

	REGIONAL SCIENTIFIC CENTER OF VETERINARY MEDICINE KALININGRAD, RUSSIAN FEDERATION		
	PRODUCT: COMBINED COLLAR FOR TREATMENT AND PREVENTION OF OSTEOARTHRITIS IN DOGS		
	Study No.: 200801-4	EFFICACY STUDY REPORT	Page 1 of 16

Combined Collar for Treatment and Prevention of Osteoarthritis in Dogs **Efficacy Study**

FINAL REPORT

Identification No.:	200801-4
Study initiation date:	September 15, 2021
Study completion date	January 15, 2022
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	PRODUCT: COMBINED COLLAR FOR TREATMENT AND PREVENTION OF OSTEOARTHRITIS IN DOGS		
	Study No.: 200801-4	EFFICACY STUDY REPORT	Page 2 of 16

CONTENT:

1. EXECUTIVE SUMMARY	3
2. COMPLIANCE.....	4
3. STUDY OBJECTIVE	4
3.1. The purpose of the study	4
4. PROJECT STAFF.....	5
5. STUDY DESIGN.....	5
5.1. Site and environment	5
5.2. Test Systems	5
5.3. Total Number of Animals	6
5.4. Test Articles	6
5.5. Route of Administration.....	6
5.6. Study Duration	6
5.7. Housing	6
5.8. Diet.....	7
5.9. Water.....	7
5.10. Methods	7
5.11. Study Raw Data Archiving.....	8
6. STUDY RESULTS DISCUSSION	8
6.1. Efficacy Study group	8
6.2. Control group	9
7. CONCLUSIONS.....	10
8. APPROVALS	10

	REGIONAL SCIENTIFIC CENTER OF VETERINARY MEDICINE KALININGRAD, RUSSIAN FEDERATION		
	PRODUCT: COMBINED COLLAR FOR TREATMENT AND PREVENTION OF OSTEOARTHRITIS IN DOGS		
	Study No.: 200801-4	EFFICACY STUDY REPORT	Page 3 of 16

1. EXECUTIVE SUMMARY

Solano LTD, Israel has designed Combined Collar for Treatment and Prevention of Osteoarthritis in Dogs (“**Collar**”).

Collar is a solid molded formulation which based on a fourth active substance.

Active ingredients: Glucosamine, Chondroitin Sulphate, Methylsulfonylmethane (MSM) and Turmeric root extract in total concentration about 20÷24%;

Non-active ingredients: Trade Secret Polymers -up to 100%

In this study, we report the results obtained in controlled veterinary study evaluating Combined Collar for Treatment and Prevention of Osteoarthritis in Dogs by around the neck for a period of 120 days (Efficacy Study).

In this study 25 dogs, diagnosed in Osteoarthritis were randomly assigned in two study groups: 15 dogs in Efficacy and 10 dogs in Control study groups.

On Day 0 (one day before application of the collars), Day 30, Day 60, Day 90 and Day 120 the study each animal in each study groups were undergo:

- Ultra Sound X-Ray examinations of problematic zones;
US examination showed reduction of bone growths, the inflammatory process has stopped, and the cartilaginous joint’s surface has become smoother and denser in animals, enrolled in efficacy group vs. control group.
- WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) score examination was used to evaluate the condition of dogs with osteoarthritis, including pain, stiffness, and physical functioning of the joints. WOMAC questionnaires were filled by animals’ owners at the enrollment and after 90 days of the Study. It shows the decreasing in the WOMAC total score index for each animal in efficacy study group in comparison with 120 days results. No significant changes were in WOMAC total score index for animal in control study group.
- General veterinary observation for: joint mobility, lameness, pain on palpation, clinical signs.

During the clinical examination of the dogs in efficacy study group, was detected that the lameness was completely gone in the sick animals; the joints became more mobile; joints’ discomfort has decreased, or completely disappeared; pain on palpation

	REGIONAL SCIENTIFIC CENTER OF VETERINARY MEDICINE KALININGRAD, RUSSIAN FEDERATION		
	PRODUCT: COMBINED COLLAR FOR TREATMENT AND PREVENTION OF OSTEOARTHRITIS IN DOGS		
	Study No.: 200801-4	EFFICACY STUDY REPORT	Page 4 of 16

decreased significantly, or completely disappeared. No pain or fatigue was observed the day after moderate activity by the owners. There were no changes in health conditions in animals, enrolled in control group. Some animals in this group suffered from the exacerbations of diseases of loco-motor system caused by cold in winter period, dampness and drafts, therefore, based on ethical considerations they were treated by anti-arthritis medication.

- Ca and P values in blood.
Normalization of the Calcium and Phosphorus in blood analysis was observed in efficacy group animals vs. control group, where no significant changes in Calcium and Phosphorus were observed.

On Day 31, Day 61, Day 91 collars were changed on new on all the animals in both Study groups.

The study was conducted in Kaliningrad, Russian Federation, during September 2021 – January 2022 by utilization of dogs from municipal animal shelter and from private sector. Animal care was in full compliance with the Russian Federation Laws for Animal Protection and Directive 2010/63/EU on the protection of animals used for scientific purposes.

The study showed that significant positive dynamics was observed in the treatment of joint diseases such Osteoarthritis in the animals, enrolled into efficacy study group in comparison with animals, treated by placebo.

2. COMPLIANCE

Study was based on the rules of OECD Principles of Good Laboratory Practice Directive 2004/10/EC and US FDA Good Laboratory Practice Regulations, 21 CFR Part 58.

3. STUDY OBJECTIVE

3.1. The purpose of the study was to evaluate:

- To evaluate the long-term efficacy of the **Collar**, for treatment and prevention of Osteoarthritis in dogs during a study period of up to 120 days, by comparing the treatment by using “ACTIVE” and “PLACEBO” collars.

	REGIONAL SCIENTIFIC CENTER OF VETERINARY MEDICINE KALININGRAD, RUSSIAN FEDERATION		
	PRODUCT: COMBINED COLLAR FOR TREATMENT AND PREVENTION OF OSTEOARTHRITIS IN DOGS		
	Study No.: 200801-4	EFFICACY STUDY REPORT	Page 5 of 16

4. PROJECT STAFF

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Sponsor's Representative:	"Vital Sense" Pharma Quality and Compliance Projects 38/11 Hakanaim, Arad, Israel Tel: +972-54-6751052 E-mail: vlozansky@gmail.com
Principal Investigator:	Prof. Alexander Muromtzev, VMD, Ph.D Regional Scientific Center of Veterinary Medicine, Kaliningrad, Russian Federation. Tel.: +7-911-4548152 E-mail: muromtsev.a@mail.ru

5. STUDY DESIGN

5.1. Site and environment

The Study was conducted by Regional Scientific Center of Veterinary Medicine, Kaliningrad, Russian Federation in private holders, municipal animal shelter in Kaliningrad (54°43'N 20°31'E, Russian Federation).

The shelters' animals were housed in indoor pens with adequate air conditions under room temperature.

Animal care was in full compliance with the Russian Federation Laws for Animal Protection and Directive 2010/63/EU on the protection of animals used for scientific purposes.

5.2. Test Systems

Adult animals which diagnosed in osteoarthritis.

	REGIONAL SCIENTIFIC CENTER OF VETERINARY MEDICINE KALININGRAD, RUSSIAN FEDERATION		
	PRODUCT: COMBINED COLLAR FOR TREATMENT AND PREVENTION OF OSTEOARTHRITIS IN DOGS		
	Study No.: 200801-4	EFFICACY STUDY REPORT	Page 6 of 16

5.3. Total Number of Animals:

25 animals, vaccinated against: Parvovirosis, Distemper, Leptospirosis, Parainfluenza, Hepatitis and Rabies.

1st group: Efficacy Study Group– Adult Dogs (15 subjects) were treated by “active” collar.

2nd group: Control Group– Adult Cats (10 subjects) were treated by “placebo” collar.

5.4. Test Articles:

Molded Plastic Strips (20-30 g.)

“ACTIVE” collar contains:

Active ingredients: Glucosamine, Chondroitin Sulphate, Methylsulfonylmethane (MSM) and Turmeric root extract in total concentration about 20÷24%;

Non-active ingredients: Trade Secret Polymers -up to 100%

“PLACEBO” collar contains only non-active ingredients.

5.5. Route of Administration

Application of the collars around the dog's neck.

5.6. Study Duration

120 days.

5.7. Housing

The shelters' animals were housed in indoor pens with adequate air conditions under room temperature.

Pens had a surface of approximately 20 m² with a mean density of 4 animals per pen. Parasites infestation was usually controlled by weekly spraying biocides on animals and on pen surfaces.

Dogs included in this investigation were not enrolled in any experimental trial and were managed according to local animal welfare regulations.

	REGIONAL SCIENTIFIC CENTER OF VETERINARY MEDICINE KALININGRAD, RUSSIAN FEDERATION		
	PRODUCT: COMBINED COLLAR FOR TREATMENT AND PREVENTION OF OSTEOARTHRITIS IN DOGS		
	Study No.: 200801-4	EFFICACY STUDY REPORT	Page 7 of 16

Dogs, enrolled in this study were housed separately from the other dogs, housed in the shelters to avoid any contact between experimental and other dogs.

Pens with the dogs, enrolled into control group were placed separately from the dogs, enrolled into efficacy and safety groups.

5.8. Diet

During the study period the animals were fed with standard commercial dry dogs' diet.

5.9. Water

Potable water was supplied *ad libitum* during the study period.

5.10. Methods

25 dogs, diagnosed in Osteoarthritis were randomly assigned in two study groups: 15 dogs in Efficacy and 10 dogs in Control study groups.

In each group the dogs were identified by color and/or number according to study group.

On Day 0 (one day before application of the collars), Day 30, Day 60, Day 90 and Day 120 the study each animal in each study groups were undergo:

- Ultra Sound and X-Ray examinations of problematic zones;
- WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) score examination, adopted for the dogs, was used to evaluate the condition of dogs with osteoarthritis, including pain, stiffness, and physical functioning of the joints (see Appendix A).
- General veterinary observation for: joint mobility, lameness, pain on palpation, clinical signs.
- Ca and P values in blood.

On Day 1 each dog in Efficacy Study group was applicated with Active collars, and in control group - with placebo-collars respectively, by the same manner as above.

On Day 31, Day 61, Day 91 collars were changed on new on all the animals in both Study groups.

	REGIONAL SCIENTIFIC CENTER OF VETERINARY MEDICINE KALININGRAD, RUSSIAN FEDERATION		
	PRODUCT: COMBINED COLLAR FOR TREATMENT AND PREVENTION OF OSTEOARTHRITIS IN DOGS		
	Study No.: 200801-4	EFFICACY STUDY REPORT	Page 8 of 16

To avoid any bias, all above examinations were performed by the same veterinary for all control points for the animals from municipal animal shelter and from private sector (except of WOMAC scores, filed by animals' owners from private sector).

In this report WOMAC total score index is presented for all animals in both Study groups.

Dogs included in this investigation were not enrolled in any experimental trial and were managed according to local animal welfare regulations.

Blood was taken by venepuncture from *v. cephalica antebrachii*.

Blood samples were collected into tubes Vacuette.

During the collection period, food was withheld, but water will be available *ad libitum*.

5.11. Study Raw Data Archiving

Study raw data, used and produced during the Study, including the executed WOMAC scores for each Study animals, related to Days 0, 30, 90 and 120, laboratory notebooks, working forms etc. is archived in Regional Scientific Center of Veterinary Medicine, Kaliningrad, Russian Federation in Study File.

6. STUDY RESULTS DISCUSSION

6.1. Efficacy Study group

Main period of the Study felt into winter period. Despite this exacerbations of diseases of loco-motor system caused by cold, dampness and drafts usually begin, however we observed during the Study positive dynamics in the treatment of joint diseases in the dogs in the efficacy study group.

Stability in normalization of Calcium and Phosphorus in blood analysis was observed during the Study (see Table 1).

During the clinical examination of the dogs in this study group, was detected that the lameness was completely gone in the sick animals; the joints became more mobile; joints' discomfort has decreased, or completely disappeared; pain on palpation decreased significantly or completely.

No pain or fatigue was observed by the owners after moderate activity.

	REGIONAL SCIENTIFIC CENTER OF VETERINARY MEDICINE KALININGRAD, RUSSIAN FEDERATION		
	PRODUCT: COMBINED COLLAR FOR TREATMENT AND PREVENTION OF OSTEOARTHRITIS IN DOGS		
	Study No.: 200801-4	EFFICACY STUDY REPORT	Page 9 of 16

WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) score examination was stiffness used to evaluate the condition of dogs with osteoarthritis, including pain and physical functioning of the joints. WOMAC questionnaires were filled by animals' owners at the enrollment and after 30, 60, 90 and 120 days of the Study. It shows the decreasing in the WOMAC total score index for each animal in this study group in comparison with each previous time points results (See Table 2).

US examination showed reduction of bone growths, the inflammatory process has stopped, and the cartilaginous joint's surface has become smoother and denser.

Note: Veterinary Portable Ultrasound Scanner Kit GDF-A10 with 3.5MHz Probe for Medium Sized Animals was used in this Study. Because of limitation of data storage and printouts of this device, the veterinary interpretation of the US scanned problematic zones was done in real time of the examination. No printouts are attached to this report.

Animals in this study group were not undergoing any additional medication or therapeutic treatment.

X-Ray examination of joints of several animals in this study group showed reduction of bone growths, the inflammatory process (See Appendix B)

The collars in this study group were exchanged on new "active" collars On Day 31, Day 61, Day 91 of the study.

6.2. Control group

Animals of the control group used collars without active substances.

After clinical observation on the 10th day of the study 3 dogs (Subject No. 18, 20 and 21), and 4 animals (Subject No. 18, 20, 21 and 24) on 102nd day were treated by anti-arthritis medication. It is because of ethical considerations. These animals suffered from joint inflammation and pain.

They received: NSAID (Non-Steroidal Anti-inflammatory Drug) injections, therapeutic dose once a day for 5 days.

No medication was received by other animals during the study.

No any positive changes in functional abilities during the Study were observed in Control group.

By examination of Ca and P in blood during the Study no significant changes were observed. For Ca and P results in blood (see Table 3).

	REGIONAL SCIENTIFIC CENTER OF VETERINARY MEDICINE KALININGRAD, RUSSIAN FEDERATION		
	PRODUCT: COMBINED COLLAR FOR TREATMENT AND PREVENTION OF OSTEOARTHRITIS IN DOGS		
	Study No.: 200801-4	EFFICACY STUDY REPORT	Page 10 of 16

No significant changes in WOMAC index for each animal in this study group, including the animals, received medication on 10th and 102nd days of the study (See Table 4)

The collars in this study group were exchanged on new “placebo” collars On Day 31, Day 61, Day 91 of the study.

7. CONCLUSIONS

The study results showed that significant positive dynamics was observed in the treatment of joint diseases such Osteoarthritis in the animals, enrolled into efficacy study group in comparison with animals, treated by placebo.

8. APPROVALS

This study report has been approved by:

<u>Principal Investigator :</u> Prof. Alexander Muromtzev, VMD, Ph.D Regional Scientific Center of Veterinary Medicine, Kaliningrad, Russian Federation.	<u>Date :</u> 28 January 2022	<u>Signature:</u> 
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	PRODUCT: COMBINED COLLAR FOR TREATMENT AND PREVENTION OF OSTEOARTHRITIS IN DOGS		
	Study No.: 200801-4	EFFICACY STUDY REPORT	Page 11 of 16

Appendix A

Western Ontario and McMaster Universities Osteoarthritis Score Examination (WOMAC)

Animal's ID: _____ Study Day: _____

Please circle the appropriate rating for each item.

STIFFNESS GROUP	NONE	SLIGHT	MODERATE	SEVERE	EXTREME	TOTAL
Stiffness in the morning	0	1	2	3	4	____/20
Stiffness during the day	0	1	2	3	4	
Ability to rise to standing	0	1	2	3	4	
General joint discomfort	0	1	2	3	4	
Stiffness the day after moderate activity	0	1	2	3	4	
FUNCTION GROUP	NONE	SLIGHT	MODERATE	SEVERE	EXTREME	TOTAL
Ability to jump up	0	1	2	3	4	____/16
Ability to jump down	0	1	2	3	4	
Ability to climb up	0	1	2	3	4	
Ability to climb down	0	1	2	3	4	
LAMENESS GROUP	NONE	SLIGHT	MODERATE	SEVERE	EXTREME	TOTAL
Severity of lameness during mild activity	0	1	2	3	4	____/16
Severity of lameness during moderate activity	0	1	2	3	4	
Lameness the day after moderate activity	0	1	2	3	4	
Owner awareness of dog's joint discomfort	0	1	2	3	4	
QOL (QUALITY OF LIFE) GROUP	NONE	SLIGHT	MODERATE	SEVERE	EXTREME	TOTAL
Decrease in general activity	0	1	2	3	4	____/8
Concerns about life length	0	1	2	3	4	
OWNER PERCEPTION	NONE	SLIGHT	MODERATE	SEVERE	EXTREME	TOTAL
QOL during the last month	0	1	2	3	4	____/4
WOMAC TOTAL SCORE	____/64					

Veterinary's Signature: _____ Date: _____

	REGIONAL SCIENTIFIC CENTER OF VETERINARY MEDICINE KALININGRAD, RUSSIAN FEDERATION		
	PRODUCT: COMBINED COLLAR FOR TREATMENT AND PREVENTION OF OSTEOARTHRITIS IN DOGS		
	Study No.: 200801-4	EFFICACY STUDY REPORT	Page 12 of 16

Appendix B

X-Ray Examination Images



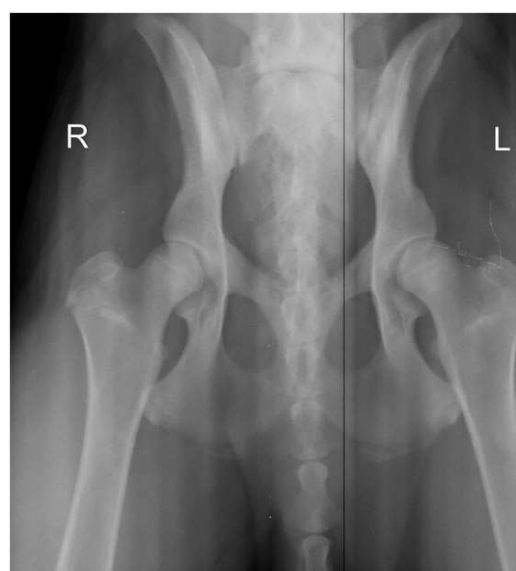
Subject 4 Before Treatment



Subject 4 After Treatment



Subject 10 Before Treatment



Subject 10 After Treatment

Table No. 1

Ca and P results in blood – Efficacy Study Group

No.	Breed	Age (y)	Weight (Kg)	Blood Tests							
				Ca (2.3-2.8 mmol/L); P (1.1-1.8 mmol/L)							
				Day 0		Day 30		Day 90		Day 120	
				Ca	P	Ca	P	Ca	P	Ca	P
1	Japanese Spitz	8	9.3	3.10	1.12	2.8	1.34	2.66	1.32	2.47	1.45
2	Japanese Spitz	6	7.2	1.82	0.97	2.34	1.25	2.55	1.40	2.71	1.39
3	Japanese Spitz	4	8.1	2.47	1.42	2.53	1.24	2.64	1.47	2.75	1.58
4	Dachshund	7	8.6	3.07	0.92	2.44	1.20	2.57	1.29	2.71	1.44
5	Mongrel Dog	4	12.3	2.65	2.44	2.74	2.30	2.67	1.87	2.70	1.49
6	Dachshund	3	5.4	2.94	0.85	2.78	1.00	2.53	1.44	2.61	1.37
7	Labrador Retriever	6	25.8	2.54	1.37	2.60	1.35	2.77	1.48	2.70	1.52
8	Welsh Corgi	2	9.5	1.10	0.84	2.25	0.95	2.25	1.34	2.77	1.52
9	Golden Retriever	5	32.7	2.37	1.95	2.50	1.70	2.70	1.65	2.64	1.48
10	German Shepherd	9	35.4	1.58	2.05	2.15	1.90	2.52	1.75	2.60	1.70
11	Yorkshire Terrier	9	2.9	1.36	0.80	2.15	1.00	2.37	1.44	2.47	1.43
12	Dachshund	4	5.5	2.45	1.23	2.50	1.35	2.67	1.49	2.48	1.40
13	Golden Retriever	5	28.1	3.20	1.95	2.94	1.83	2.71	1.63	2.75	1.65
14	Mongrel Dog	10	19.8	1.44	0.76	1.95	0.94	2.40	1.35	2.54	1.40
15	Welsh Corgi	5	11.3	2.30	1.90	2.50	1.70	2.43	1.67	2.55	1.37

Table No. 2

Summary of WOMAC Total Score Examination – Efficacy Study Group

No.	Breed	Age (y)	Weight (Kg)	WOMAC Index (Total Score)				
				Day 0	Day 30	Day 60	Day 90	Day 120
1	Japanese Spitz	8	9.3	30	15	10	7	5
2	Japanese Spitz	6	7.2	11	3	2	1	0
3	Japanese Spitz	4	8.1	20	10	6	5	3
4	Dachshund	7	8.6	35	24	14	11	11
5	Mongrel Dog	4	12.3	13	8	2	0	0
6	Dachshund	3	5.4	11	5	3	2	3
7	Labrador Retriever	6	25.8	27	14	7	4	4
8	Welsh Corgi	2	9.5	28	14	6	3	3
9	Golden Retriever	5	32.7	30	12	6	2	0
10	German Shepherd	9	35.4	13	4	0	0	0
11	Yorkshire Terrier	9	2.9	26	14	9	7	6
12	Dachshund	4	5.5	29	12	7	4	0
13	Golden Retriever	5	28.1	17	8	8	5	4
14	Mongrel Dog	10	19.8	14	9	7	3	0
15	Welsh Corgi	5	11.3	21	12	7	3	0

Table No. 3

Ca and P results in blood – Control Group

No.	Breed	Age (y)	Weight (Kg)	Blood Tests							
				Ca (2.3-2.8 mmol/L); P (1.1-1.8 mmol/L)							
				Day 0		Day 30		Day 90		Day 120	
				Ca	P	Ca	P	Ca	P	Ca	P
16	Jack Russell Terrier	6	6.1	3.80	1.30	3.20	1.50	2.87	1.53	2.74	1.48
17	Dachshund	5	7.8	1.95	1.77	2.15	1.70	2.47	1.65	2.52	1.47
18	Golden Retriever*	7	26.1	2.32	1.24	2.41	1.35	2.63	1.37	2.48	1.25
19	Mongrel Dog	7	5.9	2.72	1.93	2.75	1.47	2.72	1.49	2.58	1.24
20	Mongrel Dog*	8	9.5	2.43	1.23	2.65	1.34	2.66	1.41	2.37	1.35
21	Labrador Retriever*	9	31.8	3.69	2.38	2.95	2.15	2.92	1.75	2.84	1.45
22	Jack Russell Terrier	4	7.5	3.55	1.98	3.05	1.77	2.81	1.60	2.37	1.50
23	Golden Retriever	3	30.5	2.45	1.83	2.57	1.56	2.73	1.55	2.74	1.48
24	Mongrel Dog**	3	11.0	2.70	1.45	2.83	1.52	2.84	1.46	2.62	1.45
25	Yorkshire Terrier	8	3.0	1.48	0.71	1.97	1.15	2.35	1.37	2.24	1.27

* Animals, received medication on 10th and 102nd days of the study;

** Animals, received medication on 102nd day of the study.

Table No. 4

Summary of WOMAC Total Score Examination – Control Group

No.	Breed	Age (y)	Weight (Kg)	WOMAC Index (Total Score)				
				Day 0	Day 30	Day 60	Day 90	Day 120
16	Jack Russell Terrier	6	6.1	21	20	20	21	22
17	Dachshund	5	7.8	20	20	21	22	22
18	Golden Retriever*	7	26.1	16	7	14	16	12
19	Mongrel Dog	7	5.9	17	18	17	20	21
20	Mongrel Dog*	8	9.5	29	16	25	25	23
21	Labrador Retriever*	9	31.8	26	12	23	25	22
22	Jack Russell Terrier	4	7.5	16	16	17	18	19
23	Golden Retriever	3	30.5	23	24	24	25	24
24	Mongrel Dog**	3	11.0	11	13	12	14	15
25	Yorkshire Terrier	8	3.0	17	19	18	19	20

* Animals, received medication on 10th and 102nd days of the study;

** Animals, received medication on 102nd day of the study.