the authorized person

1. _____ May 18.2023

Prof. Dr. NedeljkoTicadate

2. _____   May 18.2023

Dr.LjubaŠtrbac, assistant professordate

3. _____   May 18.2023

   Prof. Dr. MilicaPavkovHrvojevićdate

4. _____   May 18.2023

   Prof. Dr. SrđanKolakovićdate

Appendix 1

	A.1. Scientific publications – full list of all scientific publications resulted from project implementation				
	A.1.1. Insert the full list of references with the link of all the publications which are <u>published or accepted</u>.				
	Type of scientific publication*	**Open Access (yes/no)**	**DOI or ISBN (for books)**	**Full reference title**	**Publication status****
1	Publication in conference	no	doi: 10.1109/INFOTEH 51037.2021.9400 672.	Tarjan, I. Šenk, D. Pracner, D. Rajković and Lj. Štrbac, "Possibilities for applying machine learning in dairy cattle breeding," 2021 20th International Symposium INFOTEH-JAHORINA (INFOTEH), 2021, pp. 1-6, https://ieeexplore.ieee.org/document/9400672	published
2	Publication in conference	no	isbn: 978-90-8686-385-3	Šaran, M., Despotov, M., Trivunović, S., Ivković, M., Janković, D., Štrbac, L.J. (2022): Genetic polymorphism of milk proteins in Holstein cattle population from Serbia, The 73rd Annual Meeting of the European Federation of Animal Science, Porto, Portugal 5 - 9 September, 2022. Book of Abstracts, Wageningen Academic Publishers, p. 418, no. 28	published
3	Article in journal	yes	https://doi.org/1 0.3390/ani13040 597	Štrbac L, Pracner D, Šaran M, Janković D, Trivunović S, Ivković M, Tarjan L, Dedović N. Mathematical Modeling and Software Tools for Breeding Value Estimation Based on Phenotypic, Pedigree and Genomic Information of Holstein Friesian Cattle in Serbia. Animals. 2023; 13(4):597.	published

* Type of scientific publication: article in journal, publication in conference/workshop, book/monograph/anthology, proceeding, research data etc.
** Status can only include "accepted" or "published".

	A.1.2. Insert the full list of references for all the publications which are not accepted/published yet, but <u>submitted or in preparation</u> for the submission.				
	Type of scientific publication*	**Open Access (yes/no)**	**Publication status****	**Full reference title (list all authors, tentative title and planned journal)**	**Expected deadline for publishing**
1					
2					
3					

* Type of scientific publication: article in journal, publication in conference/workshop, book/monograph/anthology, proceeding, research data etc.
** Status can include: "in preparation" or "submitted".

Appendix 2- Questions for Final Project Report Evaluators

Strengths of the Project

Weaknesses of the Project

Future Recommendations for the research team and the Project