

# 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



## **Mastitis cows and immunization**

# **MAIN CHARACTERS**

# Mastitis cows and immunization

## 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)

# Mastitis cows and immunization

## 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**

# **Mastitis cows and immunization**

## **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*

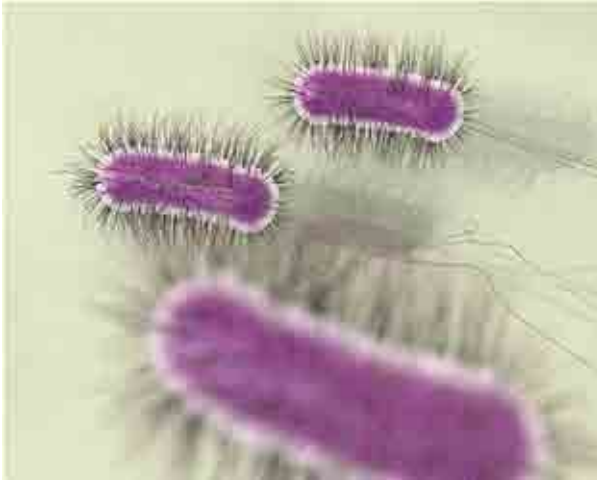
### ***E.coli:***

- **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*:**

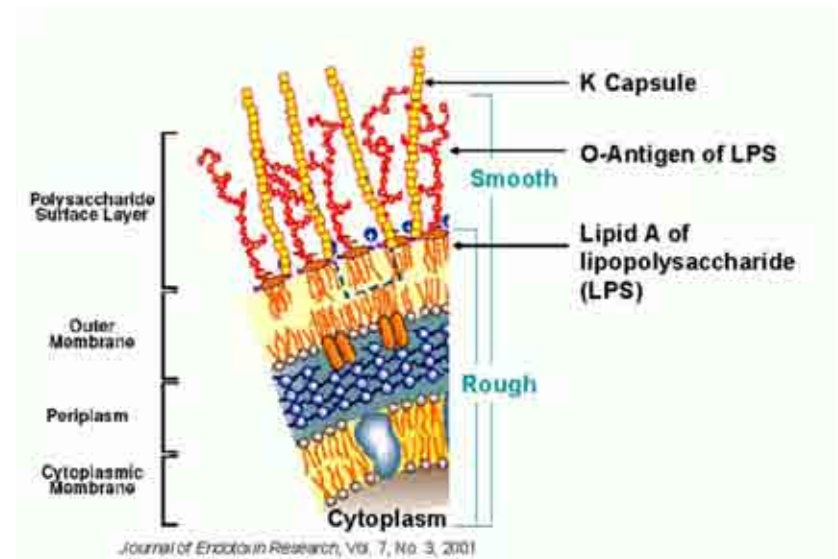
- Colonization due to the **Slime or Biofilm**, which facilitates adhesion between the bacteria and, simultaneously, does not allow the penetration of antibiotic treatments.
- **Vaccine** stops the development of micro-colonies

## Some general features of *Escherichia coli*

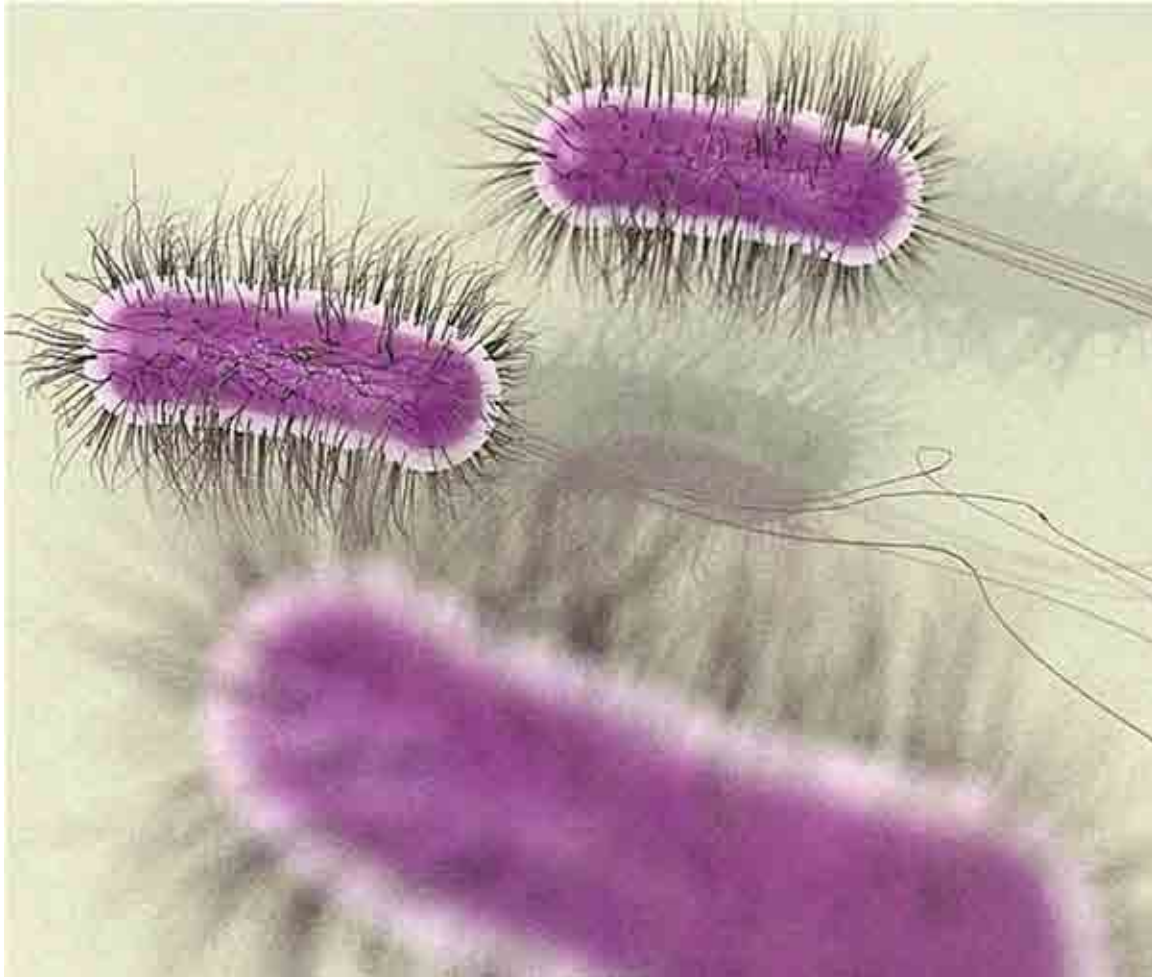


The vaccine was developed with the concept of the exposure of the core antigen common to Gram-negative organisms in the mutant J5 strain (rough strain).

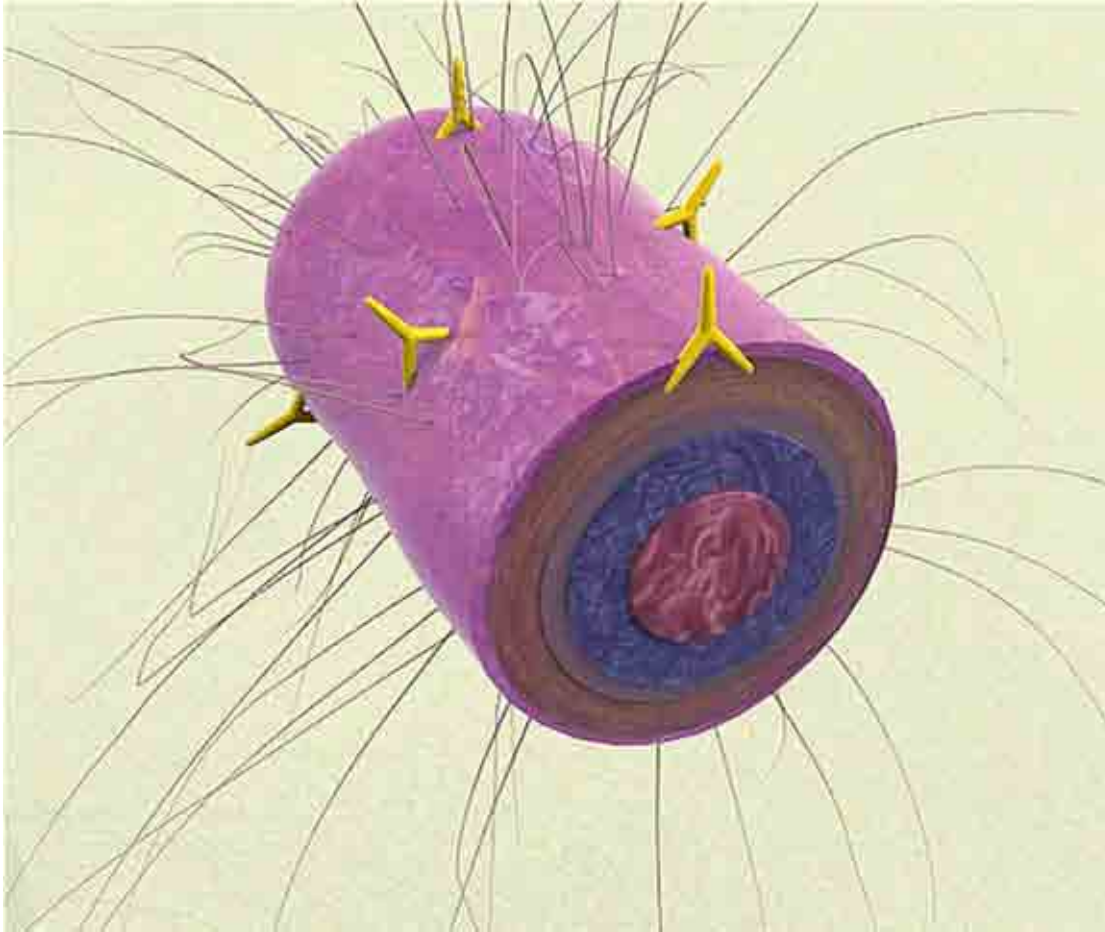
*E. coli* J5 is a strain that lacks the enzyme Uridin Diphosphate Galactose 4-Epimerase, which is responsible for binding the somatic antigen (O-Antigen of polysaccharide) to the LPS molecule of the cell wall.



# Mastitis cows and immunization



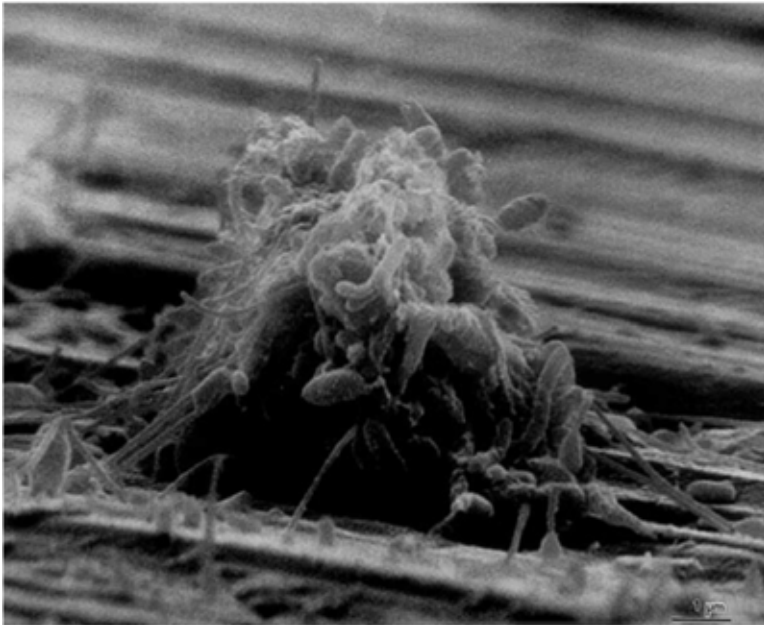
# Mastitis cows and immunization



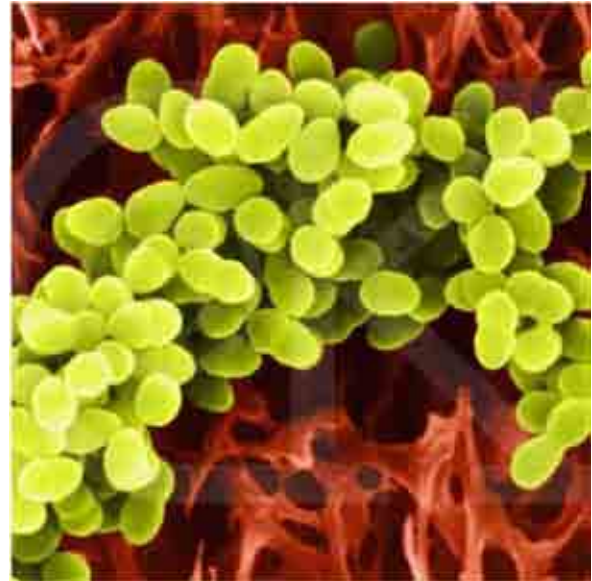
# The Biofilm as survival mechanism

**Biofilms are survival mechanisms of clinically relevant microorganisms.**

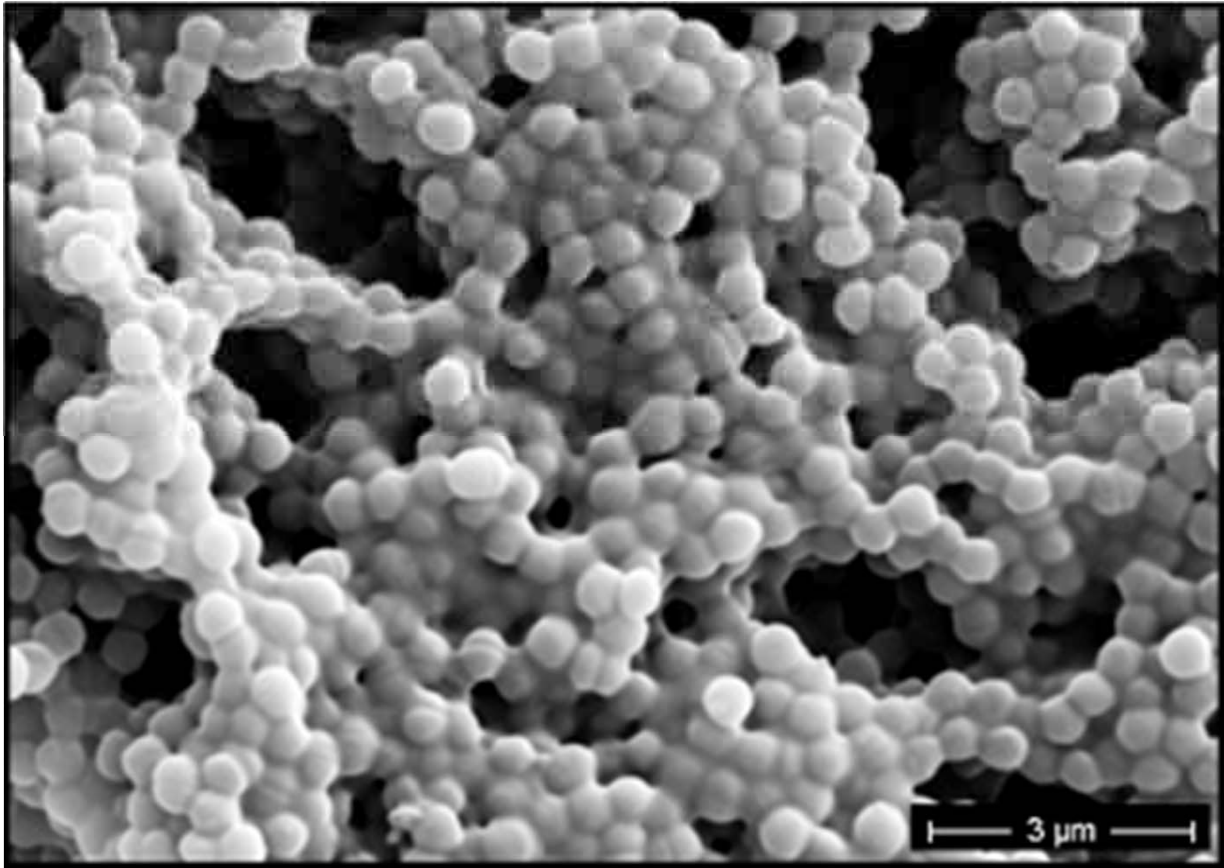
**The production of this extracellular matrix defines the ability of bacterial strains to colonize host tissues and biomaterials, participating in the intercellular adhesion among bacterial cells and subsequent development of a BIOFILM, leading to chronic infections and bacterial resistance to phagocytosis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



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



# Mastitis cows and immunization



# The Biofilm as survival mechanism

- Bactericidal effect of the antibiotics on the biofilm:

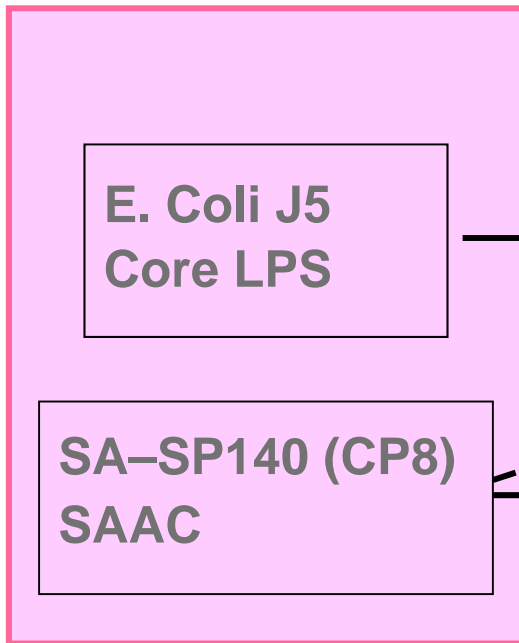
Microorganism	Antibiotic	Reference Organism Antibiotic MIC or MBC of planktonic phenotype (µg/ml)	Concentration effective against biofilm phenotype (µg/ml)
<i>S. aureus</i> NCTC 8325-4	Vancomycin	2 (MBC)	20
<i>Pseudomonas aeruginosa</i> ATCC 27853	Imipenem	1 (MIC)	1,024
<i>E. coli</i> ATCC 25922	Ampicillin	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

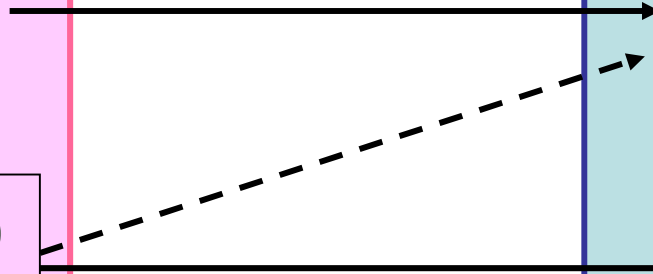
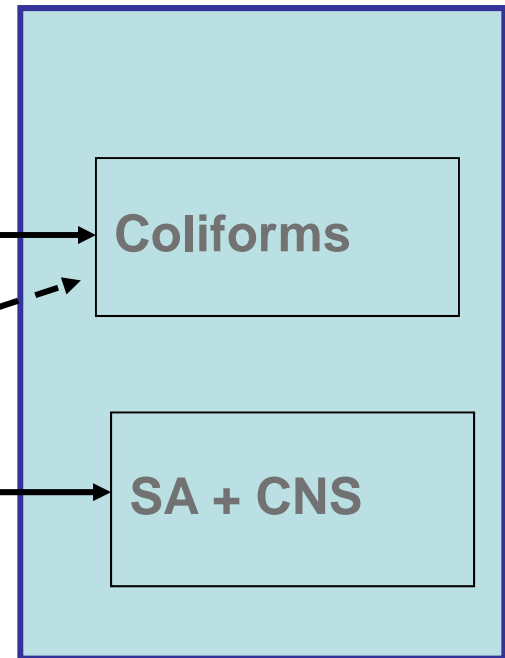
MBC: Minimum Bactericidal Concentration

# From antigens to protection

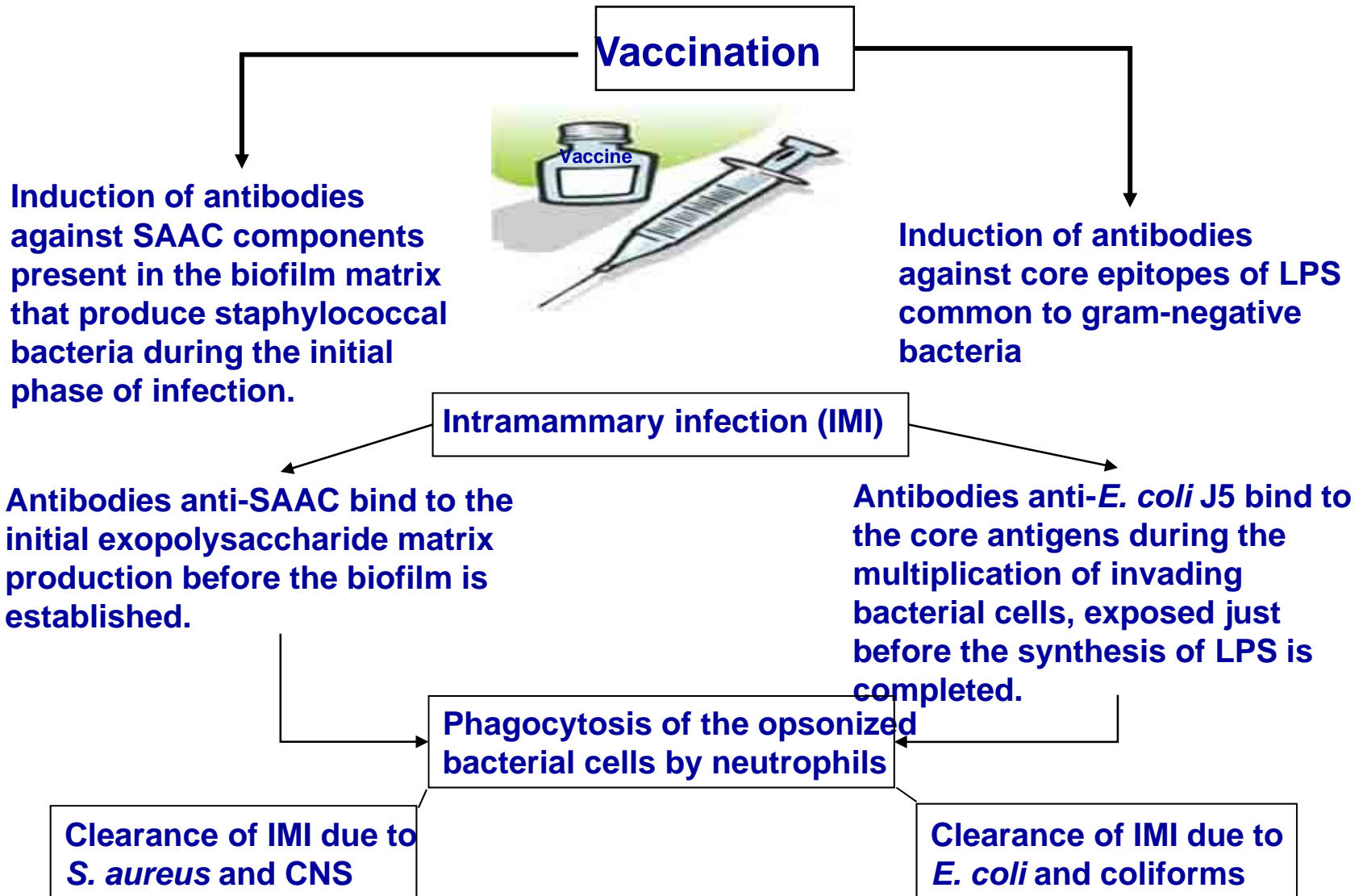
## Vaccine - ANTIGENS



## CLINICAL RESULTS



# Vaccination: Mechanism of protection

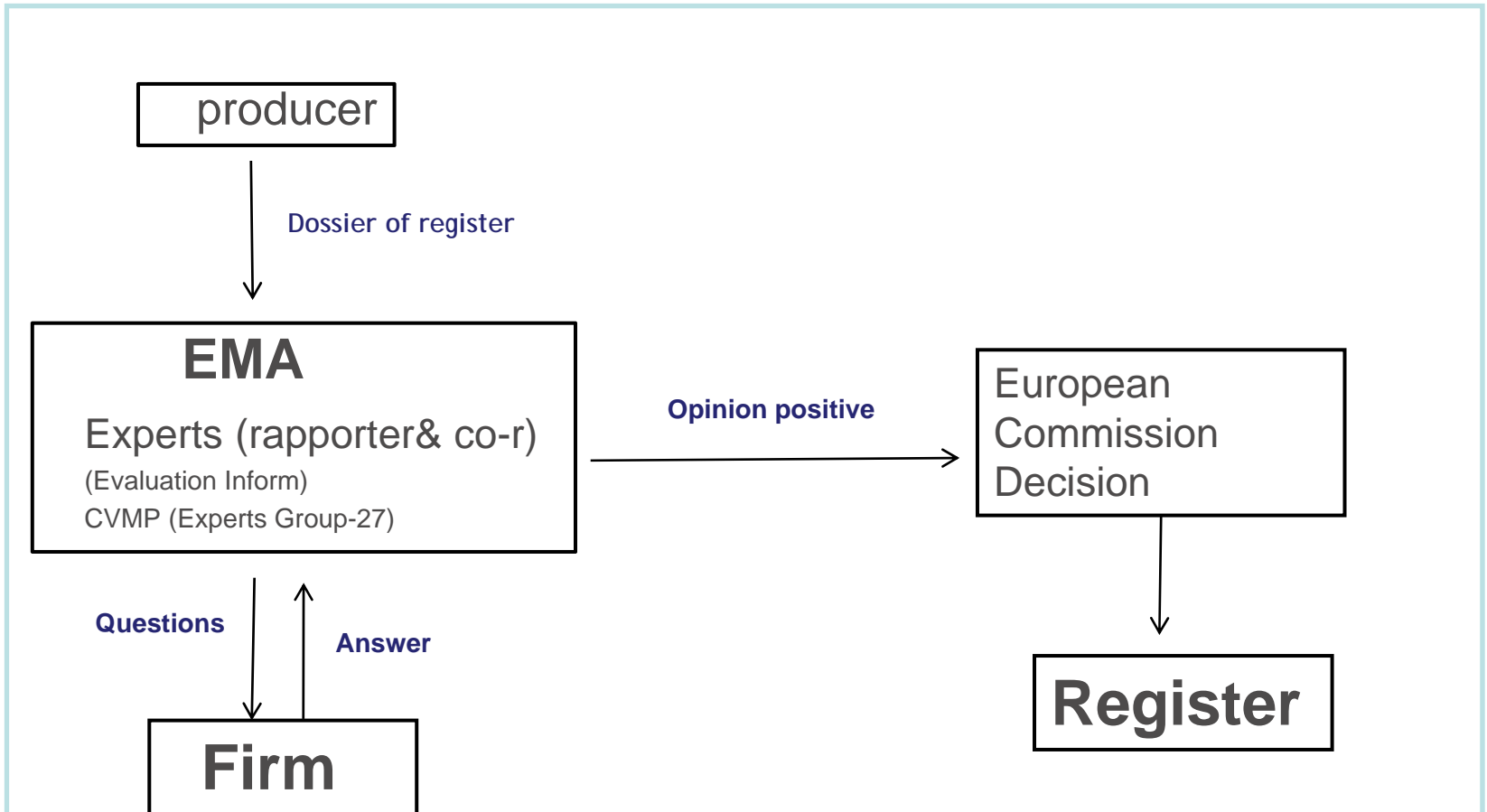


**Mastitis cows and immunization**

**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

**Mastitis cows and immunization**

# **EMEA FIELD TRIALS**

# Mastitis cows and immunization

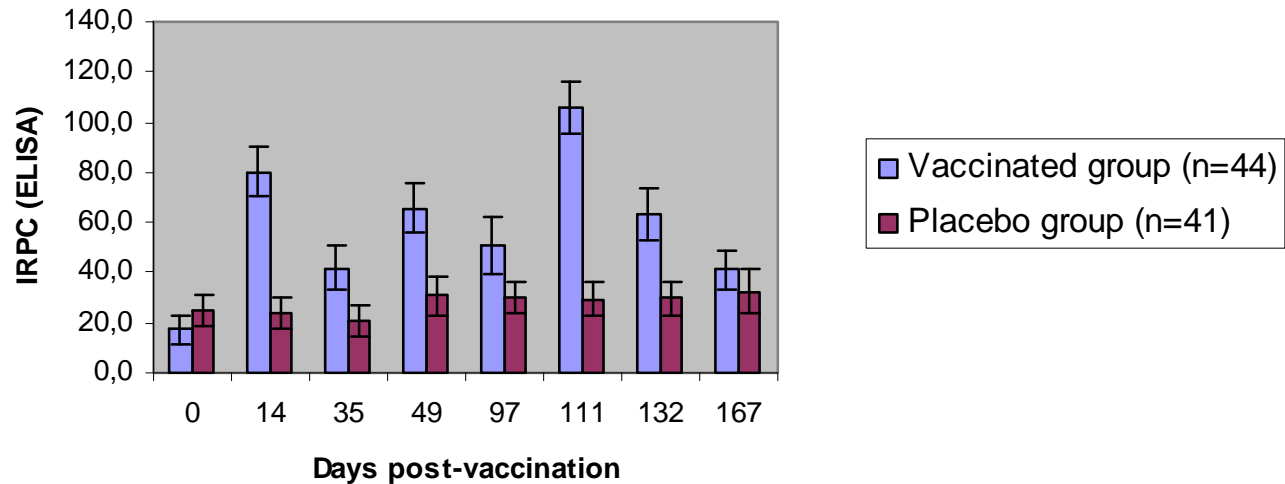
	Variable	STARTVAC Group	PLACEBO Group	STATISTICAL SIGNIFICANT DIFFERENCES BETWEEN STARTVAC AND PLACEBO ( $\alpha = 0.05$ )
Incidence of intramammary infection clinical or subclinical until day 130	<i>S.aureus</i>	1,18%	10,34%	0,001
	<i>E. coli</i>	4,14%	17,82%	0,001
	CNS	16,57%	32,18%	0,001
Incidence 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

# Mastitis cows and immunization

VARIABLE	VACCINATED GROUP	PLACEBO GROUP	STATISTICAL SIGNIFICANT DIFFERENCES BETWEEN VACCINATED AND PLACEBO ( $\alpha = 0.05$ )	OBSERVATIONS
Somatic cell count (mean SSC x 10 <sup>3</sup> )	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.

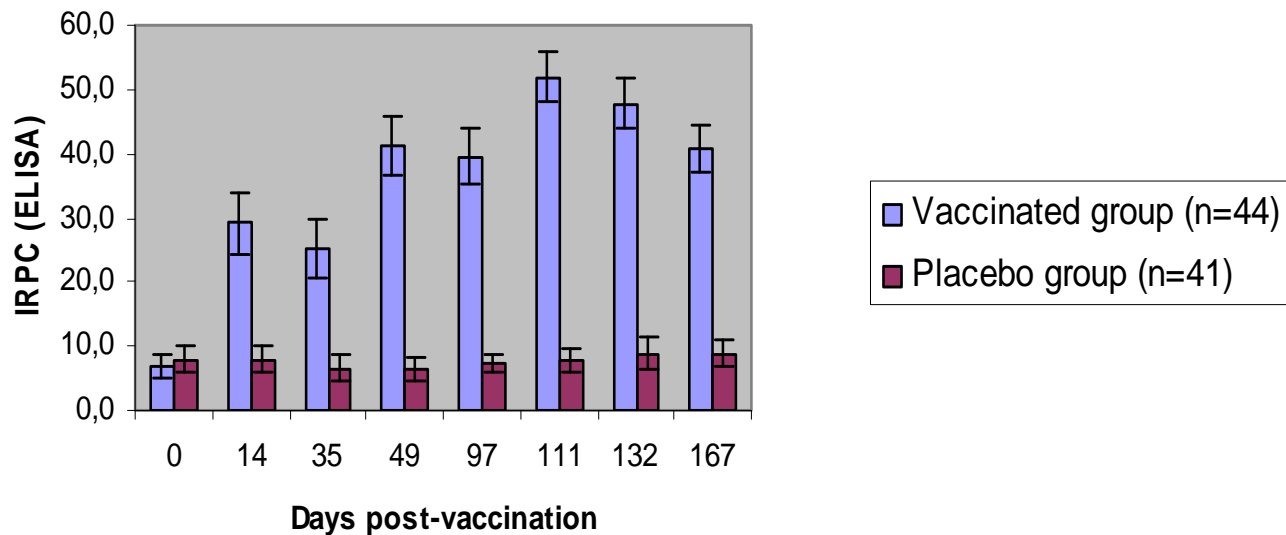
# Mastitis cows and immunization

**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)**

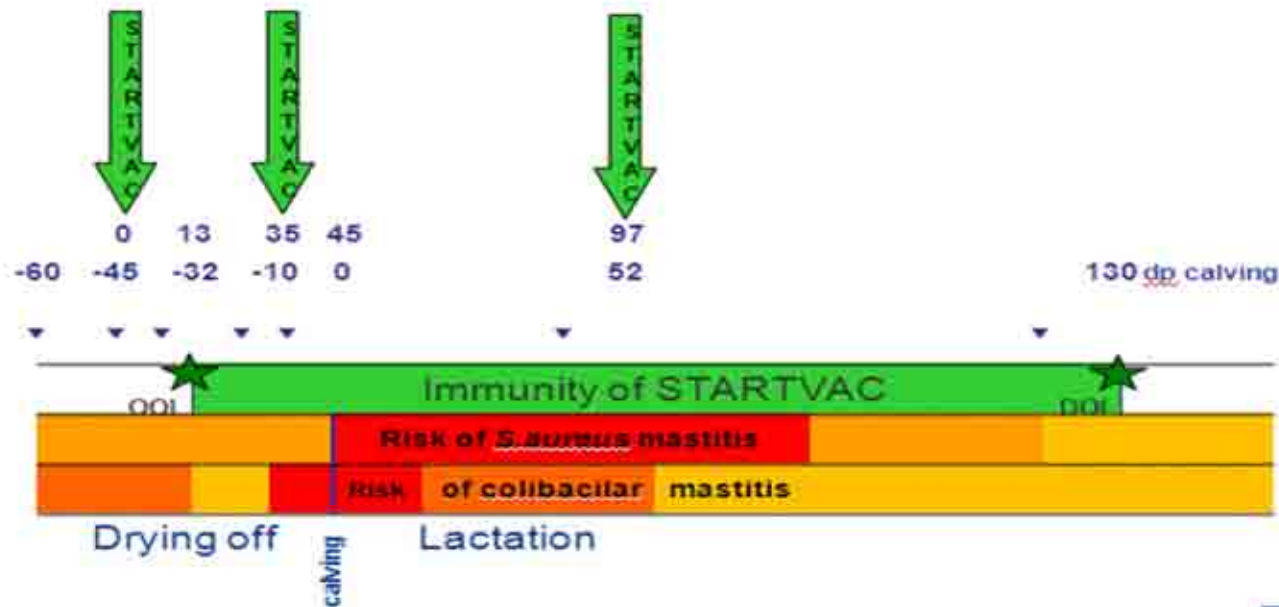


**Mastitis cows and immunization**

# **PROTOCOLS**

# Mastitis cows and immunization

## Classical Protocol



### SEGMENT:

- Highly skilled farmers and veterinarians
- Farmers with computer

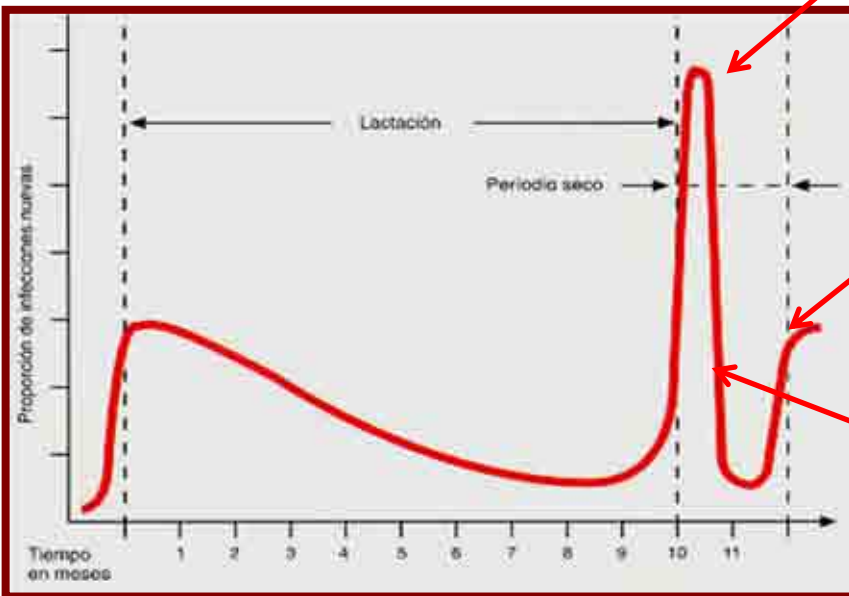
# Mastitis cows and immunization

## 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**.

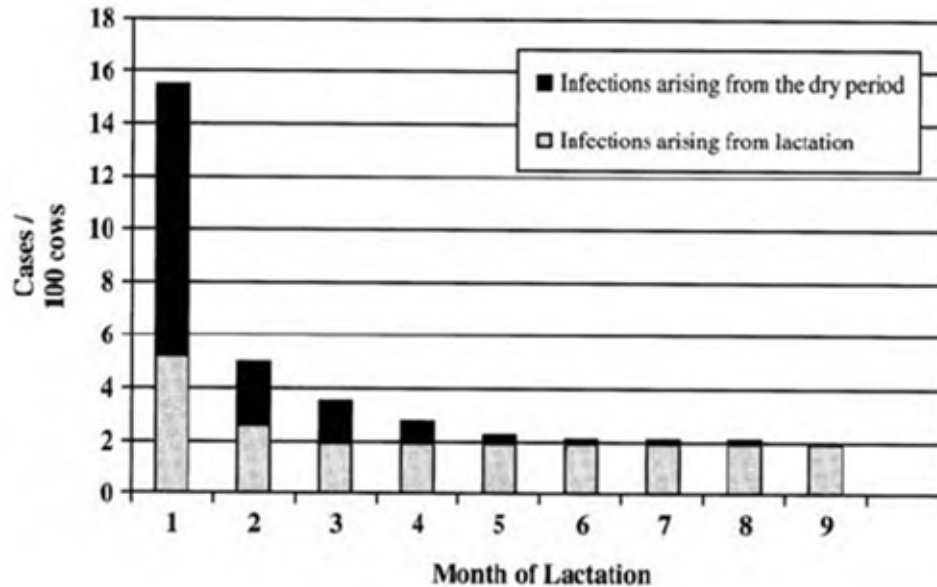
**STARTVAC** start its action at this moment (13 d after 1st application) is necessary dry antibiotics action



# Mastitis cows and immunization

## COMPLEMENTARY WITH DRY ANTIBIOTICS

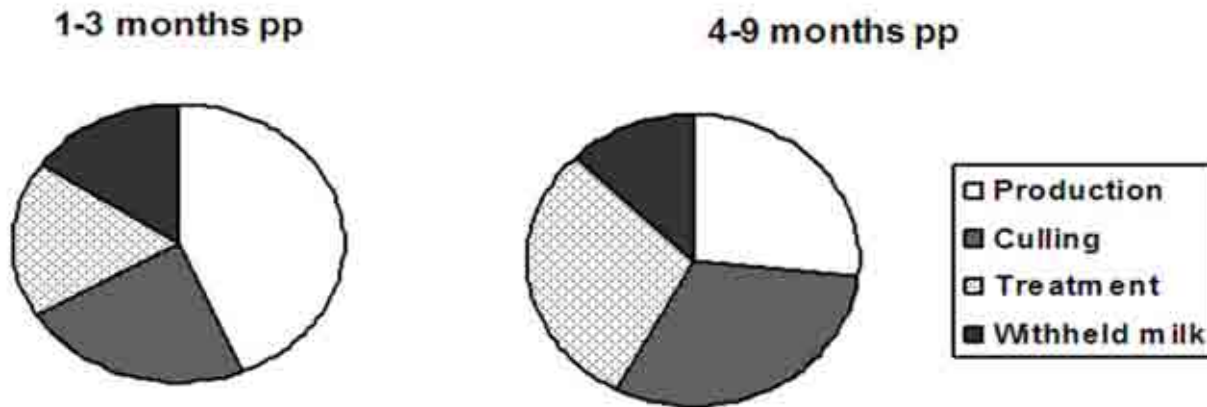
More than 50% of mastitis observed during first 100 DIM are originated in dry period



# Mastitis cows and immunization

## 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)

# Mastitis cows and immunization

## **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 Sériey)
- 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

<b>Economic Evaluation of the Intervention</b>					
<b>Control (0-130 DIM)</b>					
				<b>TOTAL</b>	
			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%
<b>STARVAC® (0-130 DIM)</b>					
				<b>TOTAL</b>	
			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%
	<b>Extra / reduced revenue</b>		milk production		NSD
			SCC premiums	€	-
	<b>Reduced / extra costs</b>		days of discarded milk	€	7
			clinical mastitis treatment	€	5
			infection transmission	€	22
			culling	€	30
			marginal feed cost		NSD
			vaccination cost	€	(17)
	<b>STARVAC® net profit per cow (direct effects)</b>			€	25
	<b>STARVAC® net profit per cow (indirect effects)</b>			€	22
	<b>STARVAC® net profit per cow</b>			€	47

47€

# Mastitis cows and immunization

**3:3:3 PROTOCOL**



**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%)

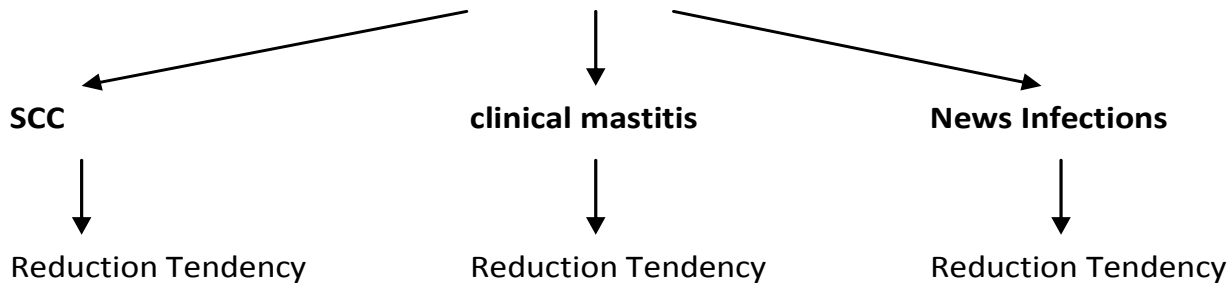
## **WEAKNESSES:**

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

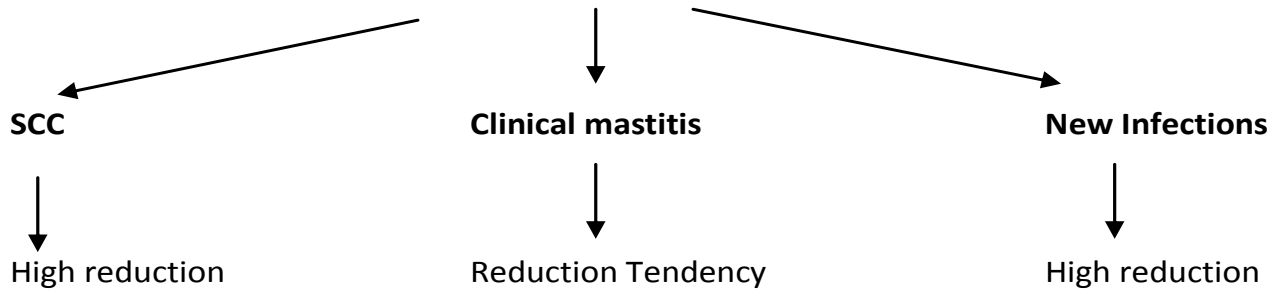
# Mastitis cows and immunization

**S.AUREUS MASTITIS (>20% Prevalence)**

**Classical Protocol** (high level farmers and veterinarians)



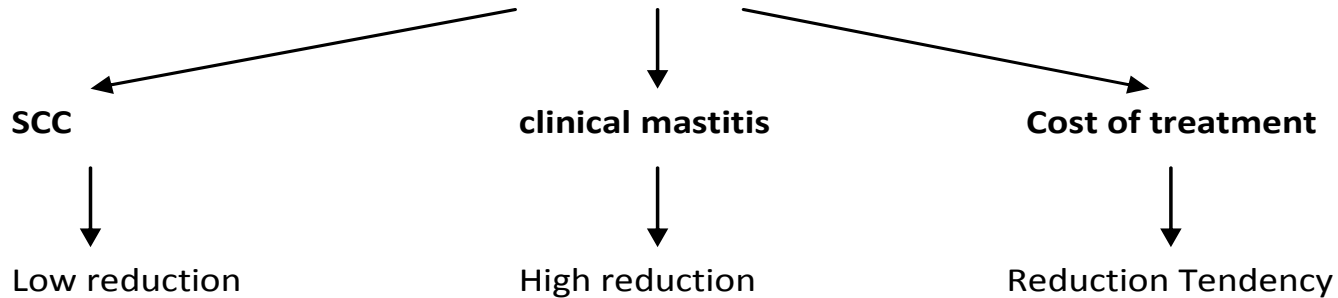
**3:3:3 Protocol** (Medium & small level farmers and vets)



# Mastitis cows and immunization

## COLI MASTITIS

### Classical Protocol (high level farmers and veterinarians)



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

