

Mastitis cows and immunization

In Spain, the antibiotherapy against mastitis moves **€12,000,000** with an interannual growth of 10.2%. Only 4 of these millions are drying antibiotherapy.

Conclusion: farmers spend a lot of money on mastitis treatment during lactation (injectables and intramammary antibiotics, NSAIDs, fluidtherapy, etc.).

The main costs for a farm are mastitis treatments followed by vaccine protocols.

Mastitis cows and immunization



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MAIN CHARACTERS

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Vaccine:

Inactivated vaccine against bovine mastitis

Composition per dosage (2ml):

Active substances:

E.coli (J5) (inactivated)

Staphylococcus aureus (Sp8) (inactivated), Slime
Associated Antigenic Complex (SAAC)

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Dosage and administration route:

- Bovine: 2ml / animal
- **Intramuscular** administration in the neck.

Recommended administration protocol:

- 1st. administration: 45 days **before** calving
- 2nd. administration: 10 days **before** calving
- 3rd. administration: 52 days **post-partum**

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KEY POINTS

Mastitis cows and immunization

1.- Action mechanism of the components in vaccine

Vaccine activates immunity in cows and heifers, and prevents intramammary infections, reducing clinical and sub-clinical mastitis against *S. aureus*, *E. coli* and *CNS*

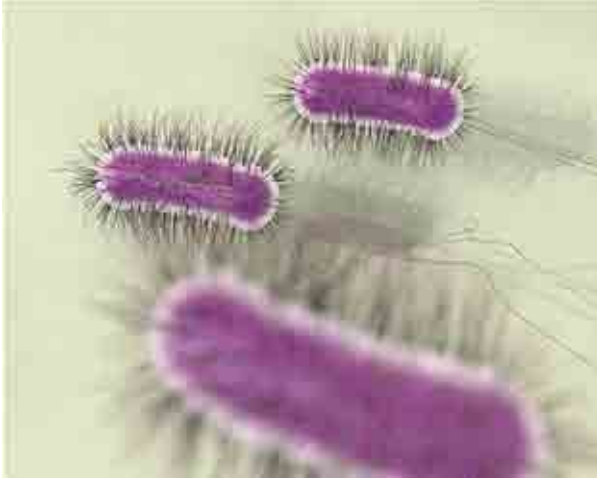
***E.coli*:**

- **Does not adhere** to the ducts and alveoli of the mammary gland; they grow quickly in milk, producing **toxic substances** that end up in the blood stream.
- **Vaccination** destroys cell wall development and enables humoral immunity activity.

***S. aureus* and *CNS*:**

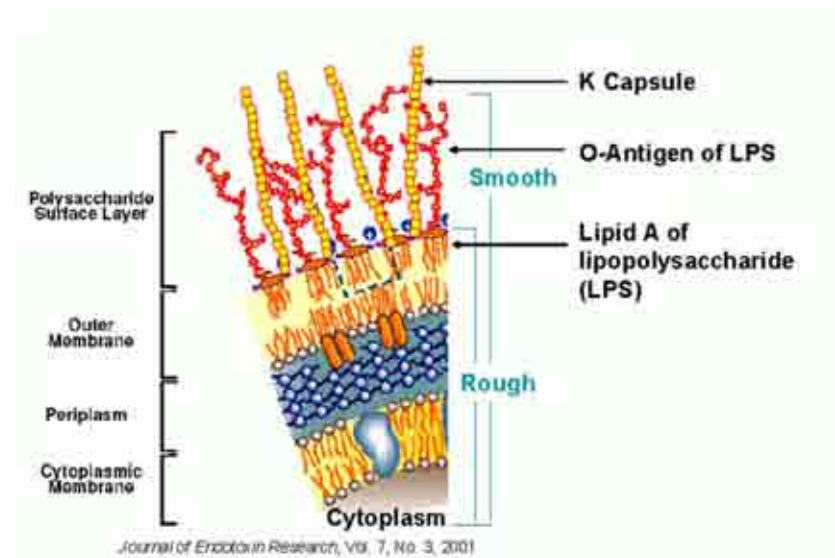
- Colonization due to the **Slime or Biofilm**, which facilitates adhesion between the bacteria and, simultaneously, does not allow the penetration of antibiotic treatments.
- **Vaccine** stops the development of micro-colonies

Some general features of *Escherichia coli*

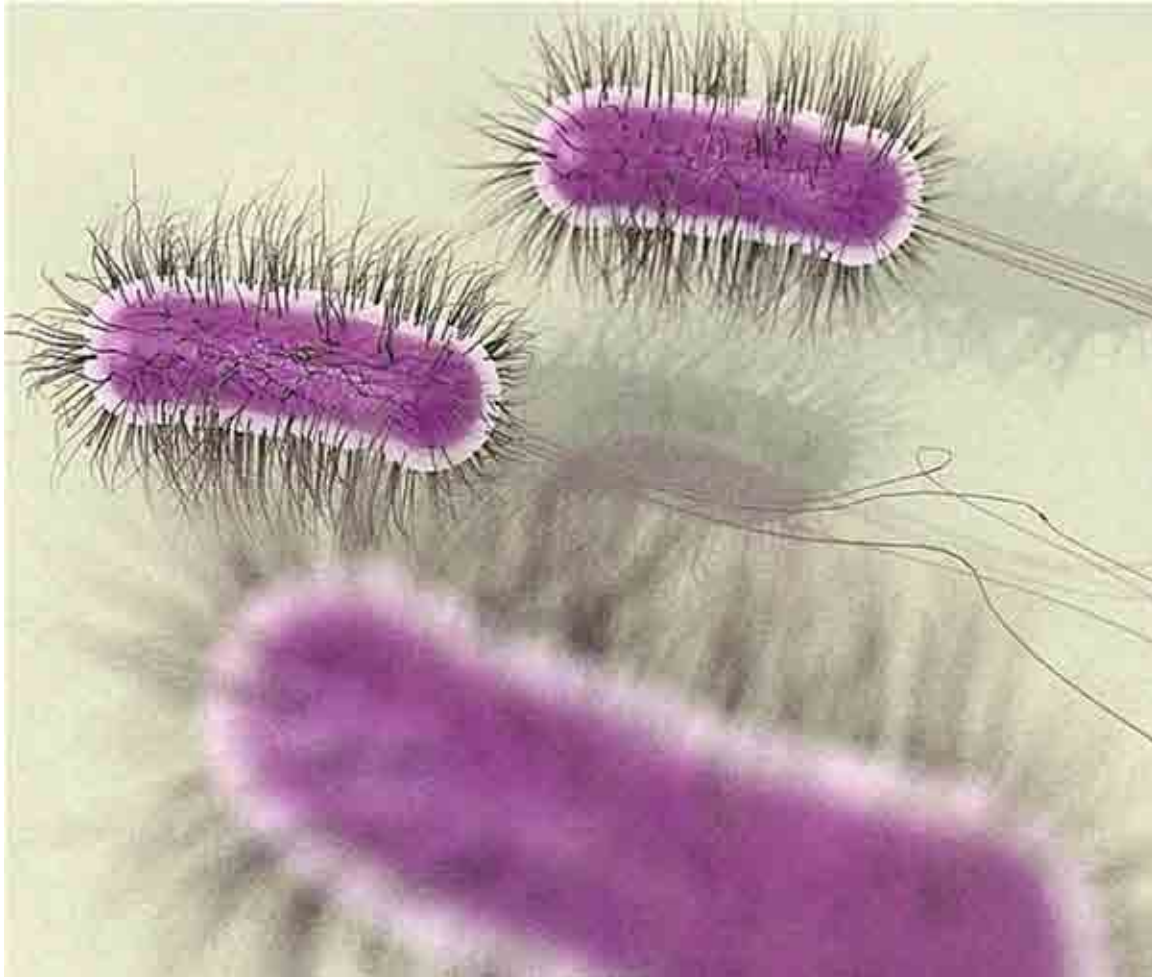


The vaccine was developed with the concept of the exposure of the core antigen common to Gram-negative organisms in the mutant J5 strain (rough strain).

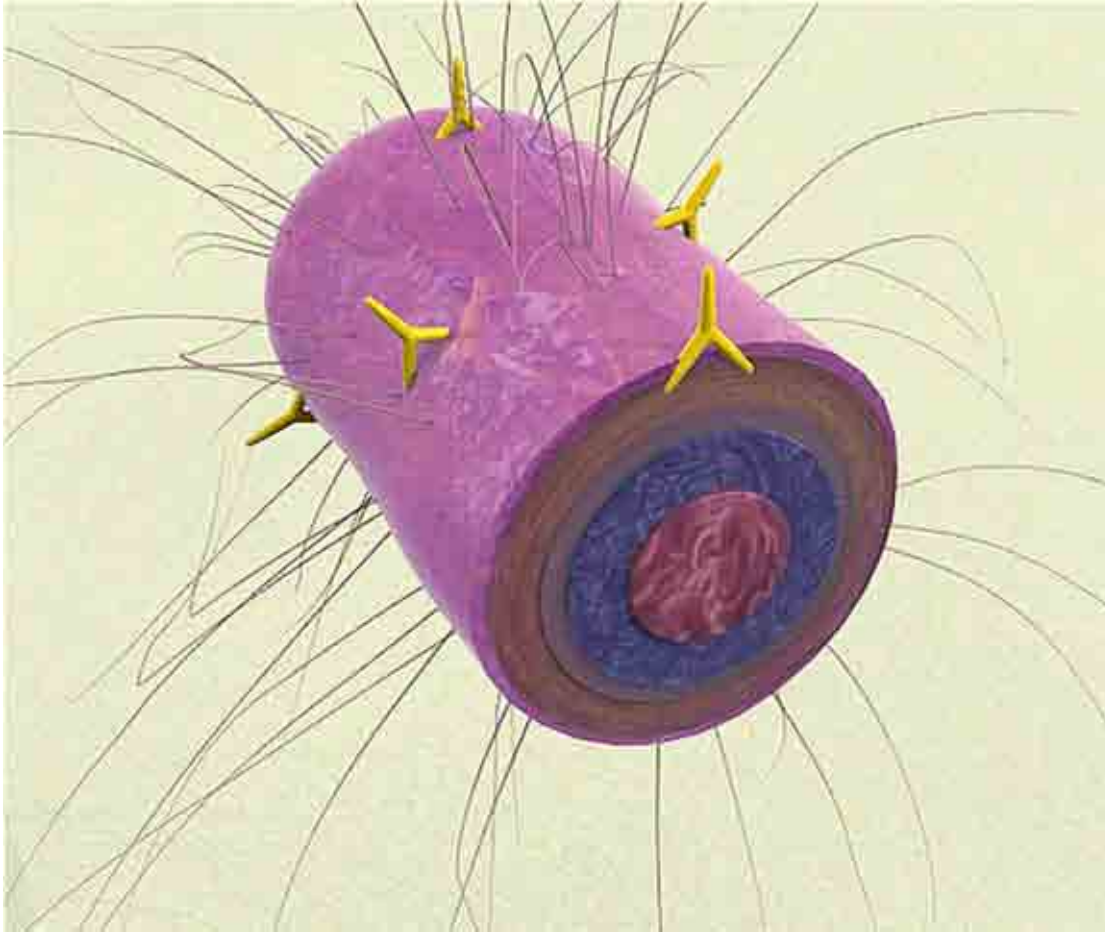
E.coli J5 is a strain that lacks the enzyme Uridin Diphosphate Galactose 4-Epimerase, which is responsible for binding the somatic antigen (O-Antigen of polysaccharide) to the LPS molecule of the cell wall.



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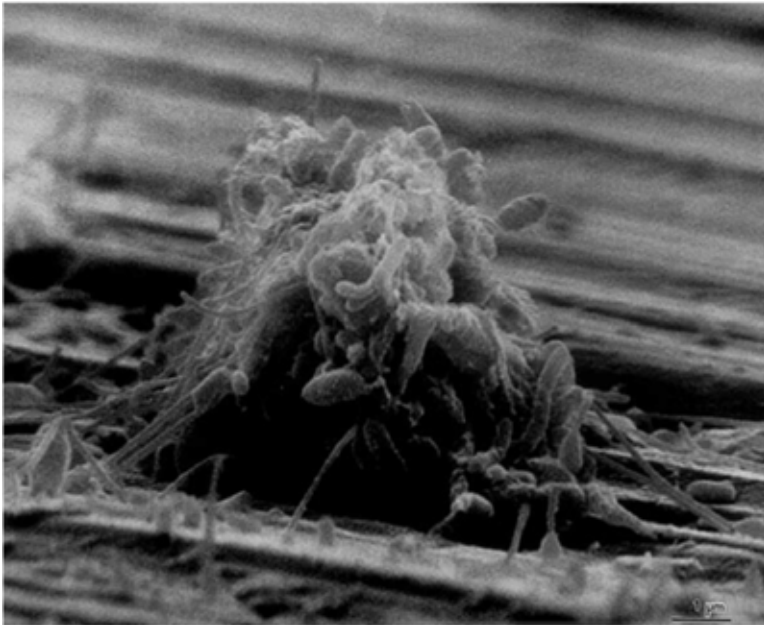
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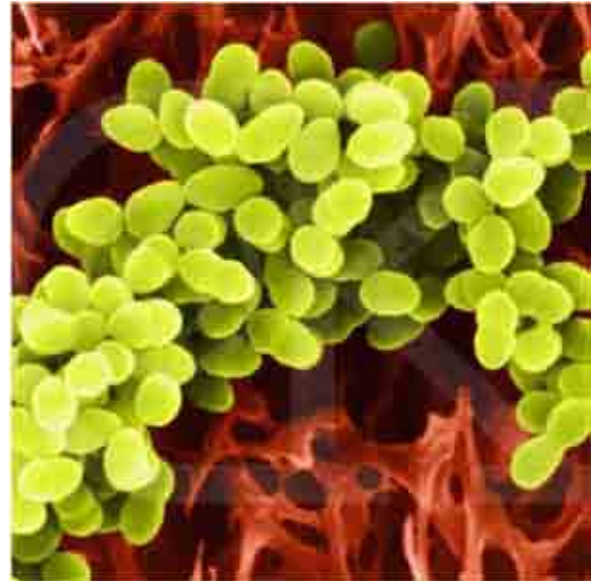
The Biofilm as survival mechanism

Biofilms are survival mechanisms of clinically relevant microorganisms.

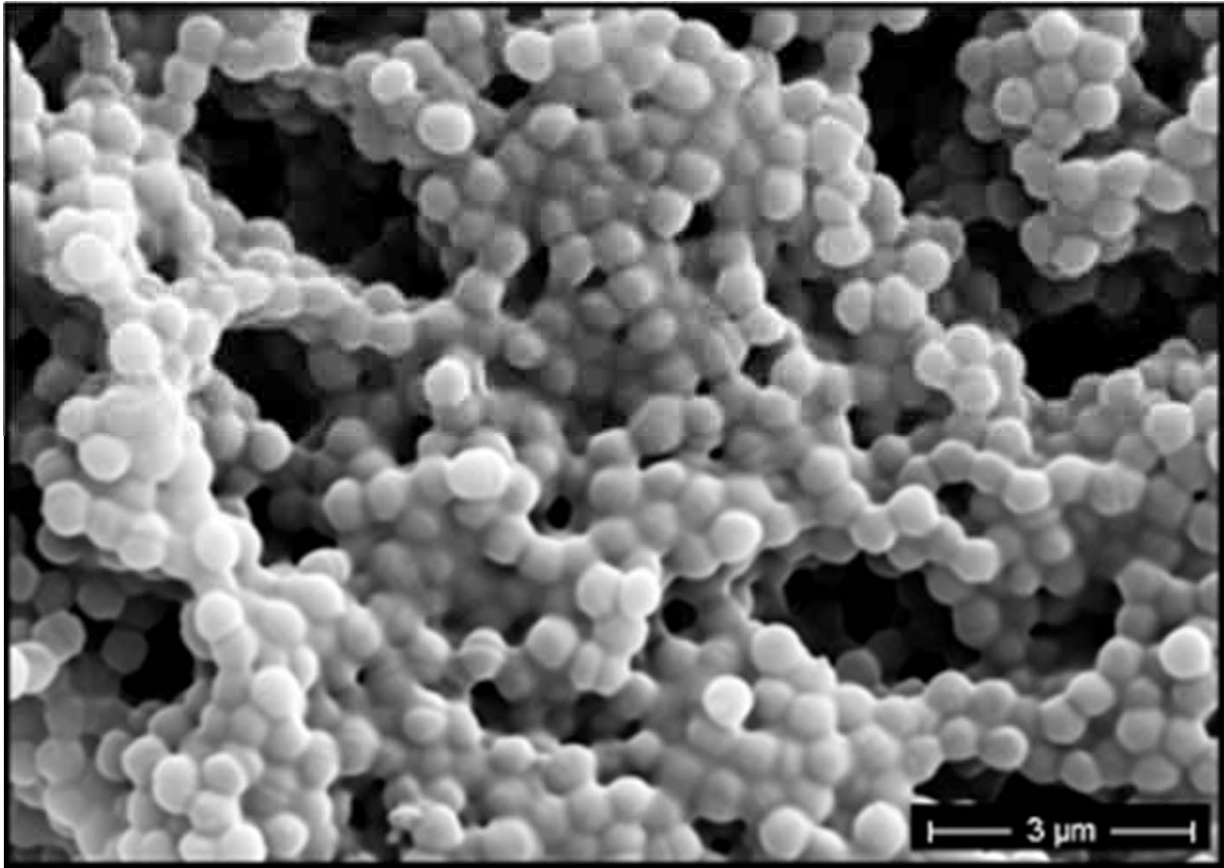
The production of this extracellular matrix defines the ability of bacterial strains to colonize host tissues and biomaterials, participating in the intercellular adhesion among bacterial cells and subsequent development of a BIOFILM, leading to chronic infections and bacterial resistance to phagocytosis and antibiotic treatments.



Scanning electron micrograph of a biofilm on a metal surface from an industrial water system.



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The Biofilm as survival mechanism

- Bactericidal effect of the antibiotics on the biofilm:

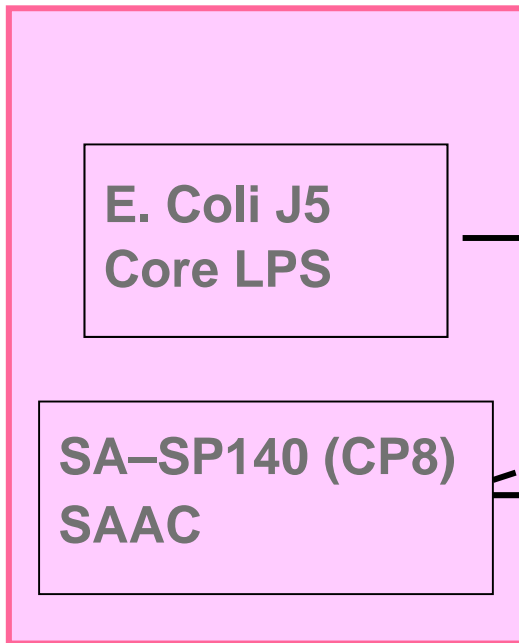
Microorganism	Antibiotic	Reference Organism Antibiotic MIC or MBC of planktonic phenotype ($\mu\text{g/ml}$)	Concentration effective against biofilm phenotype ($\mu\text{g/ml}$)
<i>S. aureus</i> NCTC 8325-4	Vancomycin	2 (MBC)	20
<i>Pseudomonas aeruginosa</i> ATCC 27853	Imipenem	1 (MIC)	1,024
<i>E. coli</i> ATCC 25922	Ampicillin	2 (MIC)	512
<i>P. pseudomallei</i>	Ceftazidime	8 (MBC)	800
<i>Streptococcus sanguis</i>	Doxycycline	0.063 (MIC)	3.15

MIC: Minimum Inhibitory Concentration

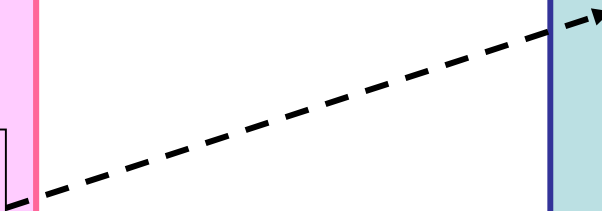
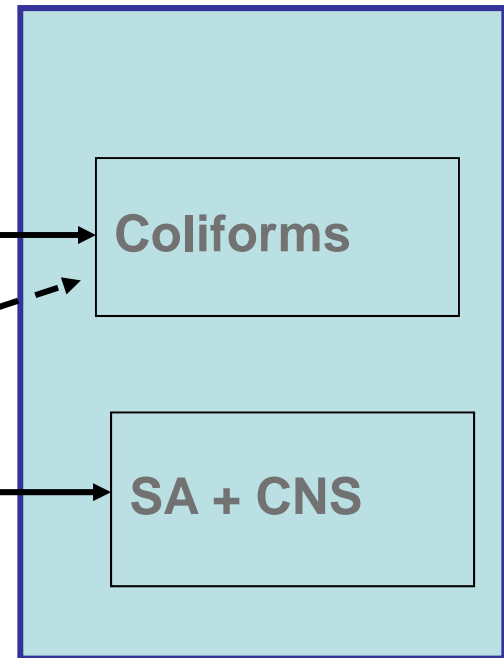
MBC: Minimum Bactericidal Concentration

From antigens to protection

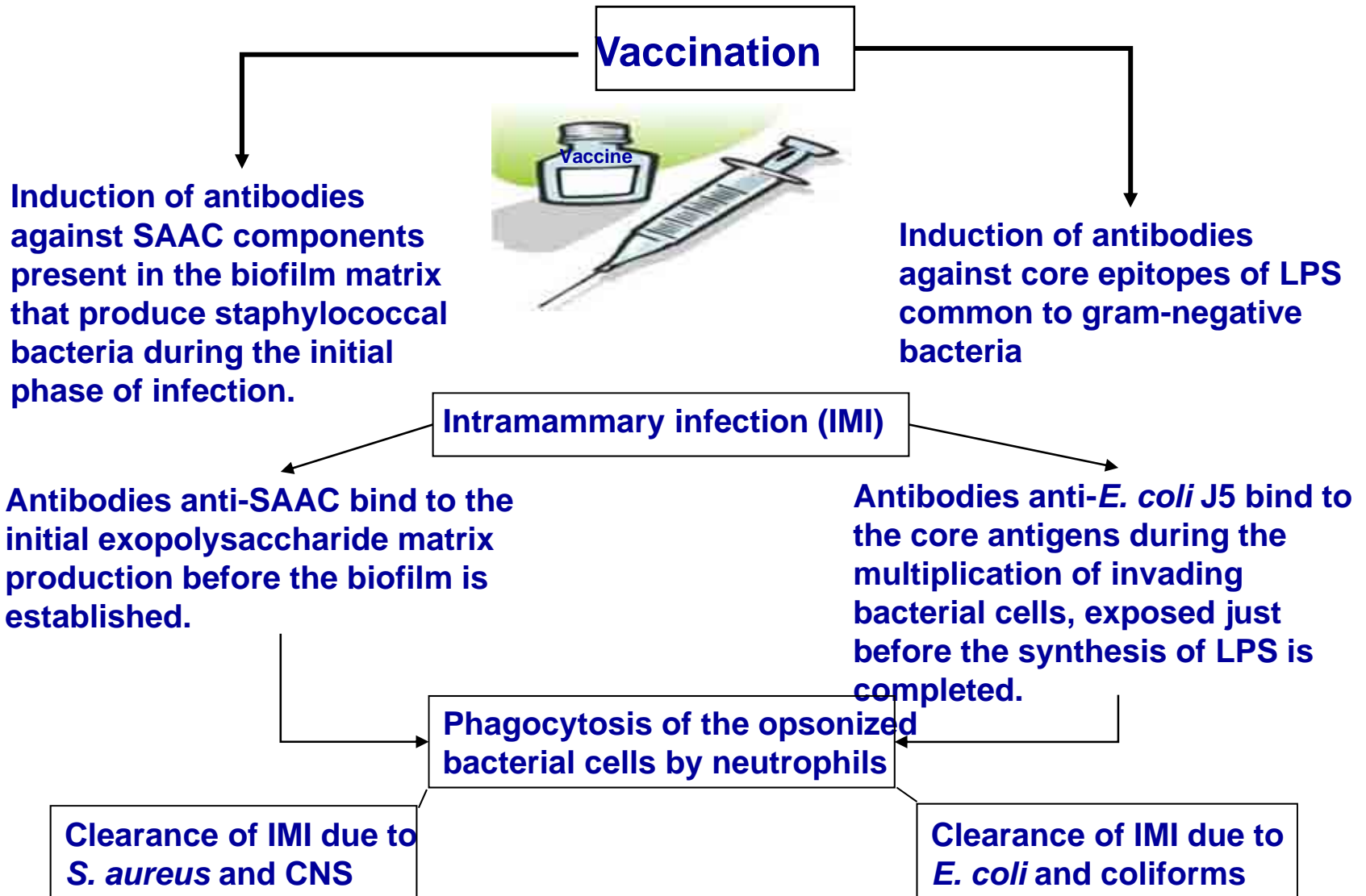
Vaccine - ANTIGENS



CLINICAL RESULTS



Vaccination: Mechanism of protection

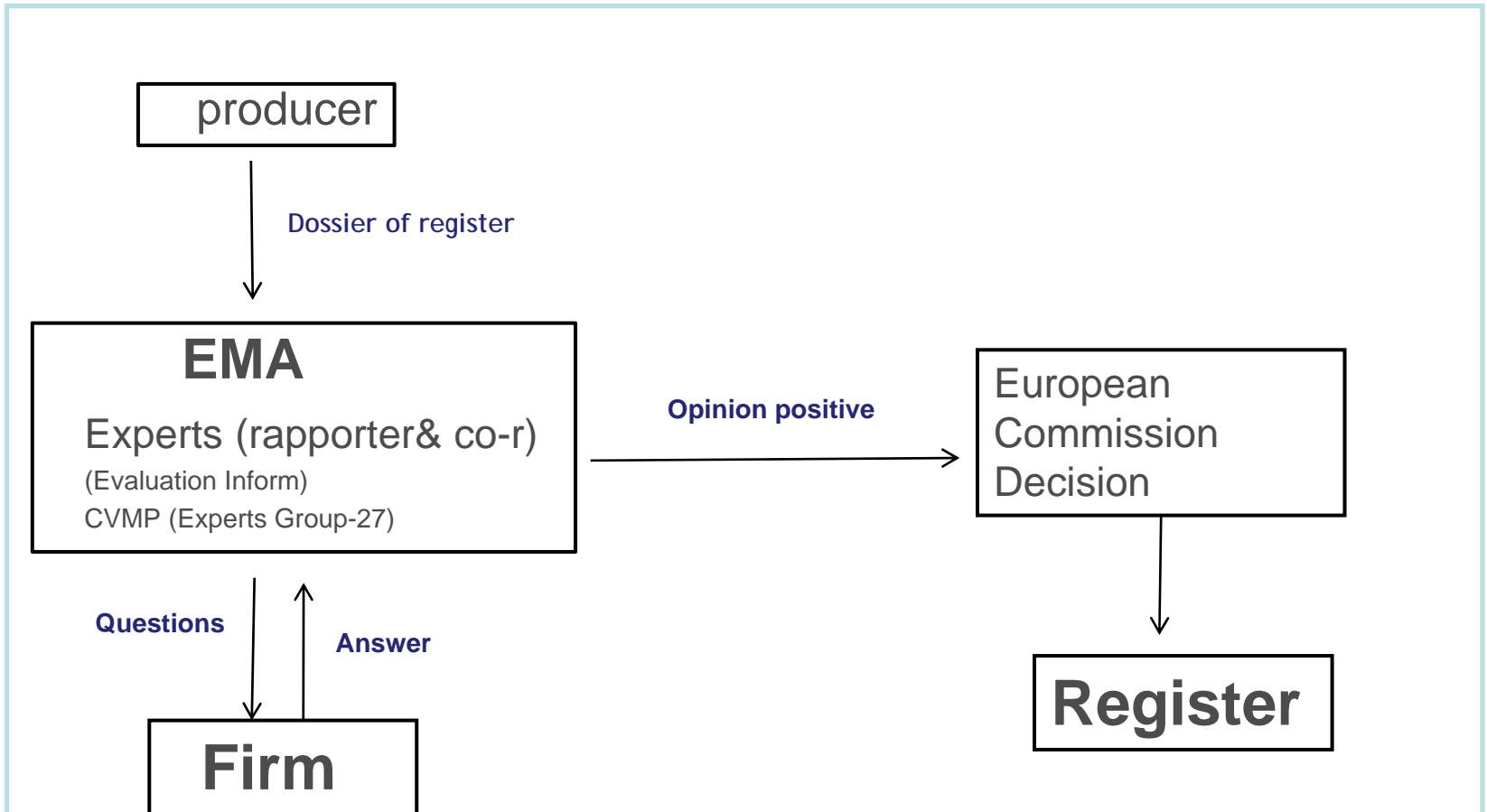


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**REGISTRATION
PROGRAM EMA**

Mastitis cows and immunization

Register Program EMEA (European Medicines Agency) :



Mastitis cows and immunization

Vaccine

EMA register conclusions:

- EMA is the most exigent system to register at this moment in the world.
- It is the first mastitis vaccine registered by this kind of method
- It has been registered simultaneously in 30 European countries

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**EMEA FIELD
TRIALS**

Mastitis cows and immunization

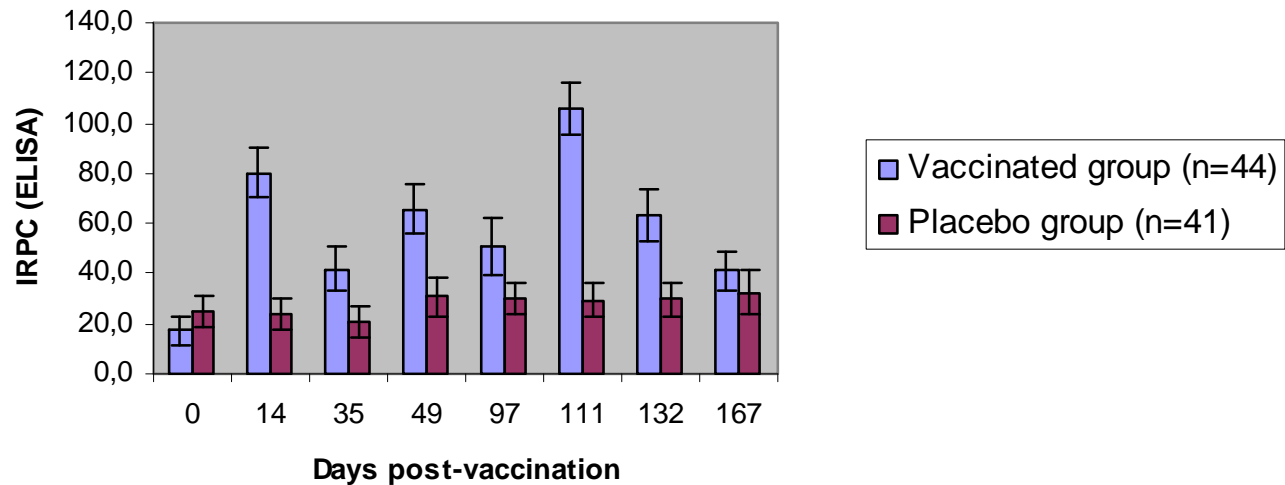
	Variable	STARTVAC Group	PLACEBO Group	STATISTICAL SIGNIFICANT DIFFERENCES BETWEEN STARTVAC AND PLACEBO ($\alpha = 0.05$)
Incidence of intramammary infection clinical or subclinical until day 130	<i>S.aureus</i>	1,18%	10,34%	0,001
	<i>E. coli</i>	4,14%	17,82%	0,001
	CNS	16,57%	32,18%	0,001
Incidence of intramammary infection clinical until day 130	<i>S.aureus</i>	0,00%	2,87%	0,032
	<i>E. coli</i>	1,78%	6,90%	0,02
	CNS	2,37%	6,90%	0,047
Incidence of intramammary infection subclinical until day 130	<i>S.aureus</i>	1,18%	9,77%	0,001
	<i>E. coli</i>	2,37%	13,22%	0,001
	CNS	15,98%	39,98%	0,002
Spontaneous Cure Rate	Multiparous	44,19%	20,45%	< 0,05
	Primiparous	53,33%	50,00%	> 0,05
	total	51,43%	32,18%	< 0,05

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VARIABLE	VACCINATED GROUP	PLACEBO GROUP	STATISTICAL SIGNIFICANT DIFFERENCES BETWEEN VACCINATED AND PLACEBO ($\alpha = 0.05$)	OBSERVATIONS
Somatic cell count (mean SSC x 10 ³)	328,2	548,6	YES (p<0.05)	Internationally recognized indicator for mastitis and milk quality
Milk aspect (>1)	11.42 %	19.79 %	YES (p<0.05)	Implies less economic losses due to lost quarters, discarded milk and replacement cows
Mammary gland aspect (>1)	14.44 %	24,03 %	YES (p<0.05)	
Treatment with pharmacological products	34 treatm 22 cows	93 treatm 40 cows	YES (p<0.05)	Implies less economic losses due to treatments and reduces the risk of residues in milk
Death of cows due to mastitis	0	3	NO (p>0.05)	Low number of deaths. Deaths due to mastitis only occurred in the placebo group.

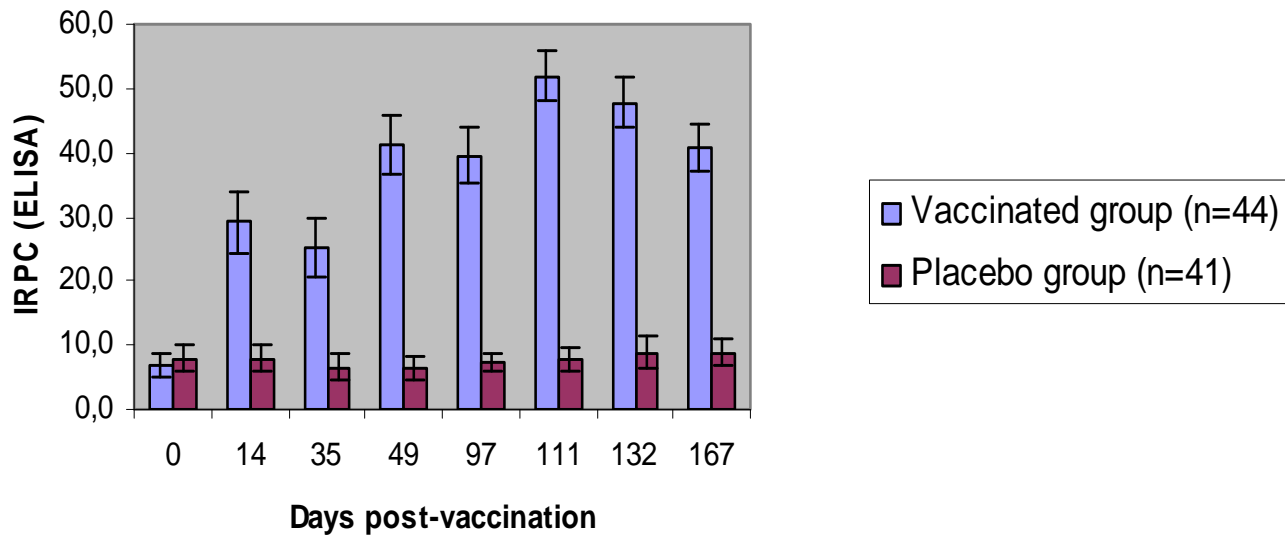
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Figure 2. Serological response anti-*E. coli* J5 in serum at days post-vaccination (EC-2005-CB-001)



Mastitis cows and immunization

Figure 1. Serological response anti-slime in serum at days post-vaccination (EC-2005-CB-001)

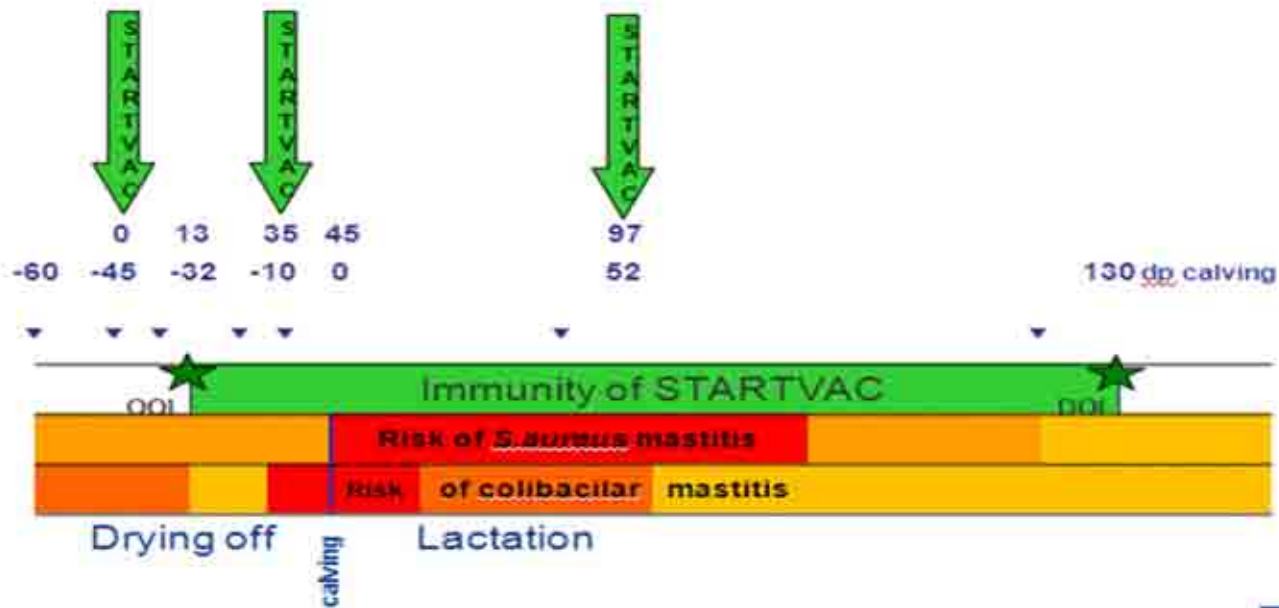


Mastitis cows and immunization

PROTOCOLS

Mastitis cows and immunization

Classical Protocol



SEGMENT:

- Highly skilled farmers and veterinarians
- Farmers with computer

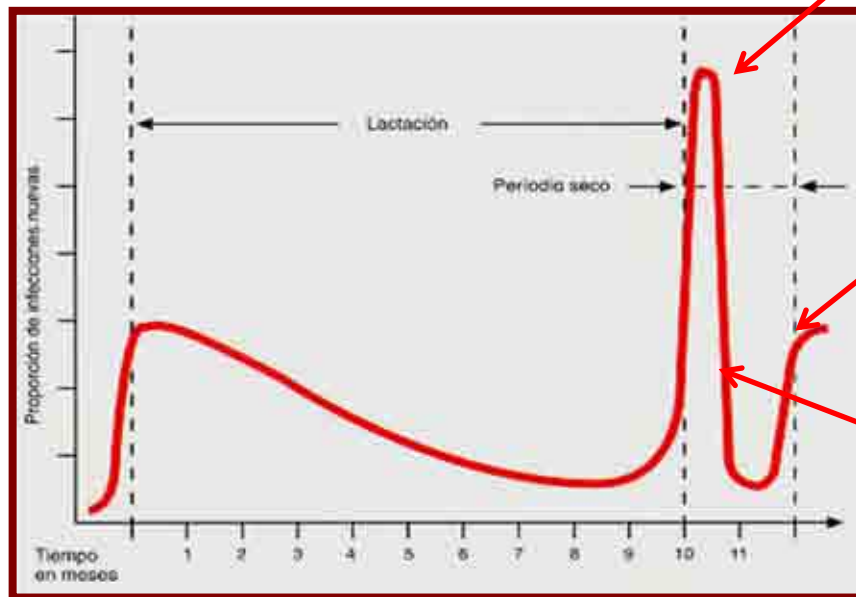
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COMPLEMENTARY WITH DRY ANTIBIOTICS

Infection risk during the first 3 weeks of dry period is **6 times higher** than during previous lactation.

High infection risk during the **10 latest days before partum**.

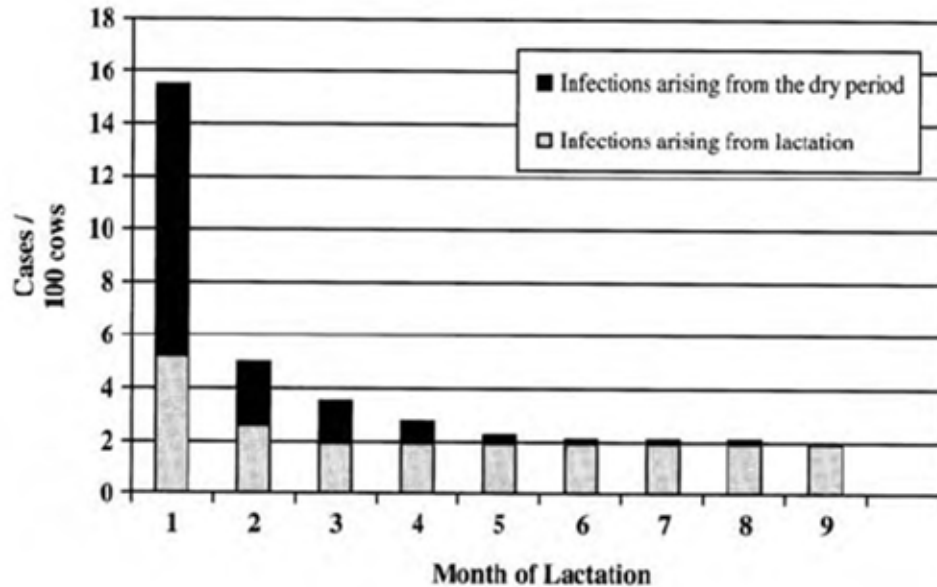
STARTVAC start its action at this moment (13 d after 1st application) is necessary dry antibiotics action



Mastitis cows and immunization

COMPLEMENTARY WITH DRY ANTIBIOTICS

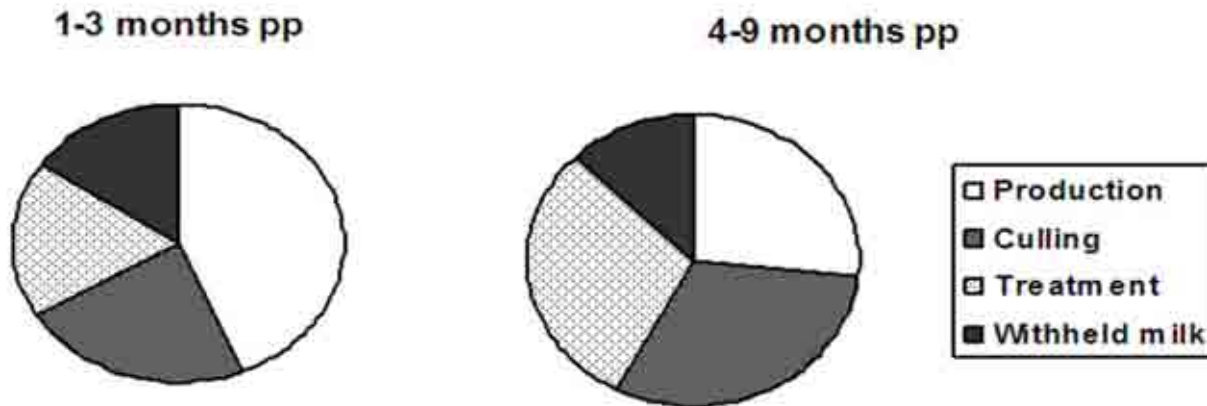
More than 50% of mastitis observed during first 100 DIM are originated in dry period



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Economic advantages with this protocol

- Distribution of the average of the economic loss due to clinical mastitis in the beginning (1-3 postpartum months) and the end (4-9 postpartum months) of the lactation



Origin: mastitis is an economic problem (Henk Hogeveen, The Netherlands)

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ADVANTAGE:

- Colimastitis:
 - it prevents when there is more risk and more mastitis cases
 - Combination with T-Sealant increase the benefit
 - Bibliography J5 vaccines in USA
 - Reduction mastitis treatment cost
 - Increase milk production
- S.Aureus and CNS:
 - Tendency to decrease new infections and tendency to decrease SCC
 - Increase the immunity in farms that separate s.aureus animals

WEAKNESSES:

- It's necessary to know the calving date
- Results are not immediate (only 15% of dry-off cows each month)
- Mistakes with protocol's dates very frequently (Study Francis Sérieys)
- Colimastitis
 - Does not decrease SCC in bull tank (5-15% of clinical case, and not all in same moment)
 - Immunity: short time, does not protect all lactation (130days)
 - Does not protect seasonal mastitis
- S.Aureus /CNS

Difficult to fit with others standard S.aureus control measures

Mastitis cows and immunization

Economic advantages with this protocol

Conclusion:

- The most important consequence of the mastitis affection is the milk reduction, due to its effect during lactation
- If we prevent mastitis during postpartum, we can obtain more benefits than if we make it during lactation

STARTVAC® - Data from a study on 6 farms

Results (0-130 DIM)

	Control	Vaccine
Discarded milk (days)	1.6	0.9
Daily production (kg/day)	30	302
SCC (cells/ml)	548,000	328,000
Risk of clinical mastitis	15%	4%
Risk of sub-clinical mastitis	46%	18%
Elimination	9%	5%

STARVAC® Partial Budget Analysis

Economic Evaluation of the Intervention			
Control (0-130 DIM)			
			TOTAL
		days of discarded milk	1,6
		average daily milk yield (kg)	32
		average SCC (cells/ml)	559.000
		clinical mastitis risk	15%
		subclinical mastitis risk	46%
		culling risk	9%
STARVAC® (0-130 DIM)			
			TOTAL
		days of discarded milk	0,9
		average daily milk yield (kg)	30
		average SCC (cells/ml)	431.000
		clinical mastitis risk	4%
		subclinical mastitis risk	18%
		culling risk	5%
Extra / reduced revenue		milk production	NSD
		SCC premiums	€ -
Reduced / extra costs		days of discarded milk	€ 7
		clinical mastitis treatment	€ 5
		infection transmission	€ 22
		culling	€ 30
		marginal feed cost	NSD
		vaccination cost	€ (17)
		STARVAC® net profit per cow (direct effects)	€ 25
		STARVAC® net profit per cow (indirect effects)	€ 22
		STARVAC® net profit per cow	€ 47

47€

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3:3:3 PROTOCOL



STARTVAC IMMUNITY **STARTVAC IMMUNITY**

ALL ANIMALS (LACTATION, DRY-OFF COWS AND HEIFERS)

SEGMENT:

- Medium low skilled farmers and veterinarians

Mastitis cows and immunization

ADVANTAGE:

- Results in a short time
- Take advantage of seasonality
- Facilities management
- Benefit: good feeling by the farmer
- Appropriate response in variable situations
- **Colimastitis:**
 - To protect all lactation
 - Seasonal campaign
 - Reduces cost of treatments
 - Reduces SCC of subclinical cases
- **S.Aureus:**
 - Increase Immunity level
 - Reduce the possibility of contagious
 - Reduce new infections
 - Reduce SCC in milk tank (farms with prevalence > 20%)

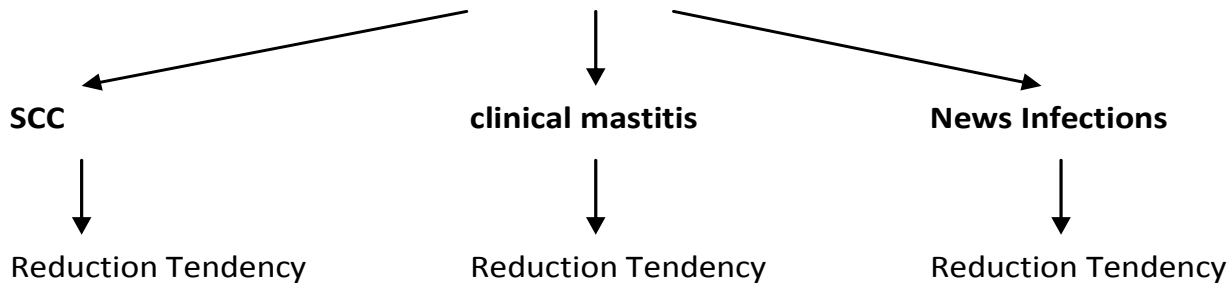
WEAKNESSES:

- There aren't official results
- E.Schmitt (from France) next May
- A.Bradley (from UK) next November

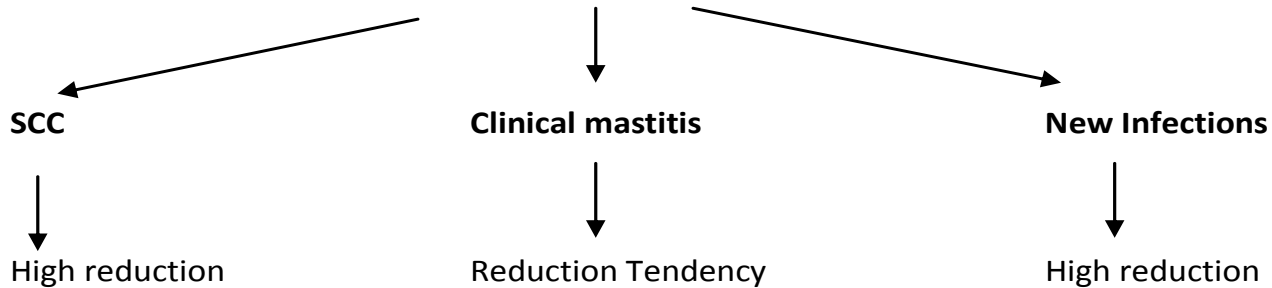
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S.AUREUS MASTITIS (>20% Prevalence)

Classical Protocol (high level farmers and veterinarians)



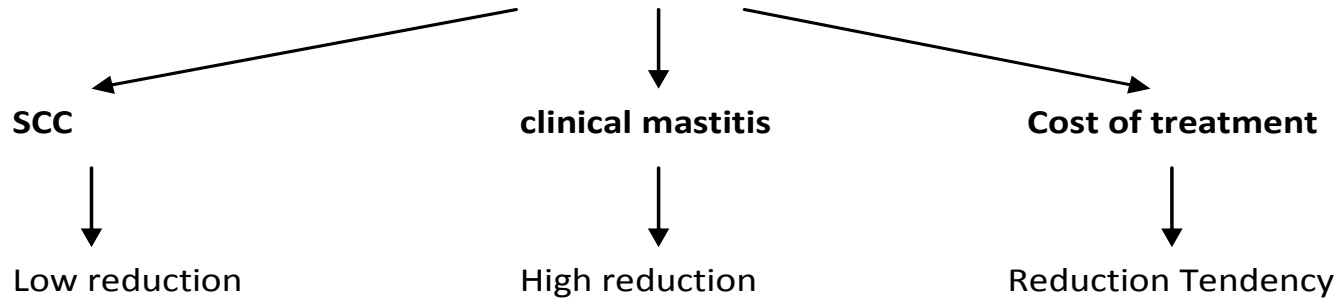
3:3:3 Protocol (Medium & small level farmers and vets)



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COLI MASTITIS

Classical Protocol (high level farmers and veterinarians)



3:3:3 Protocol (Medium & small level farmers and vets)

