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## FUNCTIONAL FOODS

Relation between Food and Pharma

Treatment and Prevention of Obesity: Approaches and Needs

ØFN/ØSR Unlimited Health conference  
Copenhagen (KU) - September 13, 2007.

Improving the quality

of **food** and **health**

for people all over the world



# WHAT IS HEALTH? - A Major Paradox

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*The scientific paradox*

Difficult to define health in absence of disease: what to measure?

*The genotype paradox*

"One size does not fit all" - we are all genetically different in our response to diet and lifestyle - but dietary recommendations are targeted to populations



*The lifestyle paradox*

Despite (1) access to high quality, safe and healthy food, (2) food industry and food safety authorities of world excellence, and (3) well-intentioned and scientifically based dietary recommendations,

The population at large has more and more healthy eating habits, which - together with the lack of physical activity - is the primary cause of the almost explosive prevalence of a range of lifestyle related chronic diseases - worldwide

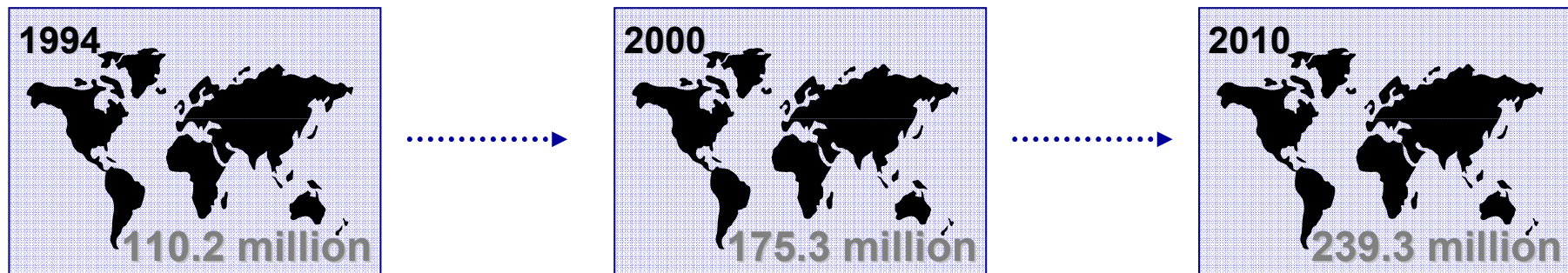
## Lifestyle related chronic diseases - 'epidemic'?

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*Urbanisation & metabolic disease*



### Incidence of diabetes (world wide projections)



McCarty and Zimmet - ISBN 0 646 20244 8

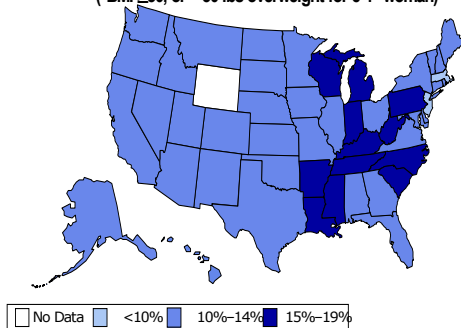
**...and that's scary!**

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6.5 bio people  
1 bio overweight  
300 mio obese (min.)

## Obesity\* Trends Among U.S. Adults 1993

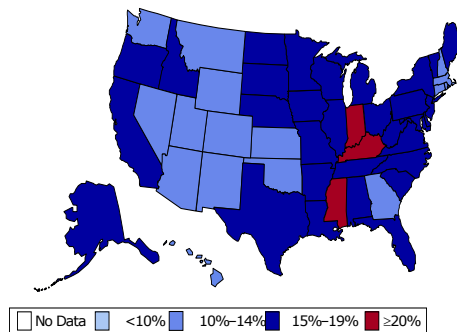
(\*BMI  $\geq 30$ , or ~ 30 lbs overweight for 5'4" woman)



Source: Behavioral Risk Factor Surveillance System, CDC.

## Obesity Trends Among U.S. Adults 1997

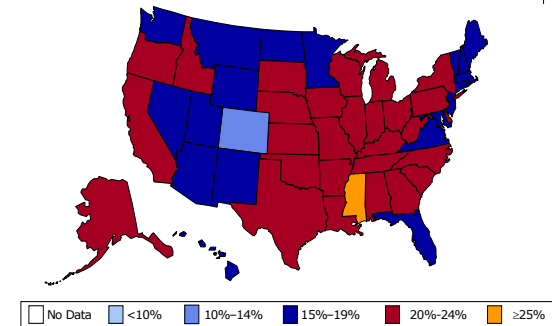
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## Obesity Trends Among U.S. Adults 2001

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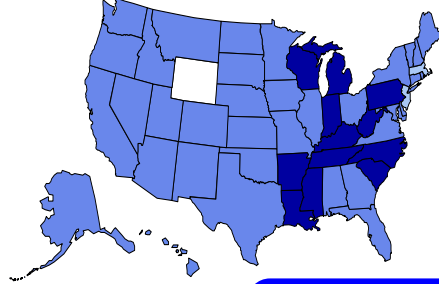
# In 2020 70% of all diseases will be related to lifestyle

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**Obesity\* Trends Among U.S. Adults**  
**1993**

(\*BMI  $\geq 30$ , or ~ 30 lbs overweight for 5'4" woman)

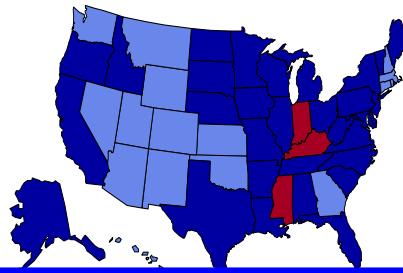


□ No Data □ <10% □ 10%–14% □ ≥15%

Source: Behavioral Risk Factor Surveillance System, CDC.

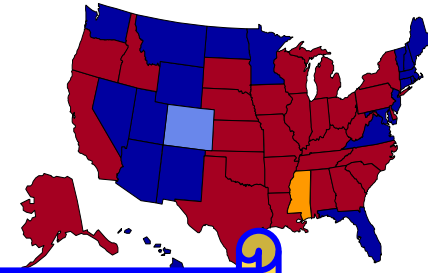
**Obesity Trends Among U.S. Adults**  
**1997**

(\*BMI  $\geq 30$ , or ~ 30 lbs overweight for 5'4" woman)



**Obesity Trends Among U.S. Adults**  
**2001**

(\*BMI  $\geq 30$ , or ~ 30 lbs overweight for 5'4" woman)



□ 19% □ 20%–24% □ ≥25%

Source: Behavioral Risk Factor Surveillance System, CDC.

Obesity now a bigger threat than  
starvation in US + (spreading...)

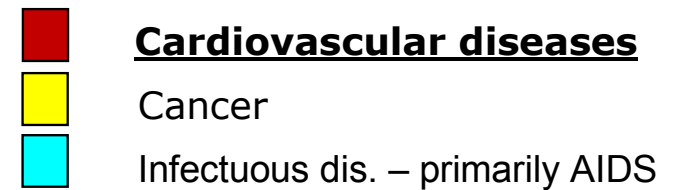
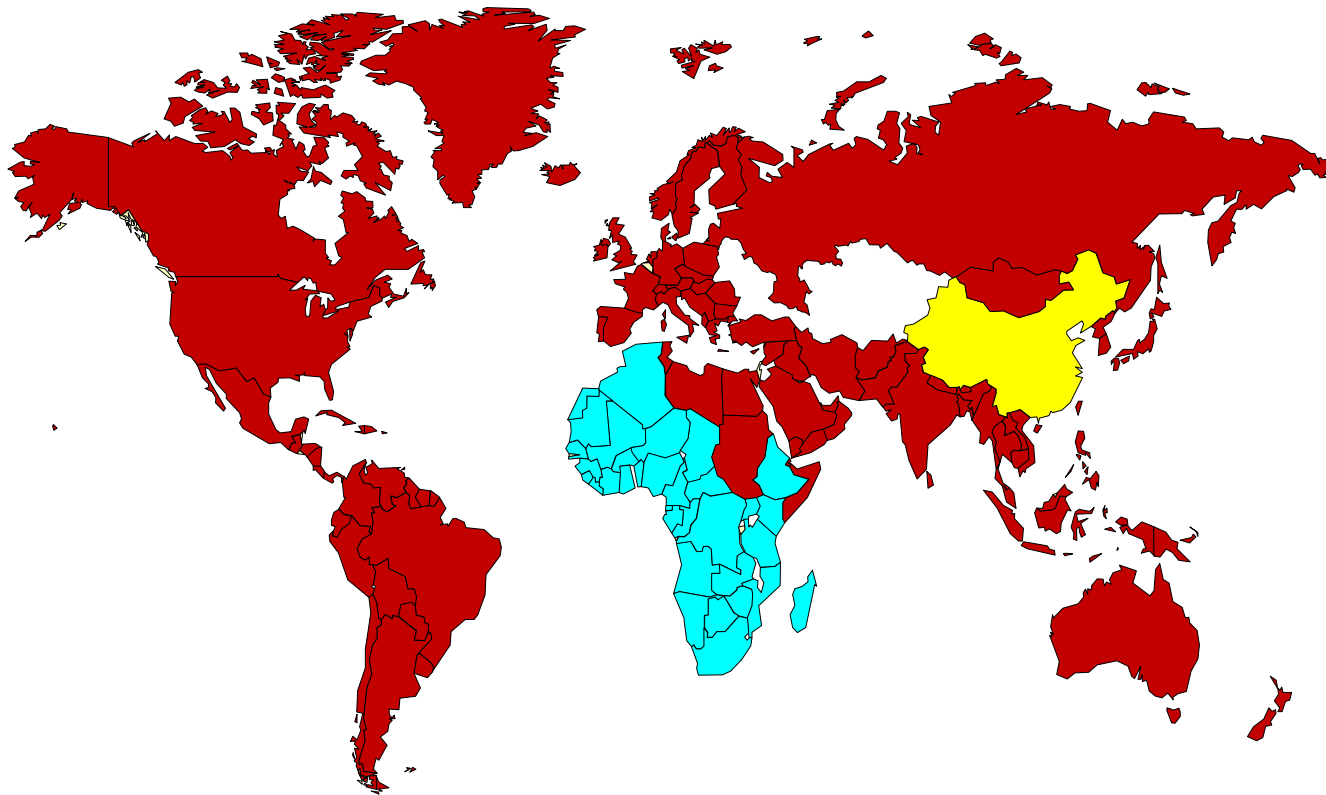




# The global picture: primary causes of death 2020

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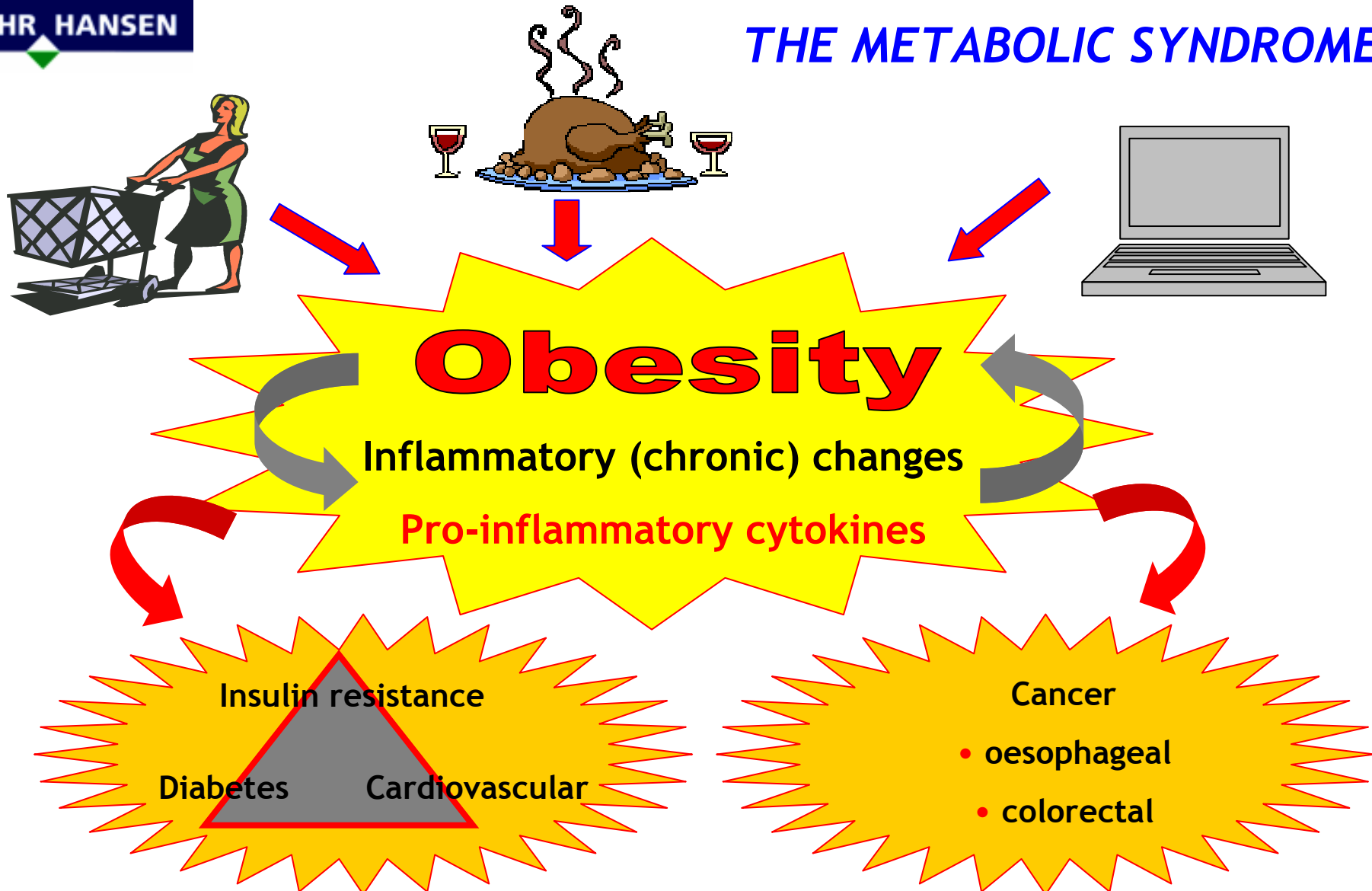
Source: WHO project 2020



# Adverse metabolic effects of western diet and lifestyle

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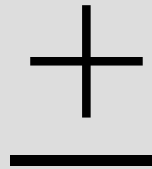
## THE METABOLIC SYNDROME



# The scientific challenge behind the lifestyle / metabolic syndrome

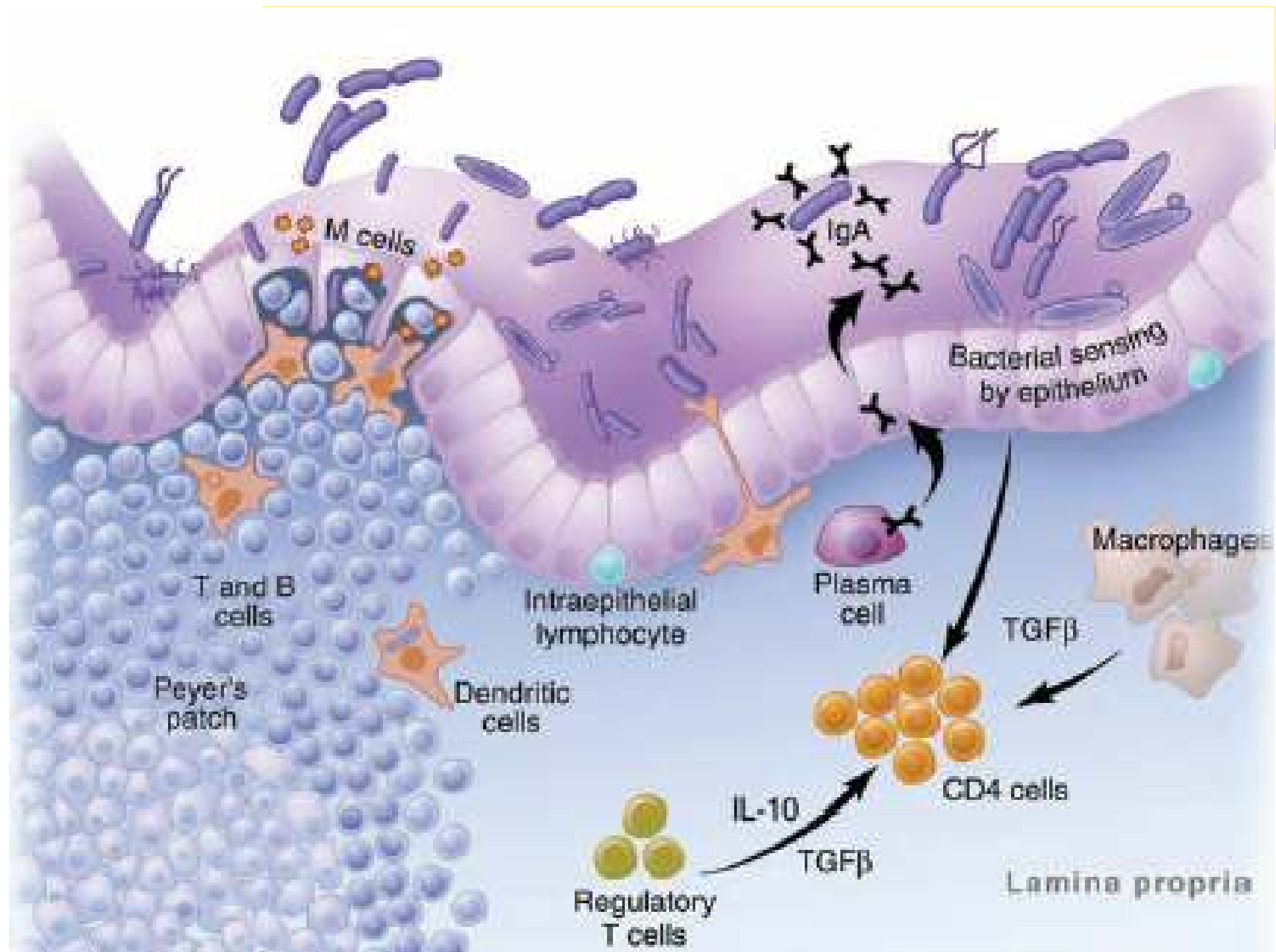
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*The nutrition challenges of the 21<sup>st</sup> century  
will need to focus on the advantages  
and disadvantages of having  
an immune system*



Professor Robert Grimble  
Institute of Human Nutrition, School of Medicine, University of Southampton, UK.





# Food and Beverage Megatrends: Industry & Society

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## A new 'Industry Standard'

1. **Health is the future of food**
2. The marketing power of intrinsic **healthfulness**
3. Fruit - the future of **functional** foods
4. Fine times ahead for fibre
5. Packaging for the "me" generation
6. The **functional** beverage boom rolls on
7. The upsurge of **functional** private label
8. Communicating the benefit is key to success
9. Asia is the place to look for innovation
10. Kid's nutrition still a strategic priority

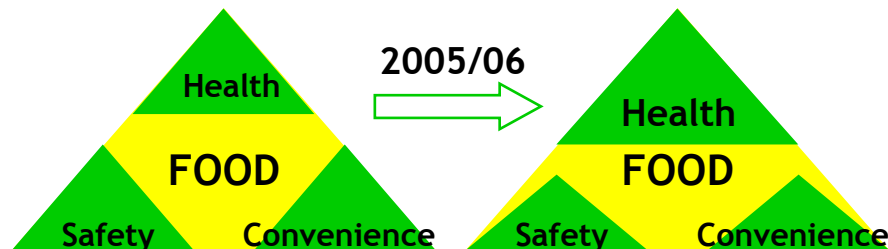
[www.new-nutrition.com](http://www.new-nutrition.com) , December 2005/January 2006

End 2004

"the tipping point for health and wellness - becoming unstoppable"

End 2005

"wellness will be for the next 15 years what convenience was for the last fifteen "



## Megatrends from a global society perspective

Diet - Culture/behaviour - Genes - Age



Lifestyle related chronic diseases:  
'Globesity' and Metabolic Syndrome



Major threat to global welfare:  
Economy and Quality of Life



Societal needs/quests for prevention  
and disease risk reduction



The Healthy Choice and Functional Food  
window of opportunity

# Functional foods: potential and challenge....

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One major strategy to combat the lifestyle paradox:  
Healthier food products - incl. functional foods

Functional foods is not just a question about fortification or enrichment - like adding vitamins to candy or masking the fat - it's dead(ly) serious!



**New product development:**

- based upon documented evidence



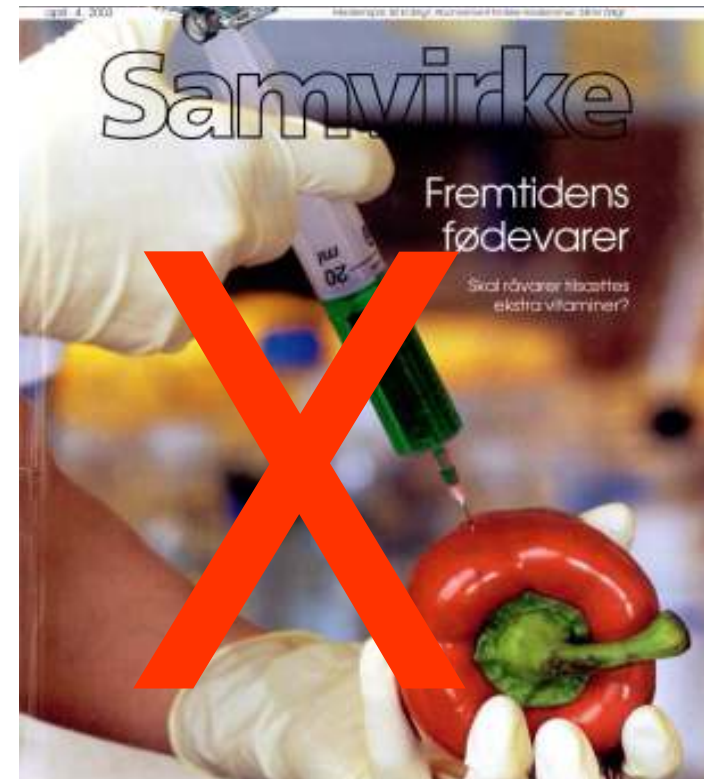
**Regulatory approval:**

- substantiated health claims
- e.g. EU/EFSA



**Acceptance & compliance:**

- choice
- consumption
- enjoyment



# The healthy revo/evolution: Potential for Chr. Hansen

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## Perfect fit with Chr. Hansen vision

"Improving the quality of FOOD and HEALTH for people all over the world"



### Market focus and leadership

Global leader dairy ingredients: enzymes, starter cultures and probiotics

Yoghurt a.o. FM products outgrow total dairy market 2-3X

CH major supplier to largest global brands



BB-12™ world's best documented Bifido - and largest single strain CH culture product

## Dairy products as perfect functional food platform



- Milk is unique 'mum-to-kid' biological nutrient
- Historical record: healthy and safe-to-use
- Positive nutrition profile (new approval dossiers)
- Any energy and taste formulations possible
- FM based beverages increasing consumer appeal

### Cardiovascular diseases and heart health

# 1 killer of chronic diseases

Major complication associated with obesity, diabetes etc.



Strong biomarkers (hypertension, cholesterol) validated for human clinical trials

CH good and proprietary entry with patented Cardi-04™ technology and product concept

(CH - Chr. Hansen; FM - Fermented Milk)

# The healthy revo/evolution: Potential for Chr. Hansen

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## Perfect fit with Chr. Hansen vision

"Improving the  
quality of FOOD  
and HEALTH  
people



*The ideal market: Combination of  
market pull and technology/science push*

G  
enzym  
Yoghurt  
outgrow to

CH major supplier to largest  
global brands

BB-12™ world's best documented  
Bifido - and largest single  
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product



## Dairy products as perfect functional food platform



- Milk is unique 'mum-to-kid' biological nutrient
- Historical record: healthy and safe-to-use
- Positive nutrition profile (new approval dossiers)
- Possible consumer appeal



CH good and proprietary entry with  
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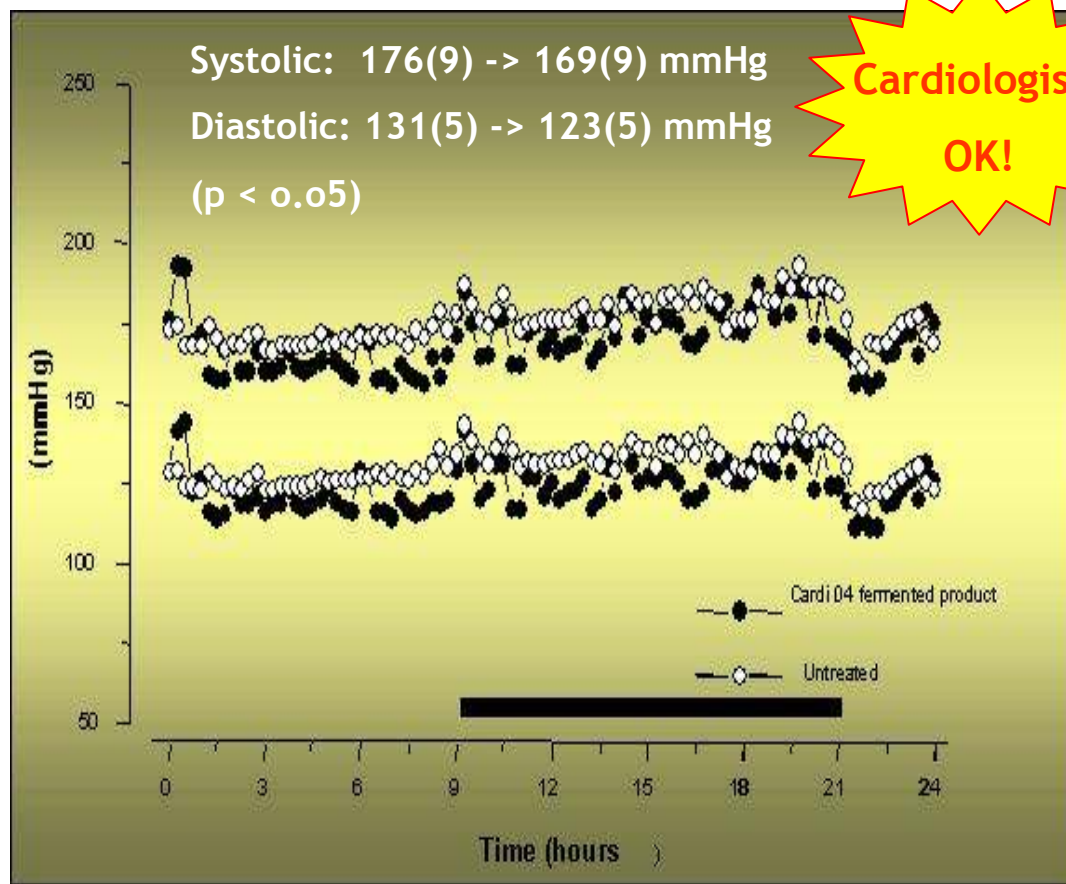
cholesterol)  
clinical trials

(CH - Chr. Hansen; FM - Fermented Milk)

# The Cardi-04 technology

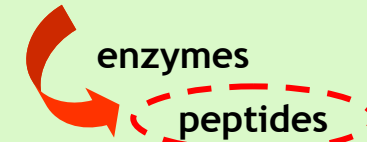
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Effect of Cardi-04 on systolic and diastolic blood pressure in spontaneously hypertensive rats, measured by telemetry - (in press)



## Fermented dairy products specific yoghurt bacteria (proteolytic)

milk  
proteins



ACE-inhibitors +



- significantly lowered BP and normalized HR in hypertensive rats (dose-dependant)
- receptor binding profile → 'arterial compliance'
- animal tests → first human
- 2 full human clinical trials running, 1st launch 2007
- 6 patent filings

# Cardi-04™ human clinical studies

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First 'tox' study  
Herlev Hospital,  
Copenhagen, DK  
(2004-06, in press)

Prospective, randomized,  
double-blind, placebo-  
controlled

43 healthy &  
normotensive  
volunteers

- No adverse effects
- Slight BPR and HRR ('barely' significant)

Efficacy + m-o-a  
Glostrup Hospital,  
Copenhagen, DK  
(ongoing, end 2007)

Randomized, double-  
blind, placebo-  
controlled dose-  
dependency study

90 patients;  
borderline ->  
slightly  
hypertensive

- Renin/angiotensin  
pathway markers\*
- Tilt test on heart  
functionality

Hypertension and  
inflammation  
TNO, Zeist, NL  
(ongoing, end 2007)

Randomized, double-  
blind, placebo-  
controlled cross-over  
study Cardi-04/BB-12

36 volunteers;  
overweight  
young males

- BPR and HRR effects
- Moderation of en-  
hanced inflammatory  
status; biomarkers

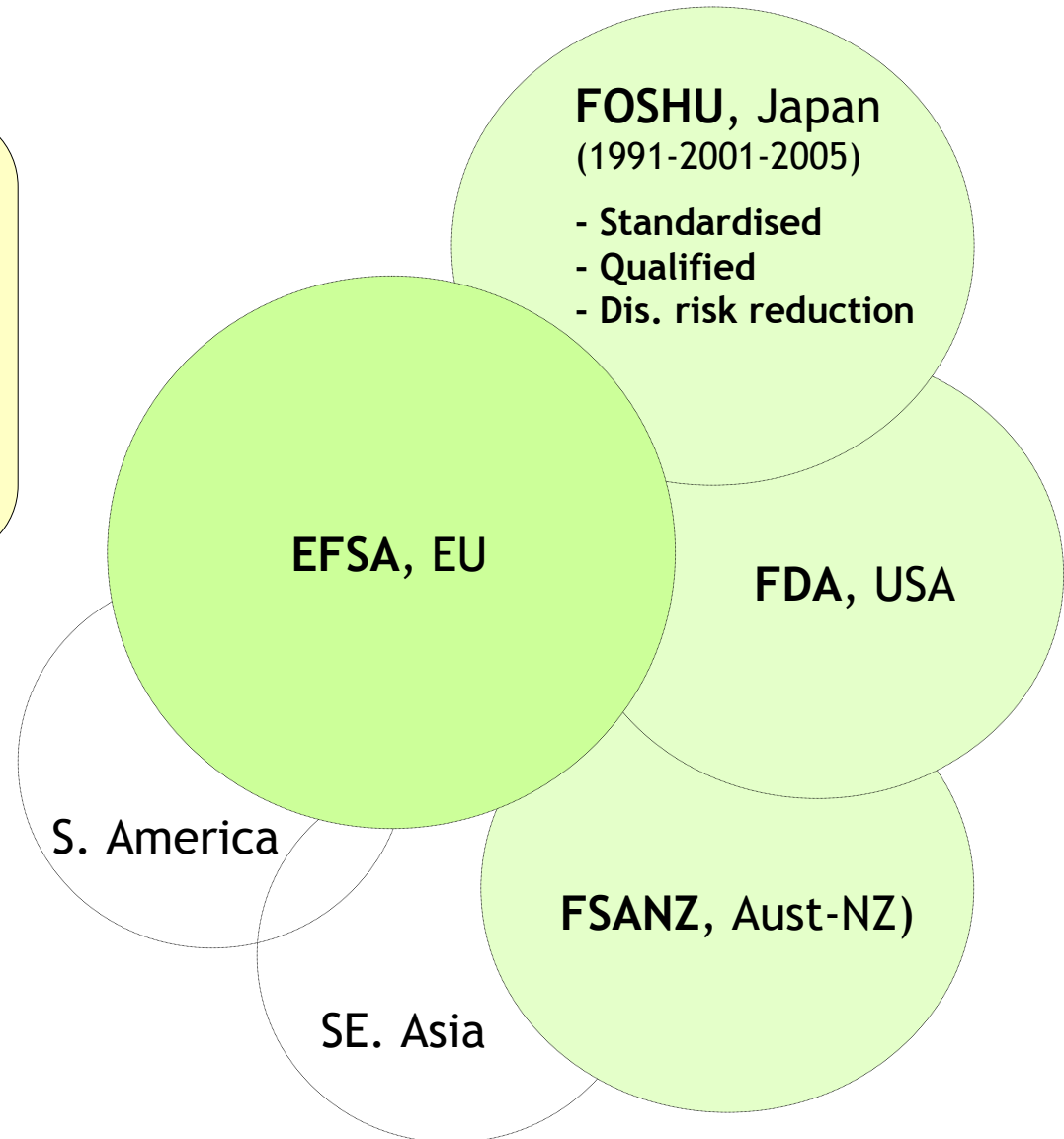


# Regulatory challenges: safety and health claims

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- ★ New EFSA 'decision tree', QPS (Qualified Presumption of Safety)
- ★ EU Novel Foods regulation: safety evaluation of strains not in use before 1997.
- *L. helveticus used as dairy starter/adjunct cultures, has some probiotic functionality*

- ❖ In legal/regulatory terms, functional foods do not constitute a specific category of food.
- ❖ Basically, health claim regulations apply to any kind of food.
- ❖ But clearly different categories of health claims can be approved.



# Regulatory challenges: safety and health claims

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★ New EFSA 'decision tree', QPS (Qualified Presumption of Safety)

★ EU Novel food evaluation before

● L. helveticus started some

❖ In legal/regulatory functional for a specific category

❖ Basically apply to any kind of food

❖ But clearly different categories of health claims can be approved.

In the future

**The Name of the Game is Claim**

EFSA, EU

FOSHU, Japan  
(1991-2001-2005)

- Standardised
- Qualified
- Dis. risk reduction

FDA, USA

FSANZ, Aust-NZ)

SE. Asia

# Regulatory challenges: safety and health claims

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- ❖ In legal function a specific

- ❖ Basic apply to



In

FOOD L

on

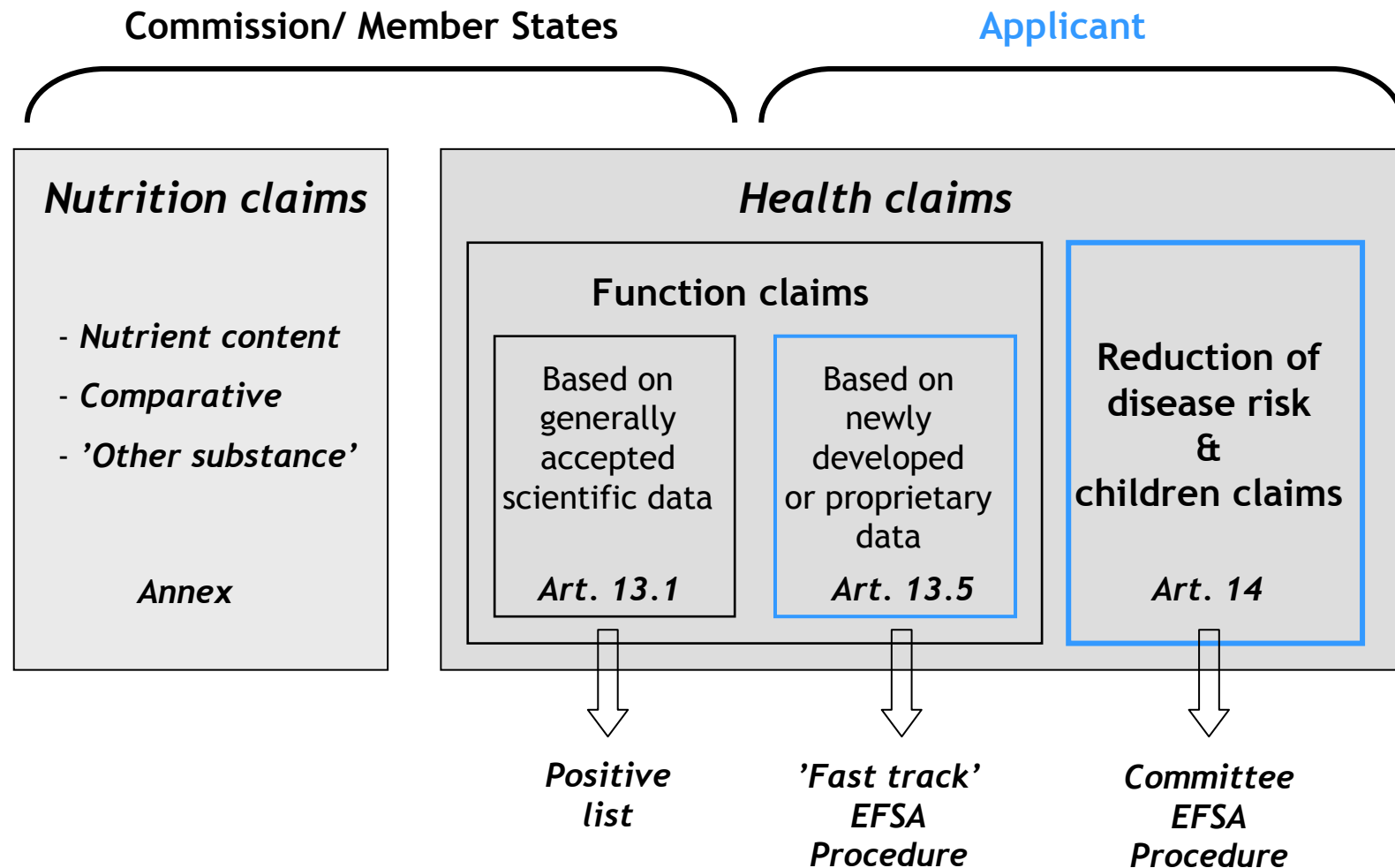
USA

(2)

# EU claims: classification and burden of proof

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"Regulation (EC) No 1924/2006 on Nutrition and Health Claims made on food"



# “Ten Key Trends in Food, Nutrition & Health 2007” by New Nutrition Business in Dec 2006 (I)

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- 1. Weight management will become one of biggest indication areas**
  - ▼ Driven by consumer shift from health benefits towards lifestyle benefits
  - ▼ Products giving “satiety” will be the winners rather than calorie-burning products
  - ▼ Second largest indication area in Japan with ~20% of functional food market
  - ▼ Danone launched in May 2006 in UK a the Lasting Satisfaction yogurt branded as “Effective Fibre and Proteins (EFP)”
- 2. Stronger link between nutrition, mood and mental health (Mood Food)**
  - ▼ Nestle announced in Nov 2006 they will invest 3M EUR annually next 5 years to research the area
  - ▼ Omega-3 largest ingredients targeting younger children and their mothers
  - ▼ Danone’s Danino kids yogurt with DHA taken 17% of kids’ yogurt market in Canada
- 3. Boundaries between health convenience and indulgence break down**
  - ▶ Snacks needs to be convenient, excellent taste, and healthy
  - ▶ Product example is PepsiCo’s Winged Pig brand being health veggie chip snack
- 4. Fruit stands strong in the future of functional food**
  - ▼ Delicious taste and intrinsic healthy preferred over science
  - ▼ Fruit drinks or smoothies with cranberry (urinary) / pomegranate (heart) / etc.



## “Ten Key Trends in Food, Nutrition & Health 2007” by New Nutrition Business in Dec 2006 (II)

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### 5. Future continues to look bright for digestive health (probiotics and prebiotics)

- ▶ 15-20% of consumers are concerned about their digestive health, but it is a hidden issue people don't admit to in public
- ▶ Gut health accounts for 64% of functional food market in Japan
- ▶ Products offer immediate effect thereby more easily creates a market contrary to e.g. cholesterol-lowering product
  - ▼ Unilever's Flora pro.active drink with Calpis patented peptides technology for blood pressure launched in 2006 but not successful and withdrawn. No immediate effect was felt by consumers
- ▶ Digestive health been big in Asia for long time, and success of Activia shows Western world also starts to care
- ▶ Prebiotic is becoming new direction on UK cereal market with Kellogg, Weetabix, and Nestle entering. E.g. Rice Krispies Muddles with 6% inulin



### 6. Drivers in kids' nutrition is brain (Omega-3), bowel (pro- & prebiotics), naturalness (free-from claims) and healthy snacking (giving snack w/o guilt)



Photo 45: Edamame, a traditional Japanese snack has migrated to the West. Unilever UK launched its version of Edamame into supermarket freezers earlier this year.

### 7. We're all turning Japanese

- ▼ Whole idea of functional food conceived in Japan in 1980'ies
- ▼ Blood pressure and cholesterol remain small part of Japanese market

## “Ten Key Trends in Food, Nutrition & Health 2007” by New Nutrition Business in Dec 2006 (III)

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### 8. Skin beauty from within

- ▶ Areas with increasing focus from P&G, Nestle, Cadbury-Schweppes, etc.
- ▶ Inner beauty trend turned out very slow in the coming as companies are still struggling with the right concept



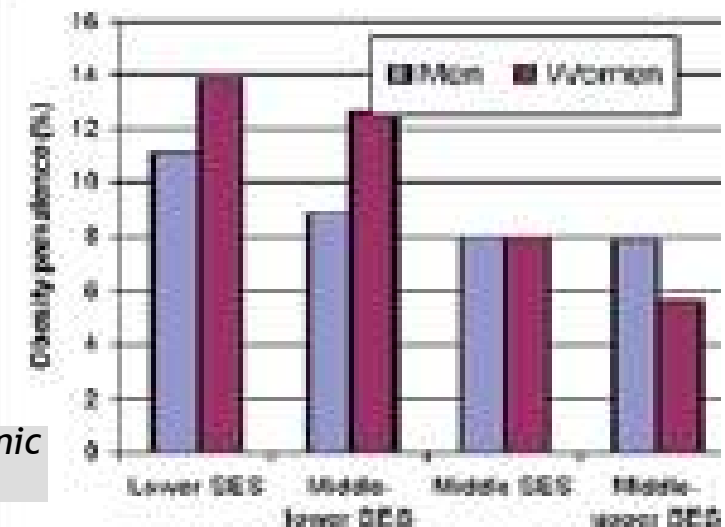
### 9. Products intrinsically healthy has strong marketing power

- ▼ In April 2006 7-Up brand switched formula cutting sodium and eliminating artificial preservatives and since advertised as “all-natural” seeing 17% sales growth



### 10. There is a clear link between low economic status and obesity

- ▼ Many cholesterol-lowering products are premium-priced and targeted higher-income consumer...
- ▼ ...but few of the poor can afford to buy cholesterol-lowering spreads priced 5 times the price of regular spreads



*Adapted from Martinez et al. Pub H Nutr 1999;2:125-33. Economic status measured by household income or by occupation*



# What's cooking in obesity...

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Antioxidants from watermelon to reduce obesity induced by oxidative stress

Body fat loss: stimulation of thermogenesis by bioactive food ingredients

## 5 groups of 'slimming ingredients'

- boosting fat burning
- inhibiting protein breakdown
- suppress appetite/boost satiety
- block fat absorption
- regulating mood

"Dairy proteins generally agreed to be most satiating macronutrient"

→ Role of bioactive milk peptides

Proteinase inhibitor II (PI2) from white potatoes: enhancing body's release of cholecystotinin (CCK), an appetite-suppressing hormone

## Some examples:

- green tea polyphenols
- CLA and DHEA
- hydroxy-methylbutyrate
- chromium picolinate
- L-carnithine
- chitosan
- calcium

Exopolysaccharide-producing probiotic bacteria (partly fibre effect?)

Appetite reduction is key for weight management - consumers

Probiotic bacteria to 'normalize' an otherwise 'fatty microflora' in obese individuals

Natural is key to UK weight loss market:

- Fabuless (DSM): palm and oat oils (sat/cal)
- PinnoThin (Lipid Nutrition): pine nuts
- Svetol (Berkem): green coffee beans

...just a few examples

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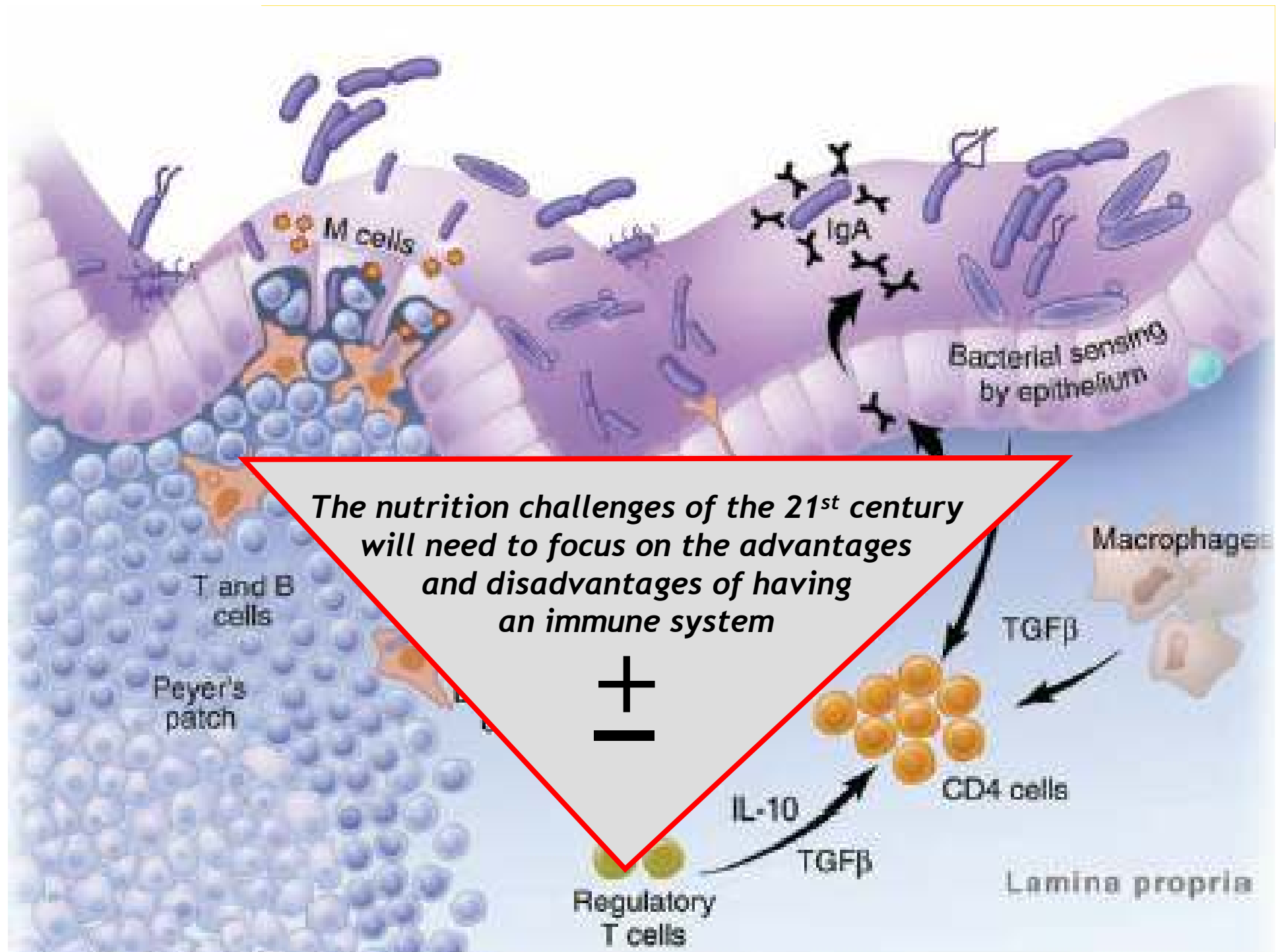
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...just a few examples



It ain't going to be that easy.....

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What makes poor people fat  
- and rich people thin?

### Other barriers / challenges to functional foods

- ❖ One size does not fit all: genotypic impact, nutrigenomics
- ❖ Which business model - food 'mass' market versus 'prescribed' prevention?
- ❖ The cultural dimension versus rational decision making
- ❖ The economical dimension - price competition and incentives

## We are all different - part of the paradox!

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Overweight: ✓✓✓

Drinker: ✓✓✓

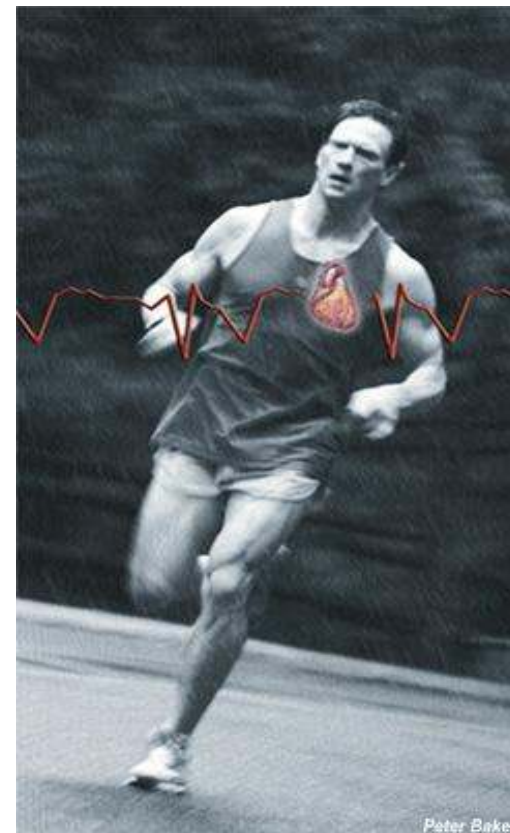
Smoker: ✓✓✓

Exercise: **XXX**

Healthy diet: **XXX**

Last job – British Prime  
Minister, Age 80

Died – Age 90



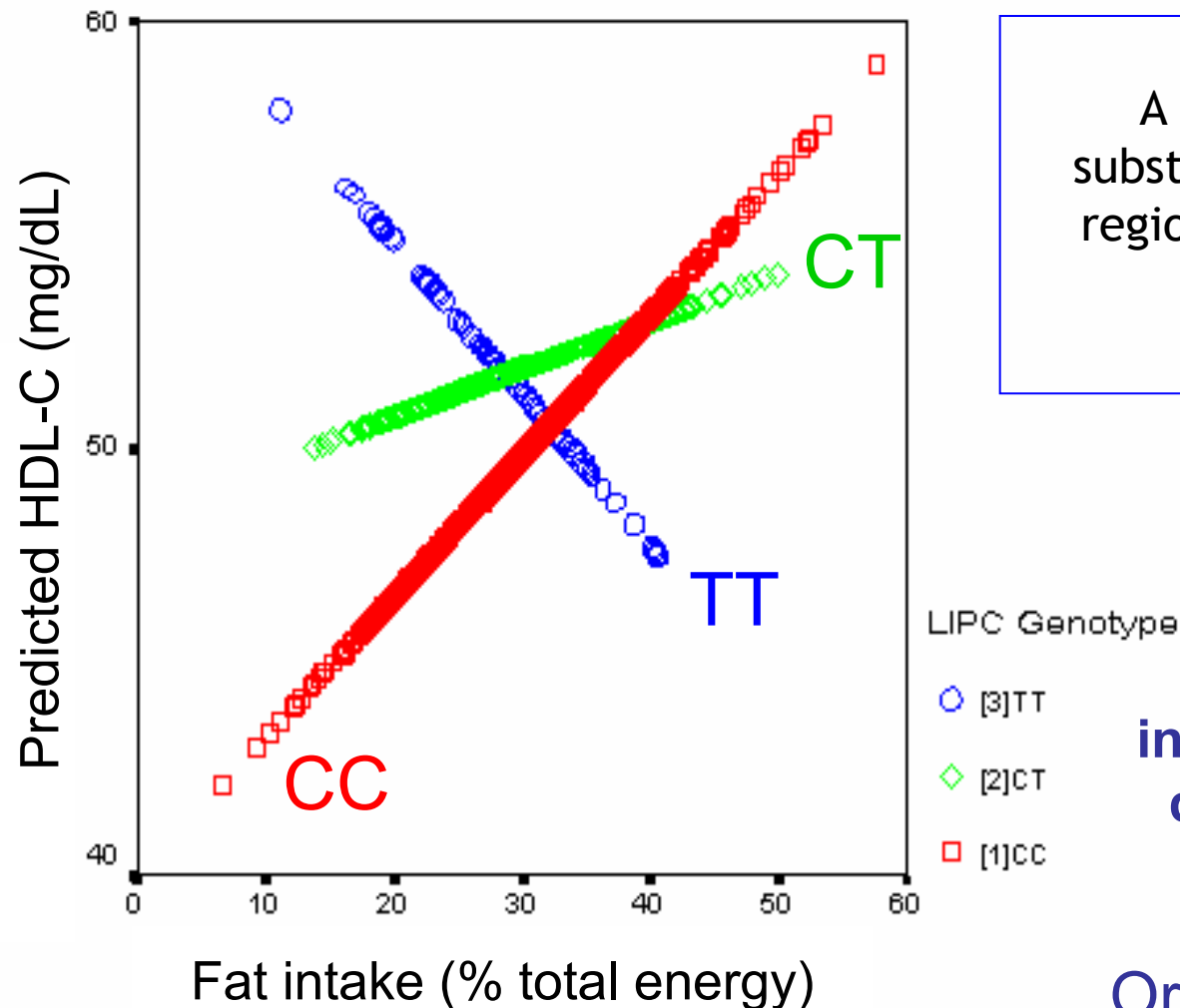
Jim Fixx

Author: *The Complete Book  
of Running*

Died, heart attack – Age 52

## People are different: Gene-diet interaction

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A common -514 C to T substitution in the promoter region of the hepatic lipase gene LIPC

**LIPC genotype influences the effect of dietary fat on HDL-C levels**

*Ordovas et al., 2002*

# "Reverse Nutrigenomics" → creating genomic diversity ?

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## Starchy diet boosts gene copy number...

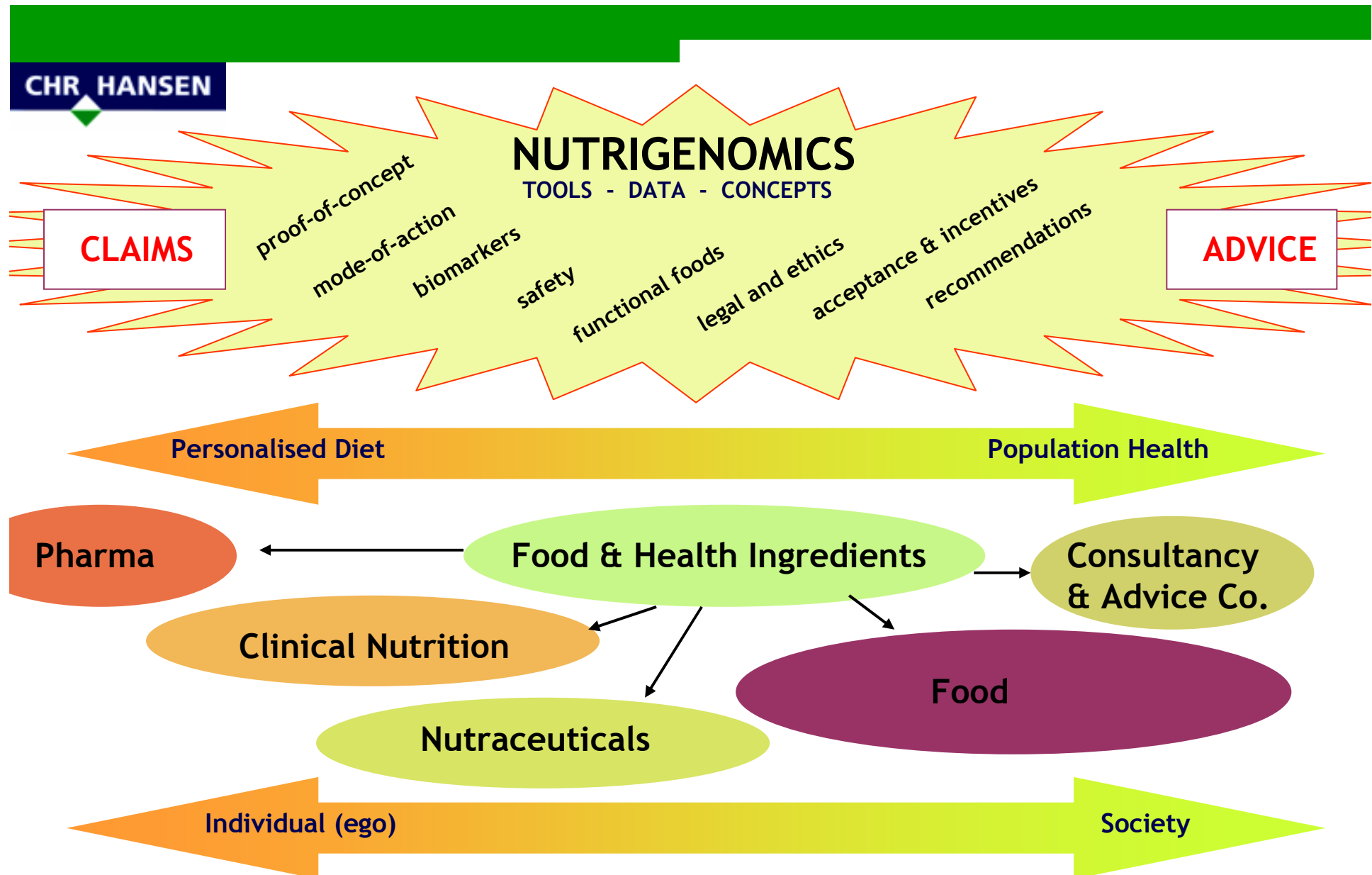
George H. Perry et al., "Diet and the evolution of human amylase gene copy number variation" - *Nature Genetics*, September 9, 2007.

- ❖ probably took place during evolution (adaptation)?
- ❖ far too early to speculate whether it might to some degree take place also in an individual lifetime period?
- ❖ - any relevance to the concept of metabolic imprinting?
- ❖ - 'food for thoughts' in relation to MS, diabetes and obesity...

...pure speculation, but...



# Commercial and Public Innovation



# Ingredients in the "hot and sweet spot"

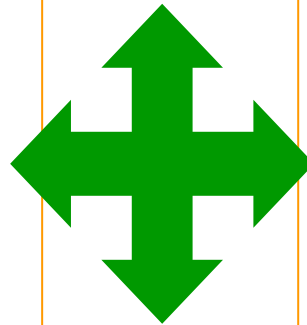
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## Food companies:

- move into **functional food** products
- **health promotion**, (i.e. prevention)
- image on **health**, not disease
- Nestlè: from world's largest Food company to " # 1 Health & Wellbeing company"
- **biomarkers** in focus
- regulatory and NGO **hurdles**
- **increased profit** margins expected
- **liability issue** for (fast) food co's
- Arla Foods: "**Nutrition** Policy"

## Pharmaceutical companies:

- move towards **prevention**, not just therapeutic drugs
- question of trustworthiness and **sustainability**
- business of the future = **health**
- needs **new business model** to evolve
- Amersham (GE): prevention as driver
- NN: **partnerships** Pharma - Food - Entertainment - Education (+ Insurance?)
- marketing budgets will shift target from GP's to **consumers**
- **decreased profit** margins expected
- NN: corporate **social responsibility** as a 'third/fourth bottomline'



Existing companies will be changing - and new companies will develop



- and they will all need innovative health ingredients

# The (food) cultural dimension of the lifestyle paradox

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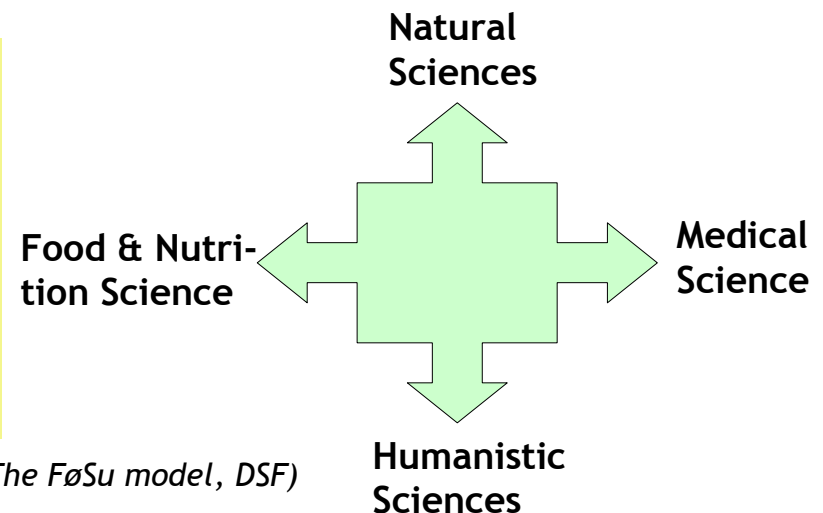


"At the heart of health campaigns lies the assumption that humans are rational decision-makers - and, if properly informed, individuals will choose beneficial health behaviours and health hazards.....

.....However, everyday experience and empirical studies show that this assumption is naïve"

*(Prof. Claus Vögele, Clin. & Health Psychology Res. Ctr., Roehampton University)*

**Nutrigenomics**, combining biology, physics, chemistry, medical, and food & nutrition sciences, **MUST** be integrated with social, psychological, economical and historical sciences



*(The FøSu model, DSF)*

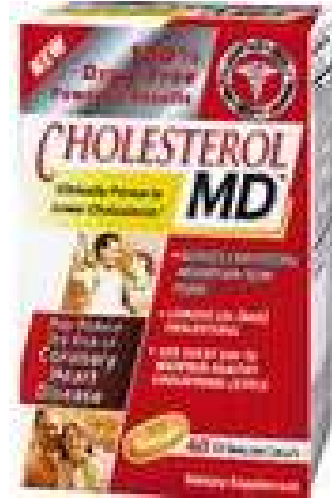
# Can dietary supplements and functional food compete pricewise with pharma products?

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70-250 DKK/40



No/low documentation



150 DKK/100  
40 mg



Strong documentation

Medicine is taken when you are ill

-

Functional food is the healthy food  
you eat all your life to reduce the  
risk of becoming ill...

# Accept and Compliance - use of Incentives

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## CASE STUDY: Refunds for healthy Dutch and French hearts

In 2005 a Dutch health insurer (VGZ-IZA Group) became first company in Europe - and possibly the world - to **reimburse policy holders who buy cholesterol-lowering food products**.

- p.t. only "Pro-Activ" products - but plans to extend the policy to other products meeting highest standards in **proof of efficacy**
- next, VGZ-IZA might reimburse women who take **folic acid** around the time of conception

In France, in November 2005, Unilever signed similar deal with healthcare insurer (Maaf), refunding customers buying Flora Pro-Activ products on their annual bill of Euro 380:

- Euro 10 if they buy/eat at least 7 such products
- Euro 22                      -                      -                      - 14                      -                      -
- Euro 40                      -                      -                      - 21                      -                      -

# Accept and Compliance - use of Incentives

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The money flow shows where the importance is  
→ well-documented biomarkers as basis for health claims

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### The culture dimension

- works well in NL
- does not seem to work in F

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- Euro 40                      -                      -                      21                      -                      -

...and there's enough for everybody!

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