Agenda

- Managing weight: context
- Fabuless: functional ingredient for weight management
- Conclusions

Context: nutritional realities

Over-nutrition

- >1 billion adults overweight; ~300 million clinically obese (WHO); type-2 diabetes and other co-morbidities on the rise, health care cost increasing.
- **Functional food solutions can be aimed at:**

  1. The overweight: **return** to normal weight.
  2. The normal weight: **maintain** a normal weight.

- **Both are relevant from a consumer health perspective.**
- Functional Food ingredients generally not well documented; represent potentially promising strategy in weight management - better compliance.

Context: efficacy of main approaches in WM

- **Pharma**: moderately effective: ~5% weight loss/year achievable. Issue: limited efficacy versus side-effects.
  - Remonabant: ~7%; Sibutramine: ~5%; Xenecal: ~3% weight loss/year
- **Slimming diets**: effective; >10% weight loss/year achievable. Issue: poor compliance and weight re-gain.
  - Virtually all weight loss by dieting neutralized by speedy yo-yo; poor compliance due to poor quality of eating experience.
- **Food ingredients**: potentially effective; <5% weight loss/year? Issue: evidence-base.
  - Potential advantages: better compliance; increased quality of life; better taste – better long-term results.
  - We are beginning to discover the possibilities of this area

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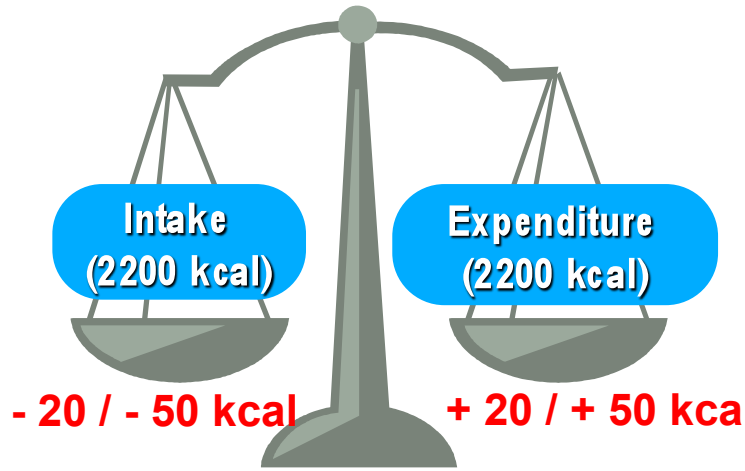
Calories and weight loss - relation

- Human calorie intake is ~2200 kcal/day; calorie expenditure: ~2200 kcal/day.
- Affecting the energy balance by ~100 kcal/day (~4% of daily calorie intake), could prevent weight gain in most of the US population (Hill, Science, 2003).
- Overweight adults consume ~100 kcal/day more than their normal-weight counterparts (US Department Agriculture, 2006).
- 20 tot 50 kcal/day extra during 1 year: 1 kg body weight (Dutch Nutrition Centre, 2007).

Relatively small sustained changes in energy intake and/or expenditure can make a big difference



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The difference between effects and benefits

Effects and benefits:

1. ***'Satiety', 'hunger control', compliance (short-term)*** : ***Effect***

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2. ***'Reduced calorie intake' (short-term)*** : ***Effect***

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3. ***'Reduced body fat mass' (long-term)*** : ***Benefit***

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4. ***'Less weight regain after dieting' (long-term)*** : ***Benefit***

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5. ***'Sustained weight loss' (long-term)*** : ***Benefit***

- *'Benefits' are scientifically substantiated to be related to improved health. E.g. there is good evidence that sustained reduction in body fat mass is related to reduced risk of cardiovascular disease. In contrast, 'effects' are not sufficiently scientifically substantiated to be related to improvements in health or wellness. Examples are satiety, satiety hormones, food intake.*

Agenda

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- **Fabuless: functional ingredient for weight management**
- Conclusions

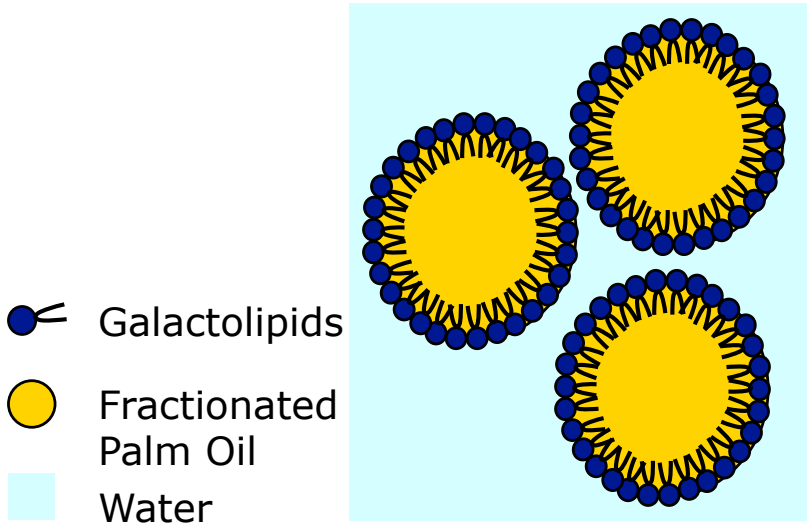
Fabuless: short history

- Past: LTP invented Fabuless - focus on ingredient development and mechanism of action in animal and short-term human studies (1 day-3 weeks).

- Present: DSM acquired LTP, focus shifted to demonstrate longer-term efficacy and mechanism of action:
  - Claims to be supported by long-term efficacy (as the body may compensate within days or weeks).
  - Substantiation to be based on weight management and health-relevant parameters, such as weight regain, BMI, waist circumference, body fat mass.
  - Short-term studies on Fabuless indicate potential mechanisms of action and *potential early signs* of efficacy.

Fabuless™ : what is it?

- Fabuless™: lipids from oat and palm
- Fabuless™: made from vegetable oils
  - Palm: 40.0%
  - Oat oil fraction: 2.5% (galactolipids)
  - Pure water 57.5%



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Fabuless™ efficacy long-term
'Regain' study

Study design:

- Placebo controlled, double blind, randomized, parallel design
- Volunteers: 50 overweight women, 18-58 years, BMI 25-32
- 6 weeks VLCD followed by 18 weeks weight maintenance
- Free living conditions; daily consumption 2x5 gr daily, dairy product

Subjects characteristics at baseline

	Fabuless group (n=22)	Placebo group (n=28)
Age (years)	40.3	41.2
BMI (kg/m^2)	28.9	28.5
Weight (kg)	81.3	79.0
Height (cm)	167.6	166.3
Waist circumference (cm)	91.1	91.5
Hip circumference (cm)	108.8	108.1
Body fat mass (%)	38.4	38.2

Fabuless™ efficacy long-term *weight regain*

• Under significant weight regain conditions (placebo group: $p<0.001$): significantly less weight regain due to Fabuless™ ($p=0.05$ ANOVA).

Fabuless™ efficacy long-term *waist circumference*

Control

Test (Fabuless™)

Diepvens et al., IJO, 2007

- Signicant difference waist circumference test (Fabuless™) versus placebo group ($p<0.05$)
- Significant increase in control group ($p<0.05$); decrease in test group ($p<0.05$)

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Fabuless™ efficacy long-term *body fat mass*

Diepvens et al., IJO, 2007

- Significant reduction in body fat mass in Fabuless™ group, compared to placebo

Fabuless™ mechanism of action long-term
GLP-1 and hunger

Plasma levels of satiety-related hormon GLP-1

Time GLP-1 (pmol/L)	Week 2 Fabuless (n=22)	 Placebo (n=28)	Week 8 Fabuless (n=22)	 Placebo (n=28)	Week 26 Fabuless (n=22)	 Placebo (n=28)
0 (min)	6.8	6.2	7.5	6.6	7.0	6.3
90 (min)	7.9	6.7	7.8	7.6	7.5	7.3
180 (min)	7.3	7.8	7.4	7.2	8.7*	7.5

* $p<0.05$ compared to week 2

These results show that:

- The satiety hormone GLP-1 was significant increased in test group (Fabuless™) as compared to placebo ($p<0.05$); no change in placebo group.
- Hunger was significantly reduced in the test group compared to the placebo group ($p<0.05$).

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Fabuless™ efficacy long-term
'Regain study' summary

Weight management-relevant benefits of Fabuless:

- A significant increase in weight was observed in the placebo group during weight regain after dieting; no difference in the test group (test versus placebo: 1.2 kg vs 3.0 kg; p = 0.05 ANOVA).
- Waist circumference: significantly decreased in test group versus placebo ($p<0.05$).
- Body fat mass significantly decreased (test versus placebo overall: 6.5 kg versus 4.1 kg; $p<0.05$).
- BMI not increased in test group, significantly increased in placebo group ($p<0.05$).

Fabuless™ mechanism of action long-term
'Regain study' summary

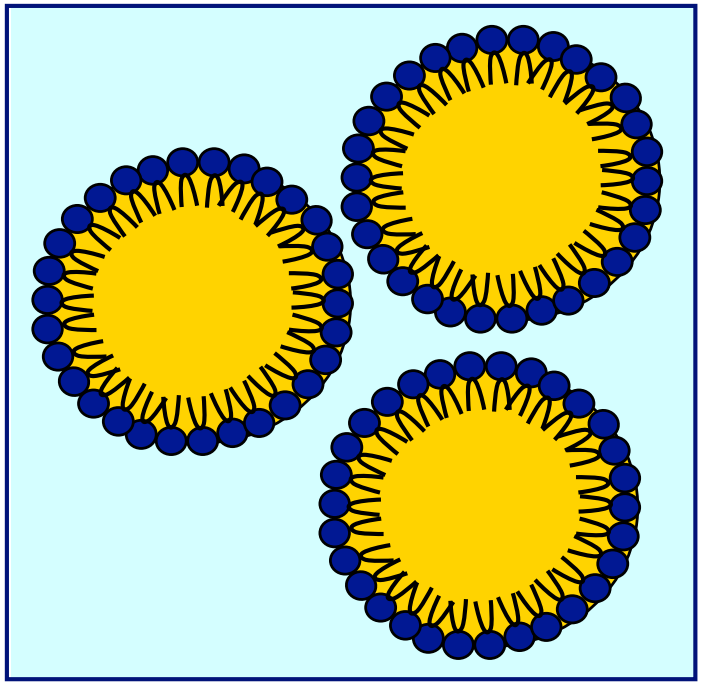
Mechanism of action (long-term).

- Hunger/satiety:
  - End weight maintenance: test group significantly less hungry, hunger 1.5 times higher in placebo; $p<0.05$ ANOVA
- Circulating blood levels of satiety hormone GLP-1:
  - End weight maintenance: test group significantly higher versus placebo ($p<0.05$).

Conclusion:

Long-term daily consumption of Fabuless (2x5 gr daily, dairy product, 4 months) supports moderately overweight women in maintaining lost body weight, reducing waist circumference and reducing body fat mass. Enhanced satiety is likely to play a role in the mechanism of action; additional mechanisms may play a role.

Fabuless™ mechanism of action long-term
'Regain study' summary



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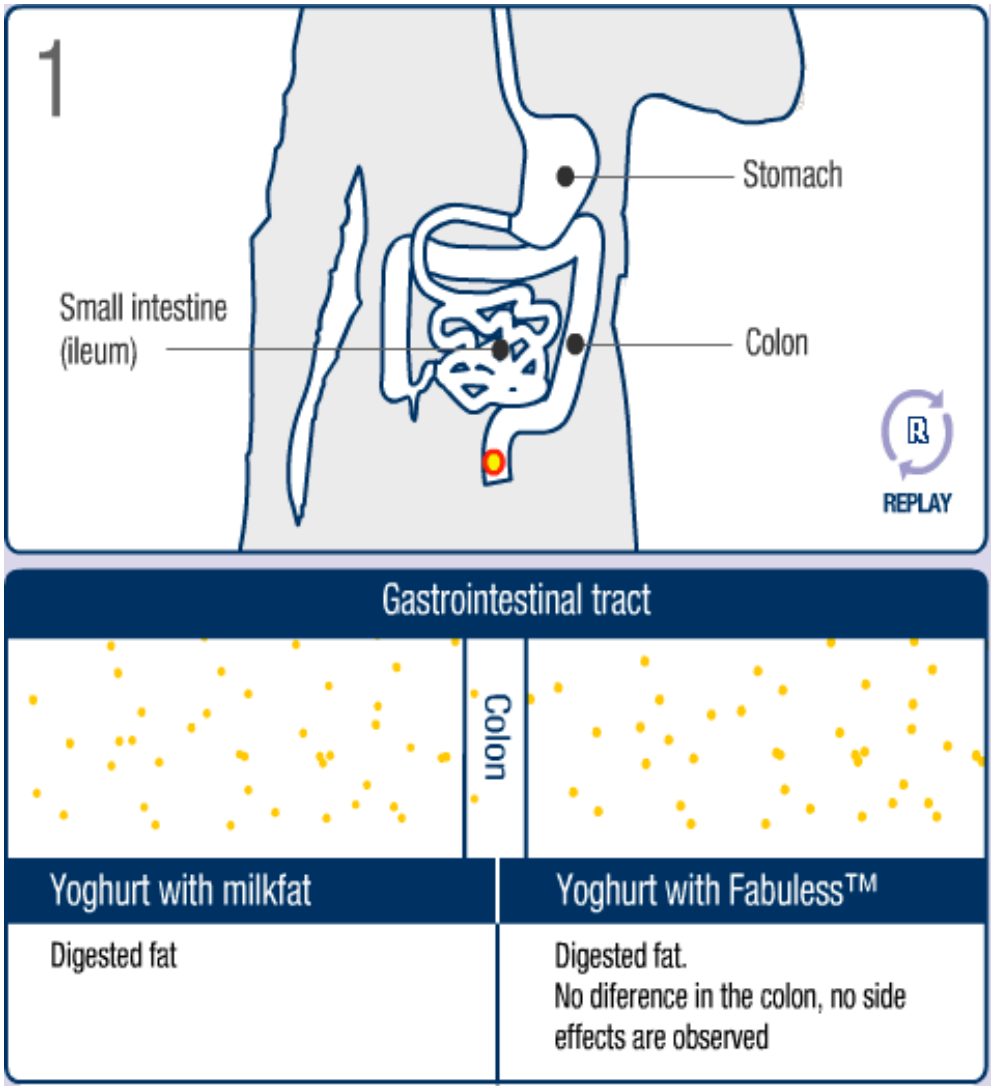
Fabuless™: how can it work?



Hypothesis: Ileal brake may be involved

Ileal brake

A natural feed-back mechanism triggered by presence of nutrients (especially fat) in the lower intestine:

- Slows down transit of a meal in the gut for nutrient absorption
- Prevents undigested food to reach colon
- Releases satiety hormones (e.g. GLP-1) to reduce or stop further eating

Fabuless™ efficacy long-term *'Maintain' study*

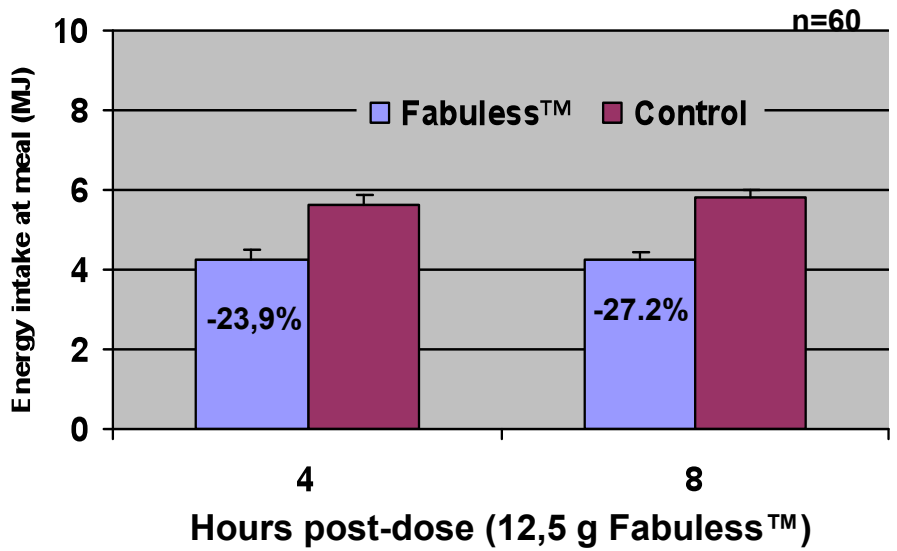
Study design:

- Randomised, double-blind, placebo-controlled, parallel design study
- Volunteers: 43 overweight females, 18-60 years, BMI 26-31
- Six weeks accelerated weight loss with meal replacement (Nutrilett powder):
  - 2 weeks with 5 portions/day (112 kcal/bag); 4 weeks with a healthy breakfast and 4 portions/day (112 kcal/bag); 12 weeks intervention with lunch replaced; Fabuless or cream (12.5 g emulsion=5 g fat) added to one portion Nutrilett

Study objectives:

- Effect on weight maintenance after dieting
- Effect on body composition with Bioelectrical Impedance and Caliper
- Effect on hip and waist circumferences
- Safety evaluation
- Retrospective evaluation of background diet and physical activities

Fabuless™ mechanism of action short-term *effects on satiety & calorie intake*



- Effects on hunger & satiety were been observed in 2 studies
- Effects on calorie intake have been observed in several studies after 4, 8 and 36 hours; reductions seen in women and men, in normal weight, overweight and obese people and after repeated exposure (short term effects not always observed)

- Increases in calorie intake or increased hunger were not observed in any study.

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Fabuless™ mechanism of action short-term *dose-response*

Dose	Energy intake	Reduction
0 g	7.4 MJ	-
2 g	7.1 MJ	4.0% (not in publ)
10 g	5.6 MJ	24.5%[a)]
15 g	5.2 MJ	29.4%[b)]

5 g

a) p<0.05 vs control
b) p<0.05 vs control and 5 g

- Short term effects on calorie/food intake are achieved by only 5-15g of Fabuless™.
- Long term study confirms satiety mechanism continues to work (no compensation).
- Data indicate small quantities of fat as effective.

Source: Burns et al Eur J Clin Nutr (2002);56;368-77

Totality of evidence Fabuless extensive

A. Efficacy

Two long-term studies demonstrate Fabuless significantly affects weight management relevant parameters, such as weight regain, body fat mass, BMI and waist circumference.

- Study 1: Fabuless affects weight management relevant parameters – e.g. Fabuless helps maintain weight after dieting.
- Study 2. Confirms effectivity Fabuless during gradual weight loss (NDA).
- Long term studies confirm weight of evidence short term studies.

B. Mechanism of action

Several independent studies show Fabuless affects satiety, satiety hormones after short- or long-term consumption.

Evidence provides clues as to a plausible mechanism of action: ileal brake.

Totality of evidence Fabuless extensive

Publications:

1. Burns et al., Int. J. Obes., Relat. Metab. Disord., 2000.
2. Burns et al., Int. J. Obes., 2001.
3. Burns et al., Eur. J. Clin. Nutr., 2002.
4. Logan et al., Eur. J. Clin Nutr., 2006 (ns).
5. Diepvens et al., Int. J. Obes. 2007.

6: 2nd long term study; in prep.

7: Meta-analysis & review; in prep.

8: Short-term effects on hunger perception; in prep.

9: Mechanism of action; human study finalised; report in prep.

Dairy concepts with Fabuless™

EXCLUSIVE HEALTH

FULL BREAKFAST

DAILY CONTROL

EAT LESS CUPS

fabuless™

EASY DIETING

PETIT SUISSE

SENSIBLE SNACK

ON THE GO SMOOTHIE

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Successful first launches
Italy and Portugal

Pineapple and Apple-Grape flavour

- Latteria Merano (Italy) with "*ActifControl*", endorsed by health guru Henri Chenot.
- Product: 200 ml drinking yoghurt with 5 grams Fabuless™. Luxury concept that is also Probiotic and lactose reduced.
- Retail price of €1.35
  (~200% of their A-Brand probiotic yoghurt drink)

Strawberry and Papaya-Passion fruit flavour

- Lactogal (Portugal) with "AdagioVersus" as part of the "Adagio" range with healthy dairy concepts
- It is 90 ml drinkable yoghurt 'shot' with 5 grams Fabuless™
- Claim: Reduces your Appetite

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Campina launched Optiwell Control in the Netherlands and Germany

- After first generation of weight management dairy products (reduced sugar and zero fat); brand innovation with additional and stronger benefit
- Claims: ‘helps to eat less’
- 102 ml drinking yoghurt in four-pack, another popular daily dosage ‘shot’
- Each bottle contains 5 gram Fabuless™
- Choice of Lemon / Raspberry in NL, Orange / Raspberry in Germany
- Room for new SKU’s: taste segmentation launched
- Premium priced at 2.49 EUR / 4pack

Optimel Control
Helpt minder te eten

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Optiwell Control: the no 1 2007 bestseller!

BESTSELLER
ERFOLGREICHSTE
PRODUKTNEUHEIT

RUNDSCHAU
für den Lebensmittelhandel

- The German trade magazine "Rundschau für den Lebensmittelhandel" announced that Optiwell Control was the best selling new product launch in 2007
- NL: 5 MIO bottles sold in 3 months!

TOP 10 BESTSELLER 2007

Optiwell Control ist die erfolgreichste Produktneuheit des Jahres 2007 – vor Ritter Sport 250 Gramm und der Pommersche Gutsleberwurst des Wurstverarbeiters Rügenwalder.

	Angaben in Euro
1. Optiwell Control 400 ml	**474.740**
2. Ritter Sport 250 Gramm	329.420
3. Pommersche Gutsleberwurst	240.560
4. Somat 7 in 1	237.270
5. Nimm 2 Lachgummi Joghurt	228.090
6. Calgonit Alles in 1 Tabs	205.850
7. Hohes C Naturelle 500 ml/1500 ml	198.800
8. Milka Sommer Tafel 100 Gramm	196.310
9. Sagrotan 4 in 1	193.270
10. Schöfferhofen Weizen + Grapefruit	179.970

Quelle: InfoScan; Basis: Durchschnittlicher Umsatz/Woche, Neuprodukt, Zeitraum 08/2006 bis einschl. 07/2007

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Fabuless™ in Meal Replacement products

- Swedish company Cederroth Intl. was first to launch Meal Replacer with Fabuless™
- Fits in their ‘Allévo’ branded weight control program
- Available in two flavours: chocolate and Orange / Banana
- Launched in March 2007 in Norway and Finland, now also available in Sweden
- Sales price: 2.90 EUR

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Fabuless offers logical fit in consumers mind in a 0% fat brand positioned around ‘balancing your weight’

- Optimel is the undisputed market leader in the ‘No fat / No Added Sugar’ segment in the Netherlands
- Campina redefined the category for the Weight Conscious consumer with Optimel Control: **Optimel Control helps consumers to eat less**

Product Brand
Dairy without fat and sugar

Lifestyle Brand
Optimel for the Weight Conscious People

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Fabuless™ now in >20 countries around the world

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General conclusions

• Weight management-relevant parameters, i.e. weight regain, fat mass, BMI, waist circumference and body composition are beneficially affected by long term Fabuless™ consumption.

• Fabuless™ can be effective during conditions of weight regain (positive energy balance) or gradual weight loss (negative energy balance; NDA)).

• The mechanism of action may include satiety, as the satiety hormone GLP-1 and subjective feelings of hunger are significantly affected by Fabuless long-term; recent findings regarding the mechanism of action provide further insights (NDA).

• Fabuless™ is a truly unique offering today; independent studies confirm ingredient efficacy on parameters relevant to *longer-term* weight management and provide clear indications of plausible mechanism of action.

• Food solutions through functional ingredients CAN be supportive in actual weight management objectives - adding a new complementary, effective and positive strategy to the existing pharma and dieting approaches.

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Claims with Fabuless

Definition of health claims (European regulations):

'Any representation that states, suggests, or implies that a relationship exists between a food, a constituent of that food, and health'.

- The evidence for Fabuless supports claims such as: *'satisfies hunger'; 'helps you to eat less', helps improve body composition, helps reduce body fat during weight loss, helps maintain weight after dieting, helps reduce waist circumference after weight reduction**
- These claims are based on scientific observations of direct relevance to weight management longer-term.
- We advise our customers not to 'over-claim', as this may lead to:
  - Consumers starting to use the ingredient as an excuse or irresponsibly, rather than as a help and support for their weight management efforts.
  - Disappointment of consumers that can be avoided.

Claims should be according to local regulations. DSM customers are responsible for product claims and communications.

DSM portfolio in functional ingredients

❖ **Food plus:**

Specialty macronutrients, micronutrients, taste - compliance in healthy eating

Linoleic acid, alpha-linolenic acid, arachidonic acid, DHA, vitamins, carotenoids, antioxidants, folic acid, biotin; better taste - compliance in healthy eating through natural yeast technology-based solutions.

❖ **Food minus:**

Reducing calories / calorie density, (saturated) fat, salt, lactose, acrylamide

Lactose (intolerance), acrylamide formation, better nutrition profiles through yeast technology-based solutions for reducing salt, sugar, (saturated) fat and calories/ calorie density.

DSM portfolio in functional ingredients

❖ **Functional ingredients:**

Scientifically proven health & wellness benefits which can be claimed

- Weight management - body shape, calorie control: Fabuless
- Type-2 diabetes - blood glucose management: Insuvital
- Cardiovascular health - blood pressure: Tensguard
- Immune function - reducing the impact of cold & flu: Lafti L10 probiotics
- Energy for active people - recovery, endurance, performance, muscle function: Peptopro
- Mood & mental performance - concentration, alertness, stress reduction: Pep2Balance
- Infant nutrition: PUFA's (e.g. arachidonic acid); InfantPro (allergy prevention)
- Lactose intolerance: Maxilact
- Various: Bonistein, Teavigo, Optisharp, more in pipeline, e.g. gluten allergy

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