

Basic training course

Enzymes



Outline of the presentation

CHR HANSEN

- ▼ Introduction to CHR HANSEN's enzymes world
 - ▶ What is an enzyme? p3
 - ▶ What is our portfolio? p7
 - ▶ Who is who? p11
 - ▶ What tools to use to find enzymes' information? p12

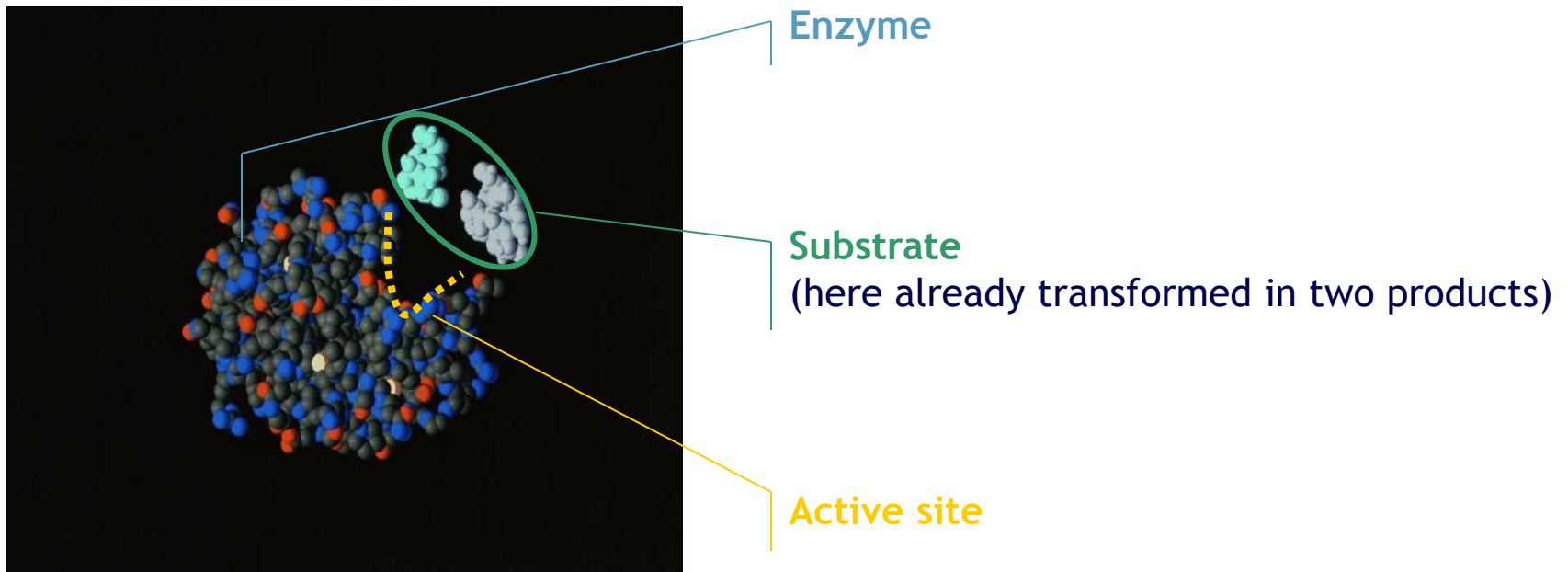
- ▼ Tour through CHR HANSEN's enzymes portfolio
 - ▶ Coagulants p15
 - ▶ YieldMAX™ PL p26
 - ▶ AFILACT™ & Chrisin p41
 - ▶ Ha-Lactase™ p47
 - ▶ Test Kits p50

What is an enzyme?

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- ▶ Enzymes are complex proteins able to catalyze (*i.e.* accelerate) chemical reactions through their active site...

Example of enzyme in action: lysozyme cutting a molecule in two new products



Source: LBNL Image Library - Collection BERKELEY

What is an enzyme?

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- ▷ Enzymes have in common a certain number of features to keep in mind that made and explained their strengths and weaknesses



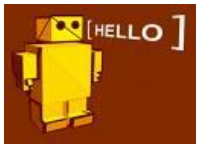
Their nature

- ✓ "biological" but not living products
- ✓ Proteins (or proteins + something else)...



Their sensibility to working conditions

- ✓ ...highly sensible to their environment (T, pH...)



Their specificity

- ✓ Very good at only one task



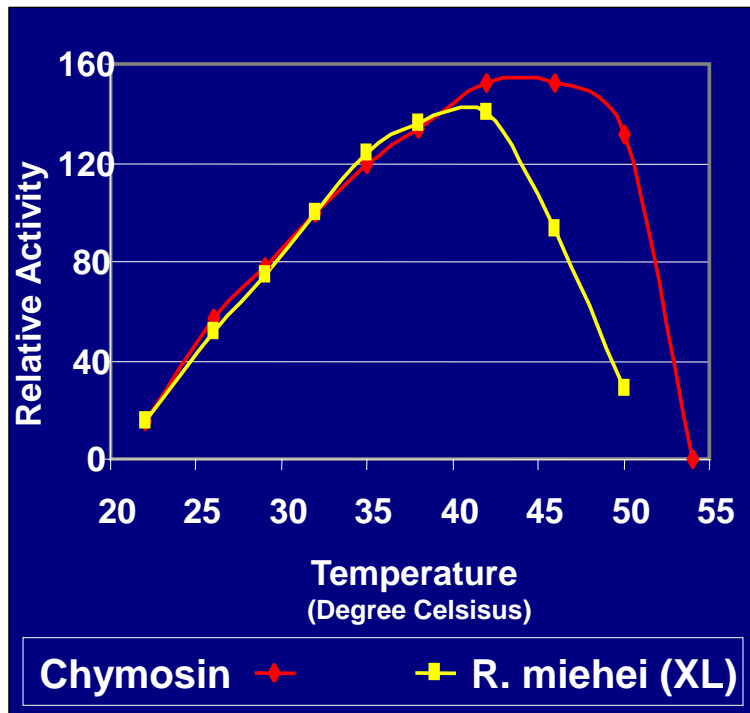
Their regulation

- ✓ Many elements regulate (+ or -) their work

How is it to work with enzymes?

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- ▷ Working with enzymes highly accelerate the production process but requires to know and respect the working conditions of the used enzyme



- ▼ Mild Processing conditions
 - ▼ Low temperature → low activity
 - ▼ High temperature → denaturation
- ▼ Specificity
- ▼ Activators/inhibitors
- ▼ More enzyme (activity) -> more reactions

Where do we find enzymes?

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- ▷ These biomolecules are wide spread both in our body and in our day to day environment through a various range of products

Examples of enzymes present in

Our body



Digestive enzymes

Energy procuring enzymes

Repairing enzymes

Products of our day to day life

Enzymes = still active products



Enzymes = processing aids



What is CHR HANSEN portfolio?

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- ▷ CHR HANSEN's portfolio is composed of these 2 main categories of products...

Enzymes = still active products



- ▶ Test kits to detect antibiotic

Enzymes = processing aids






- ▶ Food enzymes used as processing aids

What is CHR HANSEN portfolio?

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▷ ... used in cheese and dairy industries for 6 different types of applications

<i>Product name</i>	<i>Enzyme(s)</i>	<i>Industry</i>	<i>Application</i>
NATUREN™	Chymosin - Pepsin		Milk-clotting
CHY-MAX™	Chymosin		
HANNILASE™	Blend of proteases		
THERMOLASE™	Blend of proteases		
LIPASE™	Lipase		Flavors enhancement during cheeses ripening
YieldMAX™ PL	Phospholipase		Cheese yield production enhancement
AFILACT™ & Chrisin	Lysozyme Nisin		Natural protection of dairy products and cheeses
Ha-LACTASE™	Lactase		Lactose degradation to produce lactose free products for intolerant people
TEST KITS	...		Antibiotic detection in raw milk

What is CHR HANSEN in the enzyme market?

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- ▷ A DWARF regarding the global market but a market SPECIALIST on a niche segment: the dairy market



- ▼ Big enzyme markets (1.5 billion USD)
 - ▼ Detergents
 - ▼ Industrial
 - ▼ Textile/leather
 - ▼ Pulp/paper
 - ▼ Oil/fuel - alcohol production
 - ▼ Feed
 - ▼ Food
 - ▼ Sweetener
 - ▼ Baking
 - ▼ **Dairy**
 - ▼ Brewing
 - ▼ Distilling
 - ▼ ...

*Dairy enzymes: 150 million €
CHR HANSEN: 40% market share*

What is our regulatory status?

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▷ Chr Hansen's enzymes portfolio is mainly composed of "processing aids" helping customers to manage their production processes



- ▼ No harmonised European legislation yet
- ▼ Draft enzyme Regulation published
 - ▶ until then, some local legislation..
- ▼ Directive 89/107/EC
 - ▶ enzyme as additive: invertase, lysozyme
- ▼ DOC/AOC
- ▼ Allergens - fermentation exempted
- ▼ BSE
 - ▶ GBR - Geographical BSE Risk
 - ▶ SRM - Specified Risk Materials
- ▼ GMO
 - ▶ fermentation exempted
(except Japan, South Korea)
 - ▶ labelling: processing aids exempted

Who is who?

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Michel Guiraudou,
VP CD Cult & Enz



Hans Chr Bejder,
Marketing Director



David Stroo,
Marketing Director



Ole Madsen,
Marketing Manager



Laurent Hubert,
Marketing Manager



Kirsten Søndergård
Prod. Serv. Manager



Casper Christensen,
Product Service Group



Marianne Harboe,
R&D



Mikkel Laust Broe,
Applications



Jacob Jacobsen,
Production

How to find information?

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- Relevant documents regarding enzymes business for customers are stored and shared through 2 Lotus Notes databases

Business Operation Library

1

BO Document Library on DKAPPL01

Price List Document Library

2

PriceList Document Library on DKAPPL01

Business Operation Library

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Business Operations Library

BO DOC\Business Development\Enzymes

About this DB

All documents by:

- ▼ Category
- ▼ Author
- ▼ Date
- ▼ My documents



- ✓ *Range of products*
- ✓ *Product documentation, specification*
- ✓ *Presentations (CHY-MAX™, Test kits...)*
- ✓ *Sales tools (cheese yield, Excel programmes to demonstrate gains to customers...)*
- ✓ ...

BO DOC\Business Development\Certificates\Enzymes

- ✓ *Allergens, BSE*
- ✓ *GMO*
- ✓ *Halal, Kosher*

PriceList Document Library

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Document Library

Sorted by:

My Documents

All Documents

Approvers

Authors

Exit

New Document Move to 'My Documents'

Author








Price List DOC\Enzymes

- ✓ *TSP = Targeted Sale Price*
- ✓ *MSP = Minimum Sale Price*
- ✓ *Deviation report regarding MSP to fill in and send to marketing for agreement/non agreement before any deal*

Tour through CHR HANSEN 's portfolio

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COAGULANTS

Product name	Enzyme(s)	Industry	Application
NATUREN™	Chymosin - Pepsin		Milk-clotting
CHY-MAX™	Chymosin		
HANNILASE™	Blend of proteases		
THERMOLASE™	Blend of proteases		
LIPASE™	Lipase	 	Flavors enhancement during cheeses ripening
YieldMAX™ PL	Phospholipase		Cheese yield production enhancement
AFILACT™ & Chysin	Lysozyme Nisin	 	Natural protection of dairy products and cheeses
Ha-LACTASE™	Lactase		Lactose degradation to produce lactose free products for intolerant people
TEST KITS	...		...

Coagulants

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Product name	Way of production	Strategy	Remarks
NATUREN™	Extraction	Enjoy it while it lasts	Historical For AOC-DOC...
CHY-MAX™	Fermentation <i>produced by a GMM*</i>	Convert the market	OUR STAR
HANNILASE™	Fermentation <i>produced by a non GMM</i>	Grow our share	Trade product
THERMOLASE™	Fermentation <i>produced by a non GMM</i>	Niche market	Design for Swiss type cheeses

**GMM: Genetically Modified Micro-organism*

NATUREN™ - Extraction

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- ▷ NATUREN™ is Animal Rennet, extracted in Gråsten (DK) from calf or bovine stomachs...



Frozen stomachs

*Separation of meat, fat & enzymes
through several steps of
centrifugation, concentration, rinsing...*

*Optional separation of the 2 enzymes
(chymosin, pepsin)
by ion chromatography*

Production for our final range of products

NATUREN™ - BSE

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- ▷ ... as it comes from animal tissues the frequently asked question regards the Bovine Spongiform Encephalopathy (BSE) or “mad cow disease”

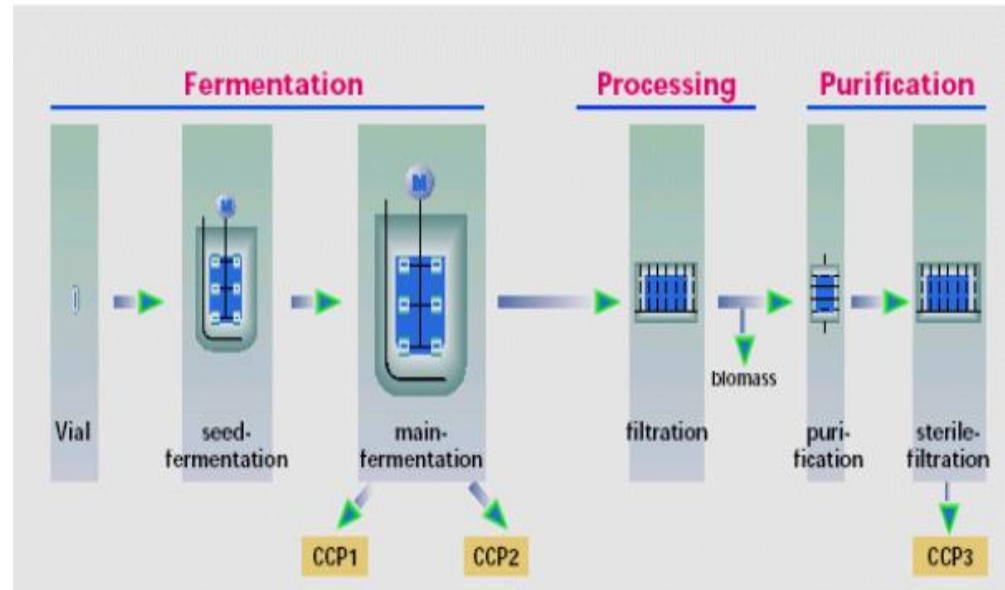


- ▼ EFSA: BSE risk from rennet is negligible (like milk)
 - ▶ Animal rennet is safe for food applications!
- ▼ Still, pharmaceutical standards (appl. to whey products for instance), target an elimination of animal tissue. (Ref: EMEA/410/01 rev. 2.).
 - ▶ BSE risk in CHY-MAX™ / HANNILASE™ is zero!

CHY-MAX™, HANNILASE™, THERMOLASE™ - Fermentation

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- These materials are produced by Fungi during fermentations, CHY-MAX™ and THERMOLASE™ are coming from our plant in Nienburg (GE)



CHY-MAX™ and GMO

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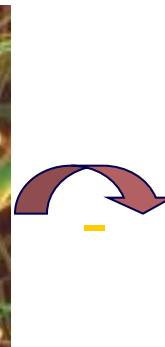
- ▷ CHY-MAX™ is produced by a genetically transformed Fungi therefore the most frequently asked question is “is it a GMO?” and the response is...”NO”...



Chymosin gene
was isolated from
a calf stomach



Gene is fully characterised
then transferred to a fungus
- *Aspergillus niger*



The transformed strain of
Aspergillus niger
produces pure chymosin
in a closed tank

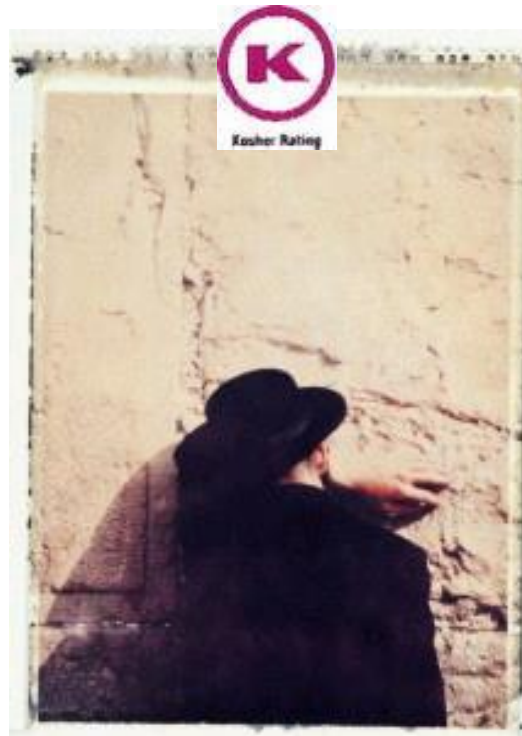
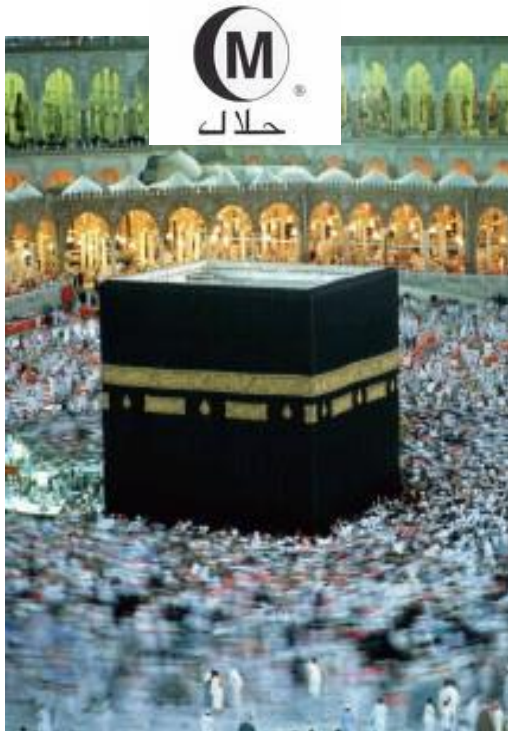
▷ ...because:

- ▼ The Standing Committee on the Food Chain and Animal Health declared on 24 September 2004 that:
- ▼ *‘Food and feed ingredients produced by fermentation using a GMM which is kept under contained use and is not present in the final product, are not included in the scope of Regulation 1829/2003’* (the GMO Regulation).
 - ▶ As CHY-MAX™ is kept under contained use and is not present in the final product (downstream process), **it is not a GMO**
 - ▶ No need to label our enzymes as GMM/ GMO origin...

Halal, Kosher, vegetarian

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- ▶ Fermented products received certificates proving that they have been produced in respect within religious restrictions or vegetarian guidelines

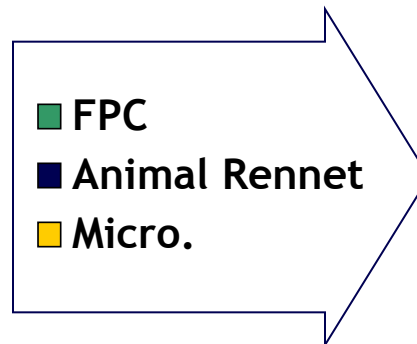
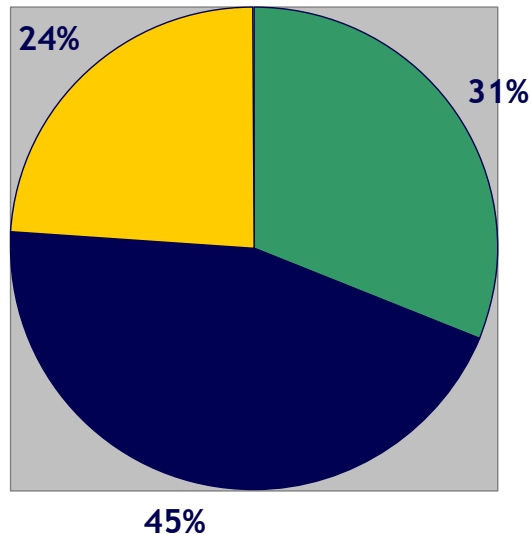


Coagulant Market trends

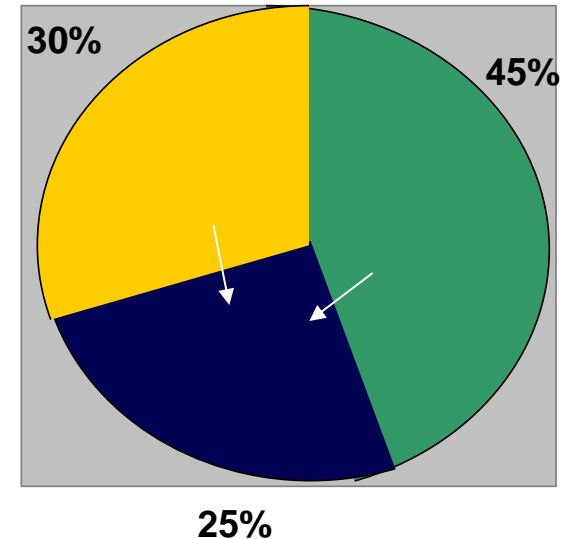
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- ▶ Animal rennet lost its first position and has now the last position while FPC like CHY-MAX™ are now used to produce about 50% of the cheeses made in the world

Market in 1999



Market in 2005








As a summary for coagulants

- ▷ If we were to start coagulants from scratch, we would only have CHY-MAX™...
 - ▼ Sell CHY-MAX™ where you can
 - ▶ + performance/price (dosage, yield, purity)
 - ▶ - perceived 'GMO'
 - ▼ Sell NATUREN™ on tradition @ AOC/DOC
 - ▶ + performance @ high chymosin %
 - ▶ - price (fluctuation), perceived BSE risk
 - ▼ Sell HANNILASE™ as 'good enough' alternative
 - ▶ + price/MIMCU
 - ▶ - yield, specificity
 - ▼ Propose THERMOLASE™ only in niches
 - ▶ only suitable for Emmenthaler-like process

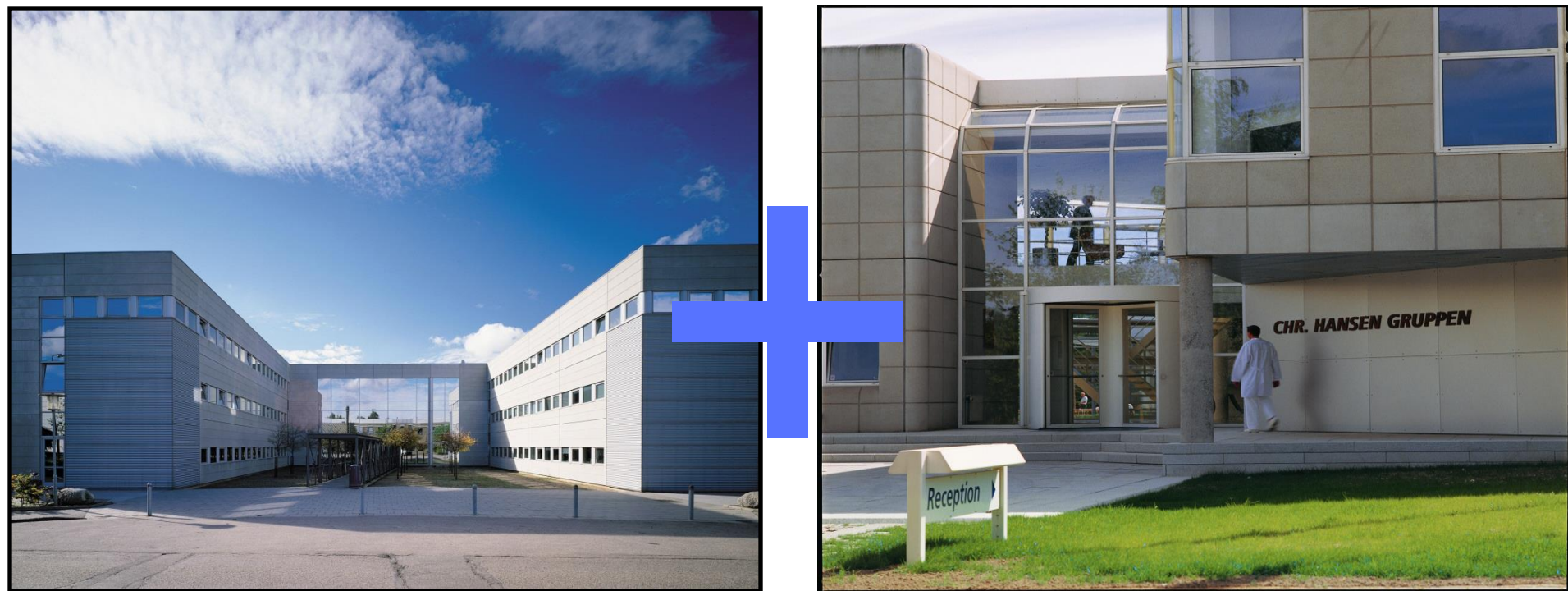
Tour through CHR HANSEN 's portfolio

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Yield MAX™

Product name	Enzyme(s)	Industry	Application
NATUREN™	Chymosin - Pepsin		Milk-clotting
CHY-MAX™	Chymosin		
HANNILASE™	Blend of proteases		
THERMOLASE™	Blend of proteases		
LIPASE™	Lipase		Flavors enhancement during cheeses ripening
YieldMAX™ PL	Phospholipase		Cheese yield production enhancement
AFILACT™ & Chrisin	Lysozyme Nisin	 	Natural protection of dairy products and cheeses
Ha-LACTASE™	Lactase		Lactose degradation to produce lactose free products for intolerant people
TEST KITS	...		...

The Milkyway Alliance

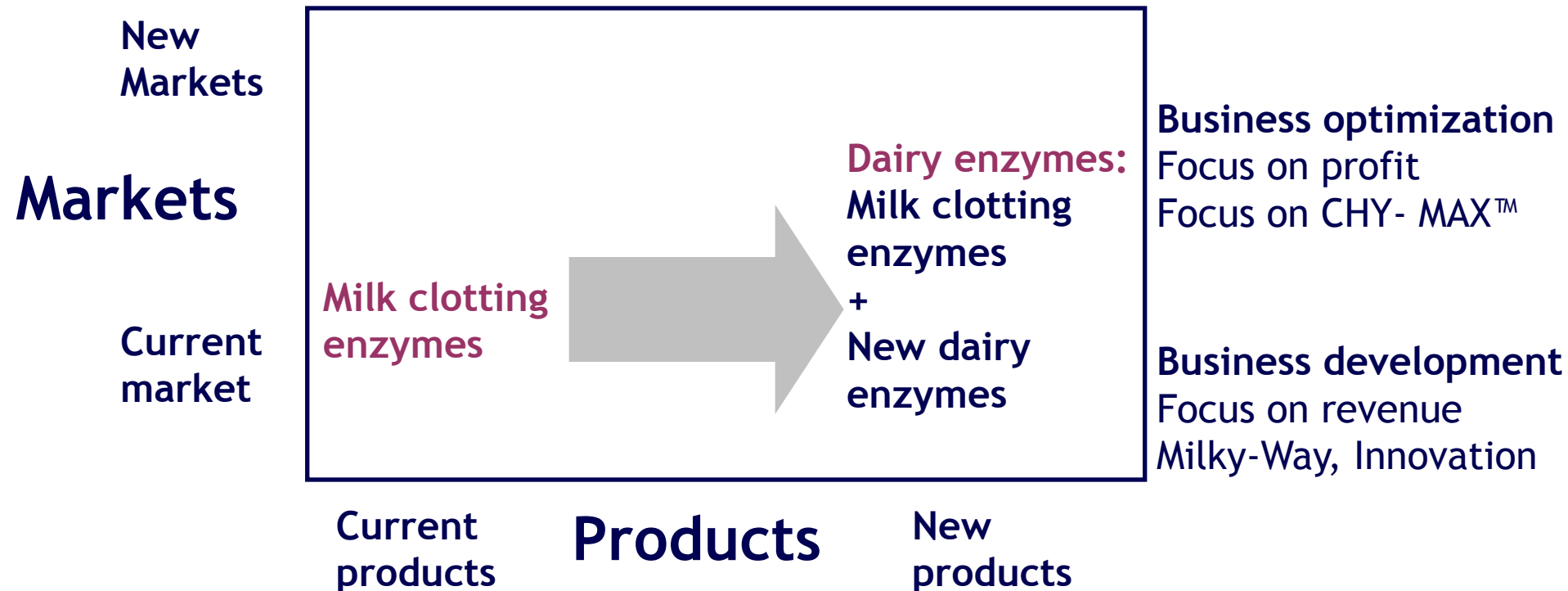


Why is it called Milkyway?

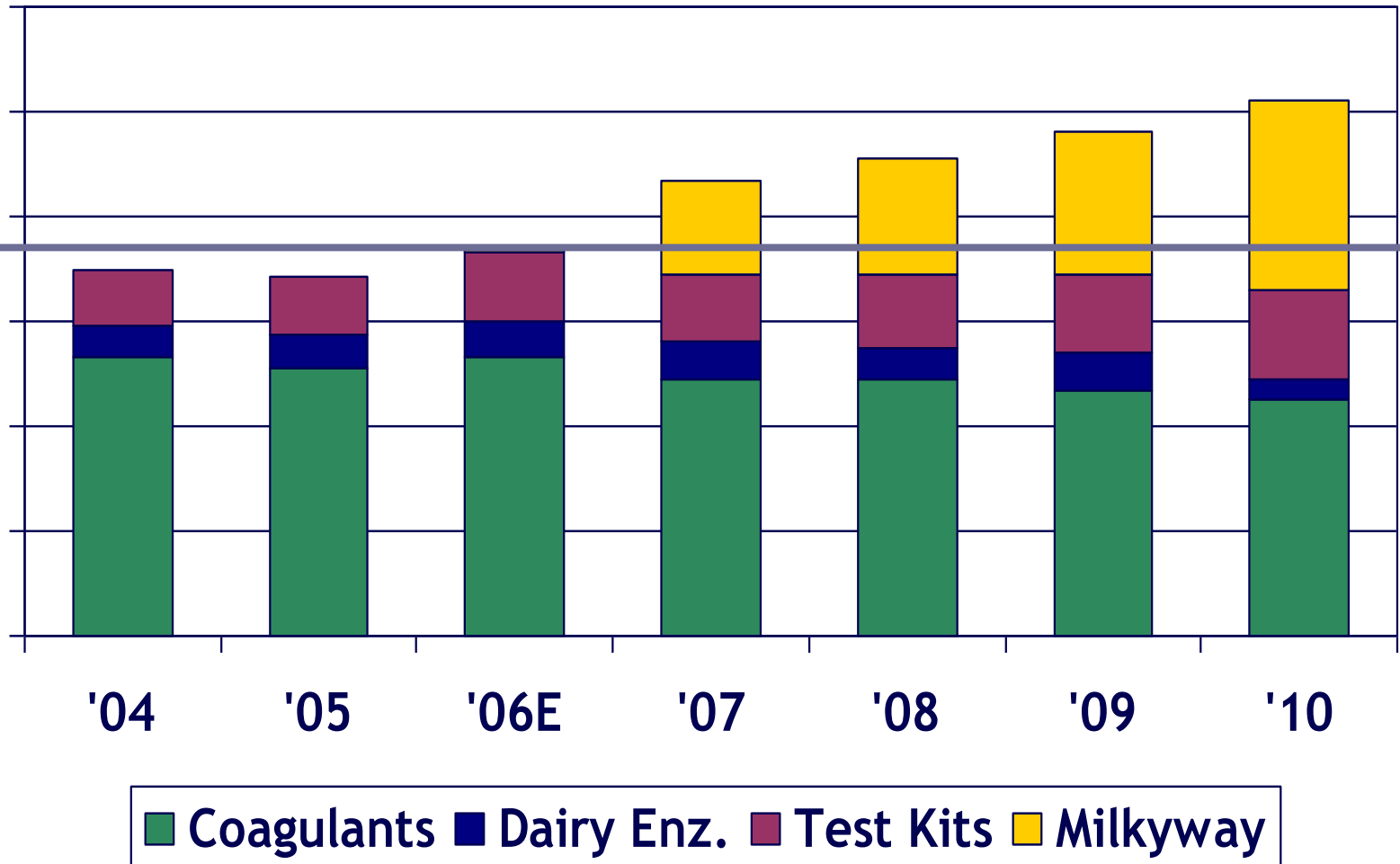




From coagulant leader to dairy enzyme leader



How much are we supposed to grow? And how?

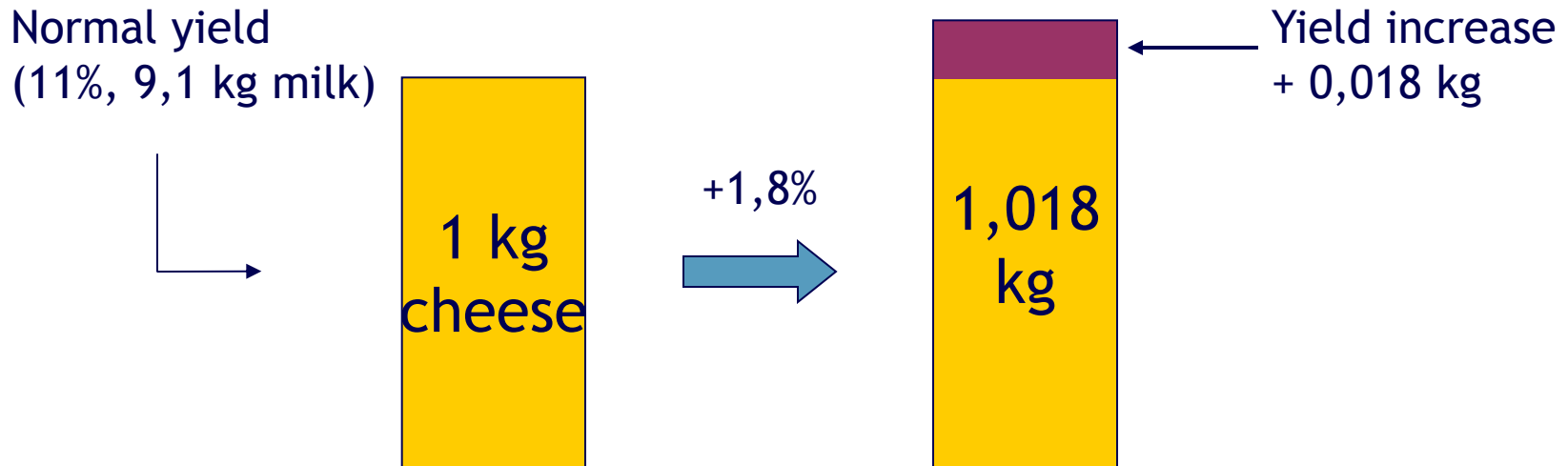




- ▼ Higher yield in production of mozzarella and pizza cheese



- ▼ 1,8% yield increase is the official figure:

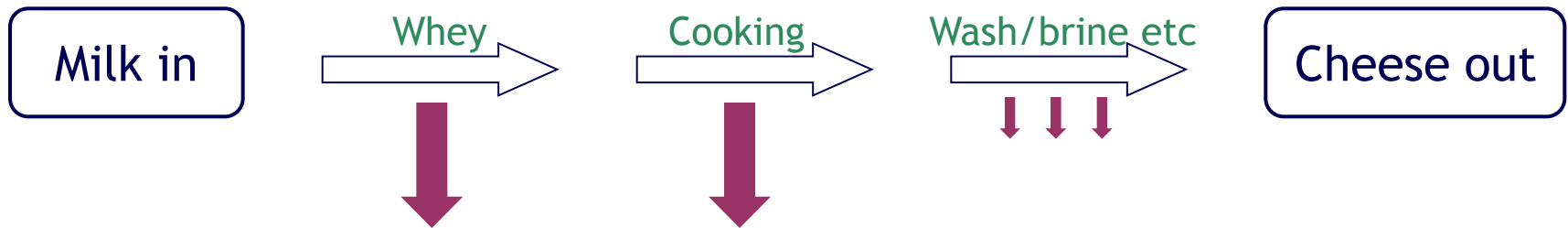


- ▼ Cheeses with higher fat content may give higher yield improvement...!

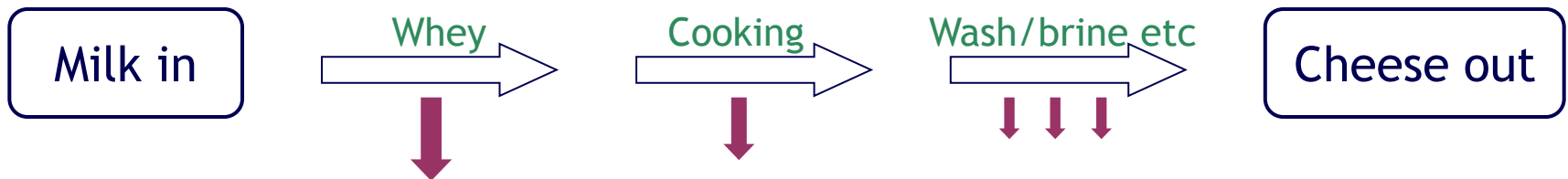
Examples of yield increases

	% increase	95% interval
Receipt 1	1,4	(0,3; 2,4)
Receipt 2	0,7	(-0,5; 1,9)
Receipt 3	2,1	(0,1; 4,0)
Receipt 4	3,8	(1,6; 6,0)

▼ Normal Mozzarella

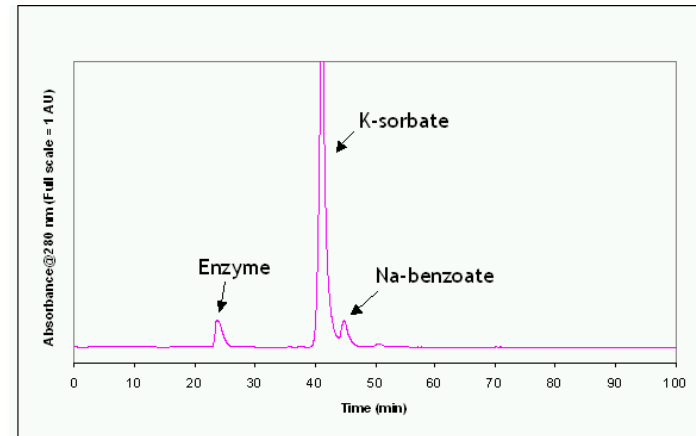


▼ Mozzarella with YieldMAX™ PL



- ▼ Side activities removed
 - ▼ Esp. amylase and glucoamylases absent

- ▼ No YieldMAX™ PL effects seen on functionality
 - ▶ Stretchability
 - ▶ Meltability
 - ▶ Browning
 - ▶ Oiling off



- ▼ Addition may lead to increased foam formation
 - ▶ Depending on process equipment, etc.
 - ▶ May be solved by using an appropriate de-foaming agent



Untreated



Treated



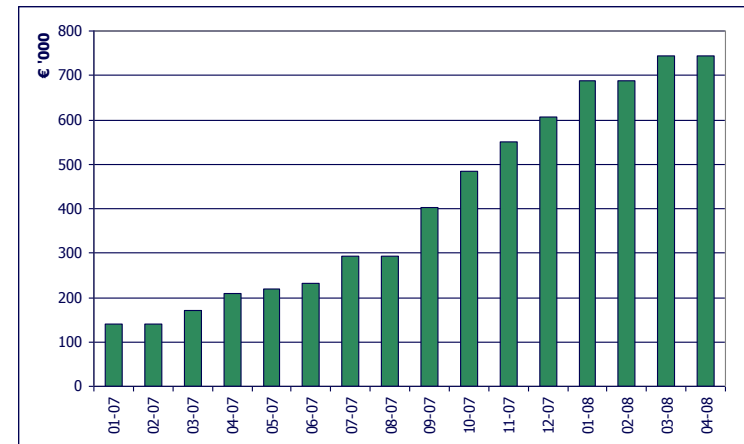
▼ Launch status

- ▼ 1st order Sep 26 2005
11:45 am CST ☺
- ▼ Currently
 - ▼ 4 US Dairies, 1 UK Dairy
 - ▼ More to come in US and IT



▼ YieldMAX™ PL targets

- ▼ Total market potential US alone is \approx 35 M EUR (815 t)
- ▼ US is 50% of world market (but rest is fractioned!)



- ▼ High need for technical resources to support customers
- ▼ Trials before purchase: Verify yield
 - ▼ Statistically proven => 200 vats or more!
- ▼ Trials after purchase: Solve problems
 - ▼ YieldMAX™ related: e.g. moisture adjustments
 - ▼ Not YieldMAX™ related
- ▼ Amount of technically capable people limited...
- ▼ Current countries: 80% of pasta filata volume globally
= they get the full set of resources
- ▼ All remaining countries: We're open for sales
 - but "you are sort of on your own"

Requirements and support for starting sales

- Check your local regulations
 - Verify that you may sell YieldMAX™ PL
- Use the support package to get started

YieldMAX™ PL
CH Launch Information,
Questions and Answers

Introduction

YieldMAX™ PL is the first product from the strategic alliance between Chr. Hansen and Novozymes - two world leaders in enzyme innovation. It is an advanced enzyme solution tailor made for production of mozzarella and pizza cheese.

YieldMAX™ PL is just the first revolutionary enzyme solution from Chr. Hansen and Novozymes - the next projects are already in the pipeline. In general, Novozymes provides most of the manpower and expertise for research and development of the new enzymes, while Chr. Hansen is responsible for marketing, sales and technical support to the customers. Profits are split equally between the two alliance partners.

What is YieldMAX™ PL?

YieldMAX™ PL is a phospholipase which breaks down certain phospholipids present in the cheese milk.

In the process of making pasta filata cheeses, most noticeably mozzarella and pizza cheese, the role of YieldMAX™ PL is to optimize milk clotting by improving the emulsification properties of phospholipids in cheese milk - which in turn results in a significant improvement of the cheese yield. The final cheese quality is not changed.

In other words, it is a highly technical new enzyme solution to get better results out of a scarce and expensive natural resource: milk!

In which countries is YieldMAX™ PL available?

At launch time, October 2005, YieldMAX™ PL is available for sale in the following countries only:

- USA
- Germany
- Italy
- UK
- Denmark

The limited availability is mainly for regulatory reasons - please refer to the section "Quick regulatory overview" for more information.

The product is only brought to the market by CH dairy technical specialists working closely with the customers to highlight and secure from very beginning the value the product will bring to the cheese makers.

Key dates:
Oct 24: Official launch, press releases
Oct 26-29: Market launch at [WFSF](#), Chicago.

The alliance between Chr. Hansen and Novozymes provides process enhancement and product innovation to the dairy industry. By teaming up with industry, the alliance develops advanced enzyme solutions based on the complementary technologies of two innovation leaders.

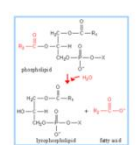

Chr. Hansen A/S - 10-12 Ege Allé - DK-2870 Hørsholm, Denmark - Phone: +45 45 74 74 74 - Fax: +45 45 74 85 85 - www.chr-hansen.com

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YieldMAX™ PL

A novel concept for increasing yield
in production of mozzarella / pizza cheese

YieldMAX™ PL
Technical presentation






19 January 2007

	A	B	C	D	E
1	YieldMAX™ PL Addition Rate in liters and kg to the vat size				
2	Fat in milk %	Vat size/ liters of milk			
3		5.000	15.000	25.000	
4	2,5	0,27	0,82	1,36	
5		0,31	0,94	1,56	
6	3	0,33	0,98	1,63	
7		0,38	1,13	1,88	
8	3,5	0,38	1,14	1,90	
9		0,44	1,31	2,19	
10	Liters per vat (top)		Kg per vat (bottom)		

Tour through CHR HANSEN´s portfolio

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AFILACT™ and Chrisin

Product name	Enzyme(s)	Industry	Application
NATUREN™	Chymosin - Pepsin		Milk-clotting
CHY-MAX™	Chymosin		
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Ha-LACTASE™	Lactase		Lactose degradation to produce lactose free products for intolerant people
TEST KITS	...		...

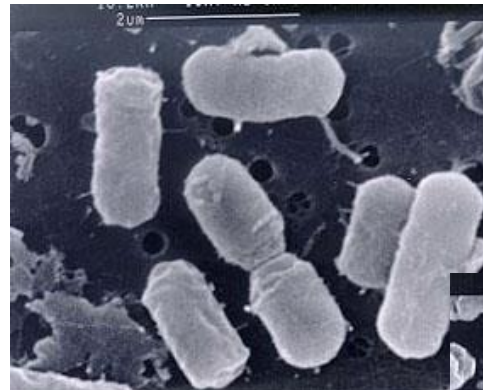
- ▼ Product characteristics
 - ▶ Lysozyme, liquid and granulate
 - ▶ Preventing late blowing in cheese (*Clostridium tyrobutyricum*)
 - ▶ Allowed in cheese and wine
 - ▶ Additive, E1105

AFILACT™

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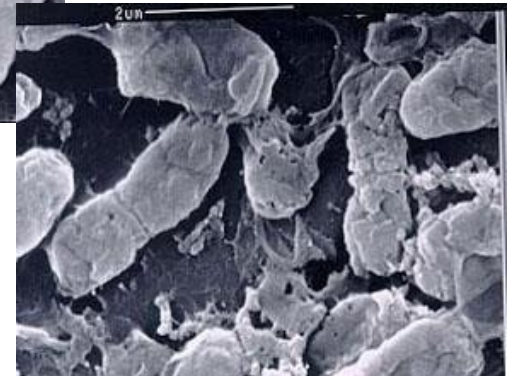
Butyric cheese

Normal cheese



Normal, vegetative
Cl. tyrobutyricum
cells

Vegetative cells after
treatment with
lysozyme



- ▼ Traded product (not intended for customer to know!)
 - ▶ CH market leader; approx 50% share
 - ▶ Price pressure, especially on liquid (DSM)
 - ▶ Countering by supply chain optimisation

- ▼ Your task:
 - ▶ Defend - and aim for growth!

Chrisin

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- ▼ Chrisin / Chrisin C
 - ▶ Nisin, an anti-microbial peptide
 - ▶ Inhibits many Gram+ bacteria
 - ▼ Including Clostridia, Listeria and Bacillus
 - ▶ Allowed in cheese (incl processed), a.o.
 - ▶ Additive, E234
- ▼ Traded product (not intended for customer to know!)
 - ▶ Danisco market leader
 - ▶ Trying to regain market after supply problems in 2003-4

- ▼ Two products available
 - ▶ "High end" - 502095, Chrisin
 - ▶ "Cheap end" - 671535, Chrisin C
- ▼ Both kosher and halal
- ▼ Your task: Go sell some!

Tour through CHR HANSEN 's portfolio

CHR HANSEN

Ha-LACTASE™

Product name	Enzyme(s)	Industry	Application
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CHY-MAX™	Chymosin		
HANNILASE™	Blend of proteases		
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AFILACT™ & Chysin	Lysozyme Nisin	 	Natural protection of dairy products and cheeses
Ha-LACTASE™	Lactase		Lactose degradation to produce lactose free products for intolerant people
TEST KITS	...		...

Ha-Lactase™

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- ▷ About 60% of the world population is lactose intolerant and do not drink milk anymore getting calcium deficient with time...



- ▼ The most concerned areas are:
South America>Africa>Asia>Near East
- ▼ Symptoms are a change in intestinal micro-organisms resulting in excessive gas and acid and cramps and diarrhoea.
- ▼ Usually peaks at the age of 40-50 years
- ▼ As a reaction people stop drinking milk
- ▼ Consequence is a calcium deficit

Ha-Lactase™

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- ▷ ...CHR HANSEN provides to the dairy industry a neutral lactase produced by fermentation and able to hydrolyze lactose naturally present in milk



▼ Not the biggest, but...
...growing rapidly

▼ Strategy:





- ▶ Top quality products
- ▶ Cost reduction achieved
- ▶ Start to improve knowledge of our market (applications...)



Tour through CHR HANSEN 's portfolio

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Test Kits

Product name	Enzyme(s)	Industry	Application
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TEST KITS	...		...

Antibiotics test kits - what's it all about?

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- Keeping the young lady happily drinking her milk
- Free from antibiotics!



Antibiotics test kits - what's it all about?

CHR HANSEN



- ▼ Ensuring that the dairy's production keep running
- ▼ Original purpose of testing

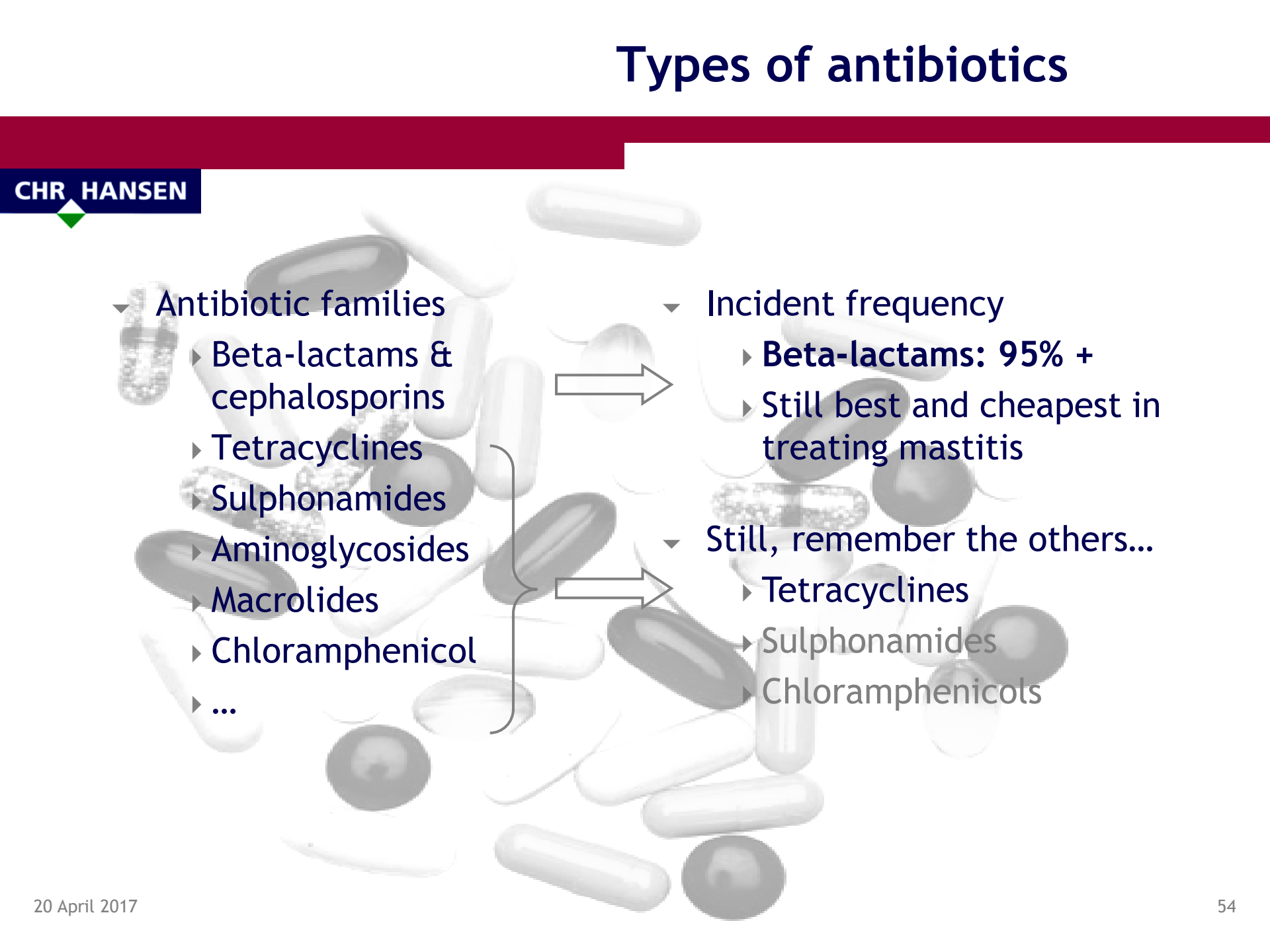
How does the antibiotics get in the milk?

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Types of antibiotics

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- 
- Antibiotic families
 - Beta-lactams & cephalosporins
 - Tetracyclines
 - Sulphonamides
 - Aminoglycosides
 - Macrolides
 - Chloramphenicol
 - ...
 - Incident frequency
 - Beta-lactams: 95% +**
 - Still best and cheapest in treating mastitis
 - Still, remember the others...
 - Tetracyclines
 - Sulphonamides
 - Chloramphenicols
- Diagrammatic flow: A bracket groups the antibiotic families listed on the left. An arrow points from this group to the 'Incident frequency' section. Another arrow points from the 'Still, remember the others...' section back to the list of antibiotic families.

Regulatory limits

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▼ EU: MRLs

Penicillin G

4 ppb

Cloxacillin

30 ppb



▼ US: Safe levels

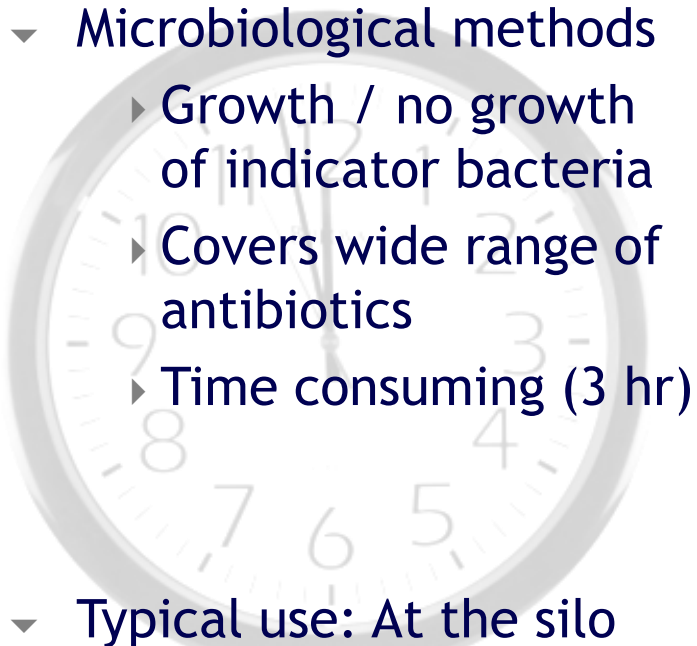
5 ppb

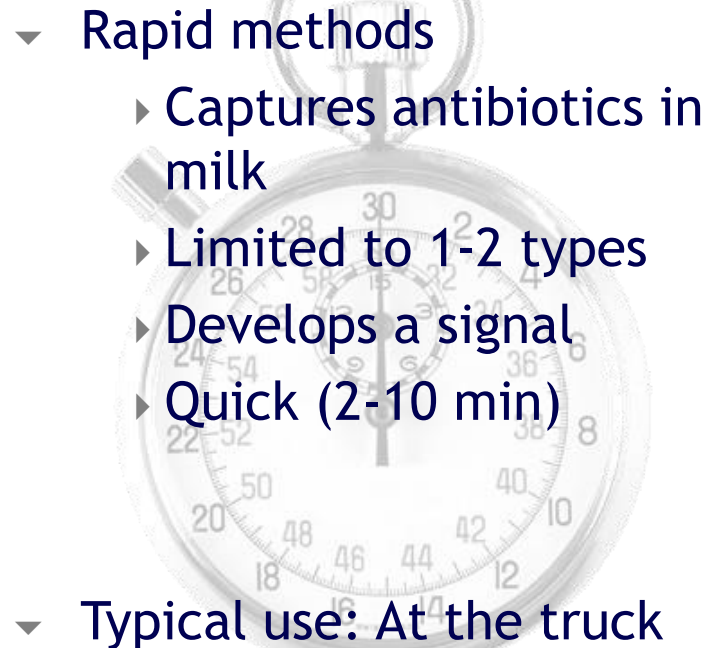
10 ppb



Types of detection

CHR HANSEN

- 
- ▼ Microbiological methods
 - ▶ Growth / no growth of indicator bacteria
 - ▶ Covers wide range of antibiotics
 - ▶ Time consuming (3 hr)
 - ▼ Typical use: At the silo

- 
- ▼ Rapid methods
 - ▶ Captures antibiotics in milk
 - ▶ Limited to 1-2 types
 - ▶ Develops a signal
 - ▶ Quick (2-10 min)
 - ▼ Typical use: At the truck

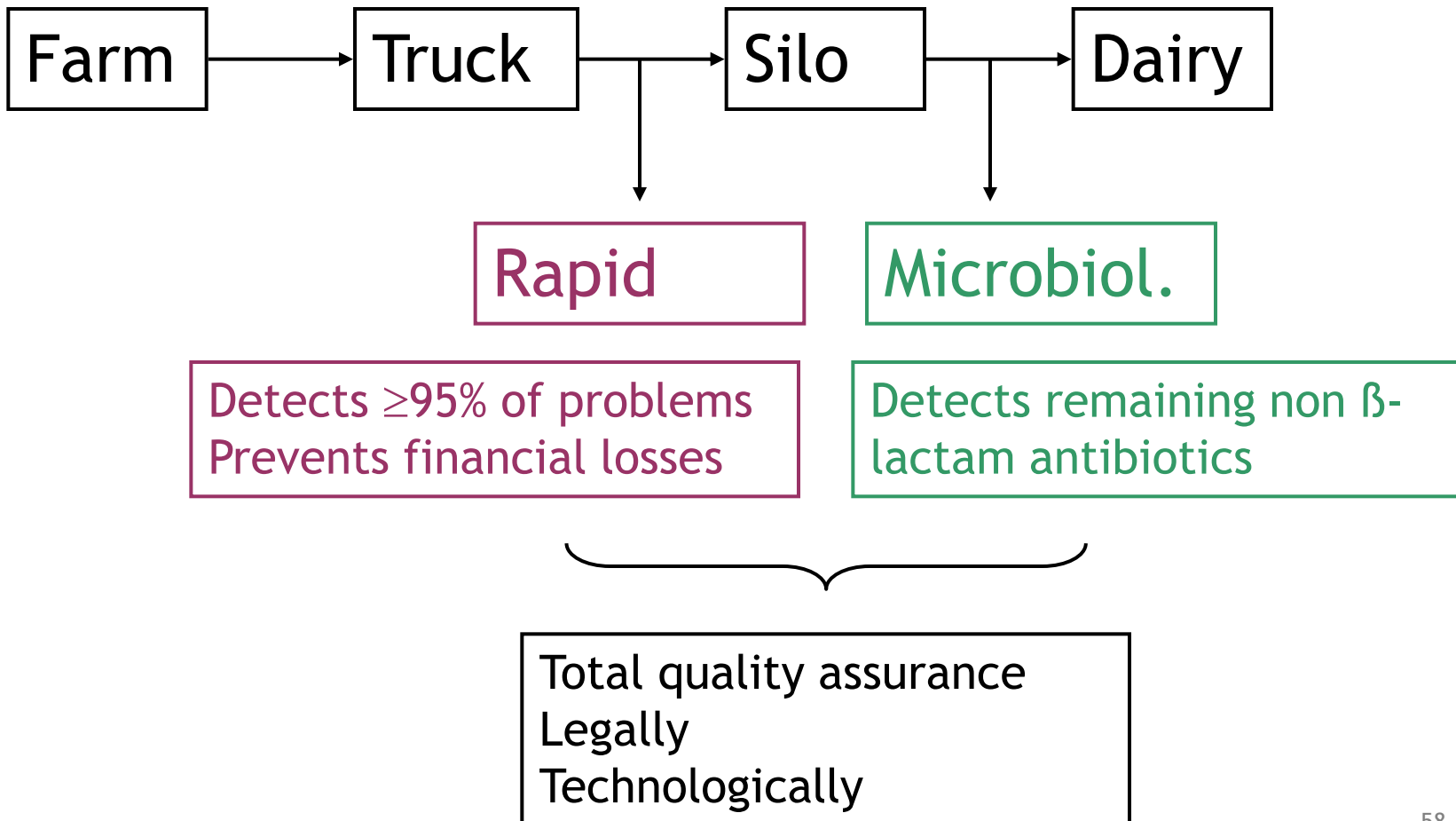
Risk management at the different levels

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Antibiotics risk management strategy

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Drivers - what do customers wish?

CHR HANSEN

- ▼ Sensible sensitivities
 - ▶ Sensitive enough to avoid issues
 - ▶ Not more sensitive than they have to be
- ▼ Efficiency
 - ▶ Covering relevant antibiotics
 - ▶ Test time and # steps
- ▼ Price & availability

Meeting market demands

CHR HANSEN

▼ Current Betastar® kit

- ▶ Wide beta-lactam coverage
- ▶ 5 min - fast!
- ▶ Visual and/or reader (reader optional)
- ▶ Very robust (timing not critical)
- ▶ Result permanent

▼ Betastar® development

- ▶ Combined stick with tetracycline
- ▶ 1+1 minute protocol for std. Betastar
- ▶ Completely new tests in idea phase



Meeting market demands

CHR HANSEN

- ▼ Copan Test
 - ▶ We also serve the microbial detection market
 - ▶ Not exclusive distribution...
- ▼ Characteristics
 - ▶ 3 hours
 - ▶ Reproducible timing
 - ▶ Good technical backup



- ▼ Rapid tests
 - ▶ Charm
 - ▶ SNAP
 - ▶ TwinSensor

- ▼ Microbiological tests
 - ▶ Delvotest SP
 - ▶ Eclipse

Good luck selling Enzymes' products

