Clusternanotech LTD
Nanostructured materials science
Office 4, 21 Knightsbridge - SW1X 7LY London UK
Company n.07961030
Capital Share: 9.080.193,00 € paid

General Manager:
Bruno Cantarelli

Scientific Director:
Dr. Arturo Sommariva

Test Papilla Seal – Sealing product for the dry period of dairy cows

Clusternanotech Group in collaboration with Dr. Giuseppe Orsi (Management of the herd, prophylaxis, CNCPS nutrition, hygiene issues, quality and rheology of milk) and Dr. Schianchi Marzio - Veterinary LP.

NOTES: the test aimed to highlight the mechanical sealing efficacy, as well as enhance the sanitizing effect within the udder during the dry period of dairy cows, was conducted on three farms. The product tested contained SynthAg with varying concentrations of both natural and synthetic beeswax.
It consists of several intervention phases entirely developed at the respective farms to evaluate the dry period process, the physiological evolution of mammary gland retraction, preparation for milk emission prior to calving, and the health status post-calving.
All these aspects were compared with standard commercial products based on bismuth subnitrate.

DESCRIPTION OF THE INTERVENTION PHASES

PHASE 1: Selection of cows to be treated in the three farms and simultaneous selection of comparison cows treated with bismuth subnitrate.

In the first farm (Attachment 3), eight cows were selected, characterized by continuous increases in somatic cell count in milk during lactation.

In the second farm (Attachment 4), twelve cows were chosen, partly with increased somatic cell counts and partly with very low counts.

In the third farm (Attachment 5), ten cows were selected, some with very low somatic cell counts and others with high counts.

All comparison cows in the various farms showed somatic cell count characteristics similar to those chosen for treatment with the Papilla product.

Clusternanotech LTD
Nanostructured materials science
Office 4, 21 Knightsbridge - SW1X 7LY London UK
Company n.07961030
Capital Share: 9.080.193,00 € paid

General Manager:
Bruno Cantarelli

Scientific Director:
Dr. Arturo Sommariva

Table 3						
FARM 1						
N°	CELL COUNT	TYPE OF COUNT	TREATMENT	DRY PERIOD CHECK	CALVING CHECK	POST-CALVING CELL COUNT
124	552	CHRONIC	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	180
135	910	CHRONIC	ANTIBIOTIC + PAPILLA	POOR	NEGATIVE	ACUTE PIOCYANIC MASTITIS
160	1250	CHRONIC	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	200
215	810	HIGH	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	160
315	1250	HIGH	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	190
360	450	HIGH	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	175
375	918	CHRONIC	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	900
400	1200	CHRONIC	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	3500
390	820	CHRONIC	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	1500
420	1200	HIGH	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	160
429	590	HIGH	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	360
510	1710	CHRONIC	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	1150
515	1310	CHRONIC	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	195

Table 4						
FARM 2						
TYPE OF ANIMALS TO BE TREATED						
N°	CELL COUNT	TYPE OF COUNT	TREATMENT	DRY PERIOD CHECK	CALVING CHECK	POST-CALVING CELL COUNT
320	552	HIGH	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	180
514	220	LOW	PAPILLA	GOOD	POSITIVE	200
745	180	LOW	PAPILLA	GOOD	POSITIVE	200
1310	810	HIGH	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	160
1430	399	HIGH	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	190
1510	160	LOW	PAPILLA	GOOD	POSITIVE	170
1674	918	HIGH	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	810
1691	1200	CHRONIC	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	2100
1741	125	LOW	PAPILLA	GOOD	POSITIVE	95
1781	515	HIGH	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	185
1789	200	LOW	PAPILLA	GOOD	POSITIVE	810
1801	140	LOW	PAPILLA	GOOD	POSITIVE	165
360	136	LOW	BISMUTH	GOOD	POSITIVE	175
368	524	HIGH	ANTIBIOTIC + BISMUTH	GOOD	POSITIVE	195
410	810	HIGH	ANTIBIOTIC + BISMUTH	GOOD	POSITIVE	120
480	1300	HIGH	ANTIBIOTIC + BISMUTH	GOOD	POSITIVE	2500
529	125	LOW	BISMUTH	GOOD	POSITIVE	1300
1125	180	LOW	BISMUTH	GOOD	POSITIVE	250
1250	140	LOW	BISMUTH	GOOD	POSITIVE	120
1290	65	LOW	BISMUTH	GOOD	POSITIVE	110

Table 5						
FARM 3						
TYPE OF ANIMALS TO BE TREATED						
N°	CELL COUNT	TYPE OF COUNT	TREATMENT	DRY PERIOD CHECK	CALVING CHECK	POST-CALVING CELL COUNT
320	552	HIGH	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	180
514	220	LOW	PAPILLA	GOOD	POSITIVE	200
745	180	LOW	PAPILLA	GOOD	POSITIVE	200
1310	810	HIGH	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	160
1430	399	HIGH	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	190
1510	160	LOW	PAPILLA	GOOD	POSITIVE	170
1674	918	HIGH	ANTIBIOTIC + PAPILLA	GOOD	NEGATIVE	810
1691	310	HIGH	ANTIBIOTIC + PAPILLA	GOOD	NEGATIVE	2100
1741	125	LOW	PAPILLA	GOOD	POSITIVE	95
1781	515	HIGH	ANTIBIOTIC + PAPILLA	GOOD	POSITIVE	185
360	600	HIGH	ANTIBIOTIC + BISMUTH	POOR	NEGATIVE	3500
510	185	LOW	BISMUTH	GOOD	POSITIVE	90
518	1790	CHRONIC	ANTIBIOTIC + BISMUTH	POOR	NEGATIVE	1525
910	180	LOW	BISMUTH	GOOD	POSITIVE	185
1314	111	LOW	BISMUTH	GOOD	POSITIVE	190

1600	680	HIGH	ANTIBIOTIC + BISMUTH	GOOD	POSITIVE	140
1620	110	LOW	BISMUTH	GOOD	POSITIVE	210

SECOND PHASE: Treatment of selected animals with the product Papilla Seal.
The treatment was carried out using the Papilla Seal product with a beeswax concentration of 20% or 15% in combination with an antibiotic for animals with high somatic cell counts (according to selective dry cow therapy protocols) and only the Papilla Seal product with a beeswax concentration of 20% or 18% for animals with low somatic cell counts.

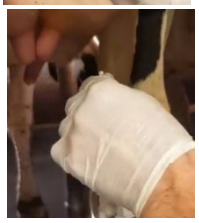
THE PROCEDURE FOR APPLYING THE PAPILLA SEAL PRODUCT TO ALL ANIMALS INCLUDED:

1. Disinfection of the teat sphincter (Appendix A).
2. Opening the sterile tube according to protocol, avoiding secondary contamination.
3. Insertion of the tube into the teat (Appendix B).
4. Insufflation of the product into the teat.

STAGES OF APPLICATION OF THE PAPILLA PRODUCT

1- DISINFECTION OF THE TEAT SPHINCTER TO AVOID SECONDARY CONTAMINATION DURING THE PRODUCT'S ENTRY

2- PREPARATION OF THE DISPENSER TUBE BY REMOVING THE PROTECTIVE CAP



STAGES OF APPLICATION OF THE PAPILLA PRODUCT:

3- INSERTION OF THE DISPENSER TUBE INTO THE TEAT

4- INSUFFLATION OF THE CONTENT INTO THE TEAT

THIRD PHASE: Visit to treated animals in the following days to evaluate the physiological evolution of mammary gland retraction until the phase is completed.

FOURTH PHASE: Visit to treated animals before calving to monitor the evolution of mammary preparation and milk production.

FIFTH PHASE: Visit to treated animals after calving, with the execution of the CMT test to assess the health status of the udder post-calving.

For all subjects, the somatic cell count was also verified during the first functional check.

EVALUATION OF THE VARIOUS PHASES

The selection of animals to be treated and comparison groups (agreed upon with the farmers) posed no significant challenges due to the large number of animals present on the farms.

During treatment, the Papilla product proved particularly difficult to flow through the teat canal, especially with the 20% beeswax concentration (a problem later resolved by modifying the product's preparation).

The phases of mammary retraction and preparation for calving did not present particular issues. However, the post-calving check revealed some cases of thickening in the quarters with altered colostrum and one case of acute pyocyanic mastitis due to the presence of pathogens in the udder prior to treatment (it should be noted that this animal had been treated in combination with antibiotics). These pathogens were resistant to any type of treatment.

The remaining cows showed entirely normal milk secretion with negative CMT results. Many animals showed residual beeswax during the first colostrum milking after calving, indicating the persistence of the product within the udder during the dry period.

CONSIDERATIONS AND CONCLUSIONS

The Papilla product demonstrated effectiveness both in the mechanical sealing of the teat sphincter and in ensuring microbiological safety. The presence of chronic subjects with

unresolved issues is considered entirely normal (the case of pyocyanic mastitis represents an exception that should not be included in the average results due to the specific characteristics of the pathogen).

The results are therefore fully comparable to treatment with bismuth subnitrate. Consequently, Papilla represents a valid alternative to this widely used molecule for the dry period of dairy cows.

TEST FOR THE COMMERCIALIZATION PLANNING OF PAPILLA SEAL

The preliminary test revealed the following parameters:

Selection of natural beeswax. Yellow natural beeswax was chosen instead of synthetic white beeswax, with no negative health effects.

Beeswax concentration at 18%. This concentration provides the product with a bacteriostatic effect due to the high presence of distilled water.

Inclusion of the patented colloidal silver preservative SynthAg. Ensures effective protection of the product against environmental pathogens.

Once the product formulation was finalized, the operational phase began, involving farmers in the use of Papilla Seal.

As a first step, approximately 1,000 Papilla Seal syringes were distributed to 50 farmers, used on over 200 cows for a 60-day period from December 2023 to February 2024. Farmers selected their cows for the product test, agreeing to send their data, which showed significant results.

Feedback was enthusiastic, both from farmers—who reported a reduction in veterinary prescriptions thanks to a naturally formulated product—and from sales agents, who found the product easy to sell due to the results obtained.

Following the first market test, 7,400 Papilla syringes were sold to 185 farmers. Each of them was asked to describe the product's performance, evaluating its effectiveness, ease of use, and appreciation for the absence of the need for a veterinary prescription.

All results collected by farmers were reported to our laboratory by veterinarians and distributors.

TABLE 1: Product Satisfaction

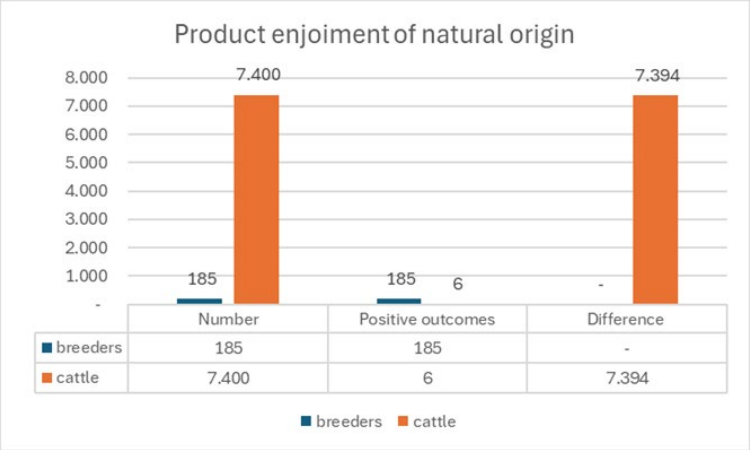


Table 1 shows the level of satisfaction with the product among the 185 farmers who used Papilla Seal on a total of 7,400 cows. The data indicates that 100% of farmers are satisfied, with 7,394 cows out of 7,400 achieving positive results. This demonstrates a high level of product efficacy based on the farmers' experience.

TABLE 2: Ease of Use of the Product

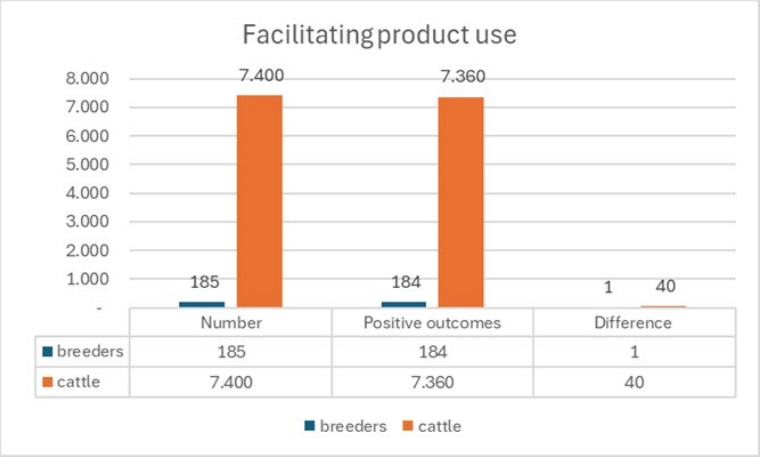


Table 2 presents the opinions of 185 farmers on the ease of use of the product. Out of 185 farmers, 184 were satisfied with its use on 7,400 cows. However, one farmer reported difficulties in applying the product to 40 of the treated cows. This suggests that while the product is generally considered easy to use, there is still room for improvement to further facilitate its application.

TABLE 3: Satisfaction Due to the Absence of a Veterinary Prescription

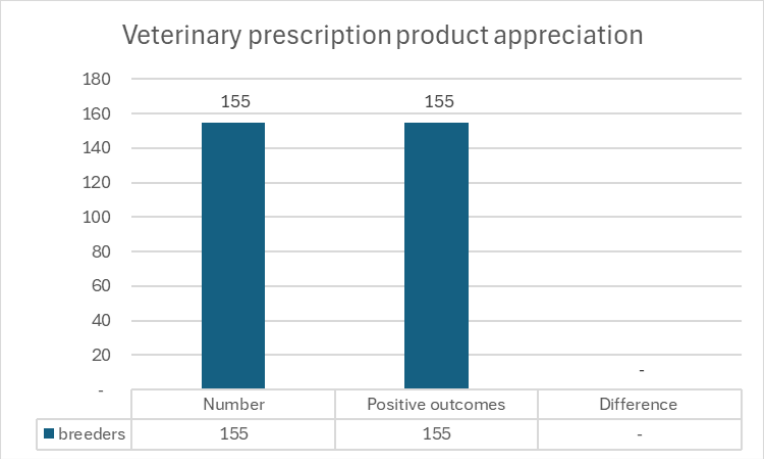


Table 3 shows satisfaction with the product in relation to the lack of a veterinary prescription. All 155 farmers surveyed are satisfied and appreciate the ability to use the product without a veterinary prescription. This is considered a significant advantage, making the product more accessible and easier for farmers to manage.

MARKET SITUATION AS OF AUGUST 1, 2024

As of today, August 1, 2024, sales of the Papilla product have reached 500,000 units, with a projection of up to 700,000 units by the end of the year. The forecasted demand for the upcoming year is 1 million units. One of the main clients is IZO, part of the Vaxxinova group. Currently, the Papilla product must be pre-ordered at least 90 days in advance for delivery. In the case of customization, the pre-order time may extend up to 120 days.

BRIEF OVERVIEW OF THE IMPLEMENTATION OF THE PAPILLA SEAL PRODUCT: PHASES, RESULTS, AND PROSPECTS

TABLE OF KEY RESULTS

Indicator	Result	Comments
Satisfaction level	100%	Among 185 farmers
Ease of use	99%	One reported case of difficulty
No need for a prescription	100%	All farmers appreciated the convenience