



EFSA update on gut and immune related health claims

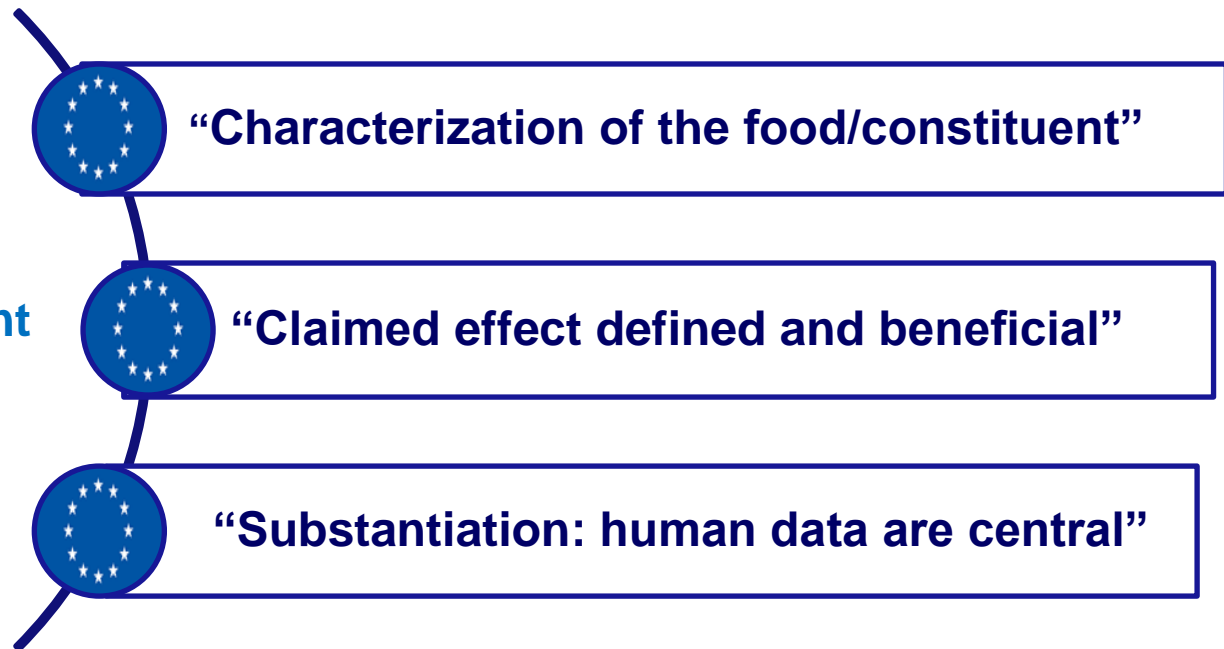
Yolanda Sanz
EFSA NDA Panel
IATA-CSIC, Valencia, Spain

MAIN CRITERIA OF HEALTH CLAIMS REGULATION

Reg. (EC) No 1924/2006

- Authorization of health claims in the EU is based on a **scientific assessment** following the highest possible standards.
- **Consumer protection, fair competitiveness and innovation**

EFSA assessment



Scientific substantiation requires a favourable outcome in ALL



HEALTH CLAIMS CLASSIFICATION

Regulation (EC) 1924/2006

Art.13.1

**Generally
accepted
scientific
evidence**

Art.13.5

**Newly
developed
scientific data /
proprietary data**

Art.14

**Reduction of
disease
Risk**

**Children's
development &
health**

List Claims

Applications

FAVORABLE HEALTH CLAIMS (ART 13.1)

Out of **421** IDs related to this area: **42 with favourable outcomes**

- ✓ **14** related to immune function (essential nutrients i.e.: copper, folate, iron, selenium, vit D, A, B12, B6, C, and zinc)
- ✓ **15** related to GI function
 - **10 bowel function** (e.g. dried prune, lactulose, wheat bran fibre, rye fibre, oat and barley grain fibre)
 - 4 GI discomfort caused by lactose intake in lactose intolerant (e.g. foods with reduced lactose content)
 - 1 reduction of intestinal gas accumulation (e.g. *Activated charcoal*)
- ✓ **13** related to absorption/digestion
 - 7 Absorption of micronutrients (e.g. Vit C, D, meat or fish, fats)
 - 2 Digestion (e.g. Ca, chloride)
 - **4 lactose digestion**:
(i.e. lactase, **live yoghurt cultures**)





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FAVORABLE HEALTH CLAIMS (ART 13.5, 14)

Of **155 applications** related to this area (07/2015):

- ✓ 7 applications under evaluation or validation
- ✓ 90 applications withdrawn during the evaluation
- ✓ **58** applications with opinions adopted/published
 - ✓ 1 with the food not characterised
 - ✓ 5 with insufficient evidence
 - ✓ 45 with cause and effect relationship not established

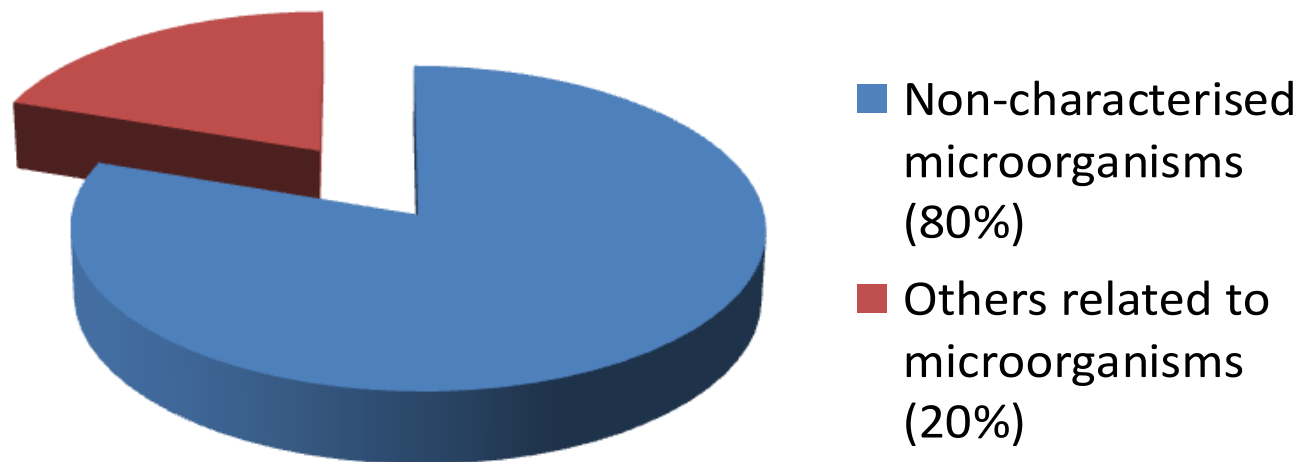
✓ **7 with favourable outcomes:**

- 3 Immune system (e.g. Vitamin D, Zinc)
- **3 bowel function (i.e. sugar beet fibre)
chicory inulin, hydroxyanthracene derv.)**
- 1 Absorption of micronutrient (e.g. Vitamin C)



FIRST GUIDANCE ON GUT-IMMUNE CLAIMS (2011)

Lack of characterization a major reason for unfavourable opinions (Art 13.1)

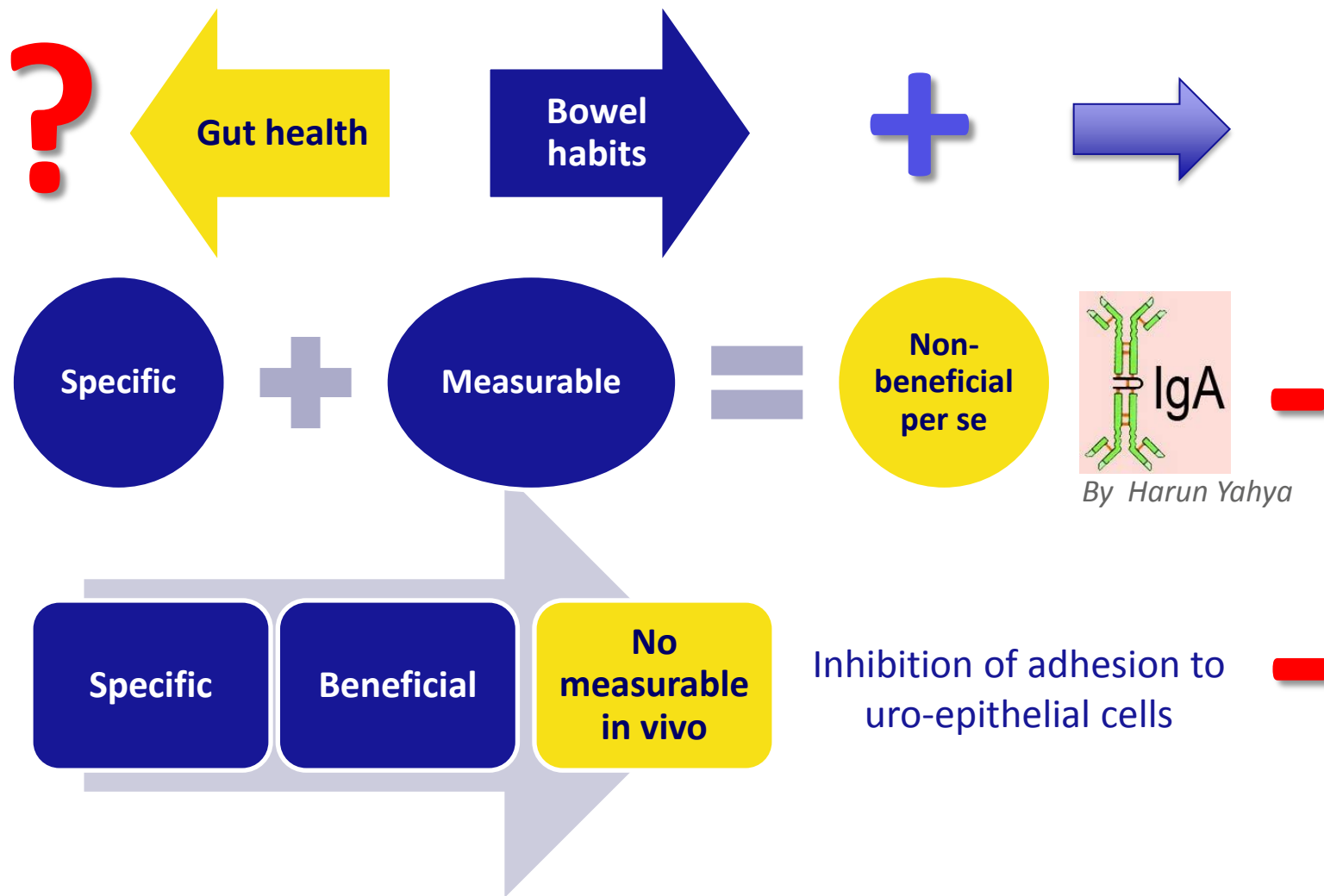


Not just a recommendation as in the past

(Joint FAO/WHO Working Group Report on Drafting Guidelines for the Evaluation of Probiotics in Food London, Ontario, Canada, April 30 and May 1, 2002)

FIRST GUIDANCE ON GUT-IMMUNE CLAIMS (2011)

The claim effect: specific, measurable and beneficial



FIRST GUIDANCE ON GUT-IMMUNE CLAIMS (2011)

Altern Ther Health Med. 2011 Jan-Feb;17(1):72-9.

Clinical utility of probiotics in inflammatory bowel disease

Cain AM, Karpa KD.

York Hospital, Pennsylvania, USA

Studies oriented to the treatment of diseases

Probiotics and prebiotics: clinical effects in allergic disease.

Tang ML, Lahtinen SJ, Boyle RJ.

Department of Allergy and Immunology, Royal Children's Hospital, Melbourne, Australia

Studies on reducing incidence of a disease failed to identify risk factors

Prevention of acute rotavirus diarrhoea. A randomized, double-blind, controlled trial using two different probiotic preparations in Bolivian children.

Grandy G, Medina M, Soria R, Terán CG, Araya M.

Paediatric Centre Albina Patiño, Department of Gastroenterology and Nutrition, Cochabamba, Bolivia. ggrandy@inta.cl

PROBIOTICS IN (SOME) PROFESSIONAL GUIDELINES



WGO Practice Guideline - Probiotics and Prebiotics

October 2011

Treatment of acute diarrhea:

Hepatic encephalopathy

Allergy Treatment of atopic eczema

Inflammatory bowel disease (IBD)


Necrotizing enterocolitis

Radiation-induced diarrhea:

Pouchitis:

Ulcerative colitis:

PROPOSALS TO CIRCUNVENT THE PROBLEM FROM (SOME) STAKEHOLDERS

- 
- **Clustering probiotic strains** for claims, while it was generally accepted that probiotic effects were strain-specific unless the opposite is demonstrated.
 - Use of the nutritional claim “**contains probiotics**”, which will not allow the differentiation of products/effects.
 - **Ignore claims** (just lines on a label) and use marketing strategies.

META-ANALYSIS FOR ASSESSING PROBIOTIC EFFECTS ?

Probiotics for the Prevention and Treatment of Antibiotic-Associated Diarrhea A Systematic Review and Meta-analysis

Susanne Hempel, PhD

Sydne J. Newberry, PhD

Alicia R. Maher, MD

Context Probiotics are live microorganisms intended to confer a health benefit when consumed. One condition for which probiotics have been advocated is the diarrhea that is a common adverse effect of antibiotic use.

The main limitations

to this result are residual unexplained heterogeneity, poor documentation of the probiotic strains, and lack of assessment of probiotic-specific adverse events.

Conclusions The pooled evidence suggests a reduction in AAD. More research is needed to identify the probiotic strains associated with the greatest efficacy and for the duration of antibiotics.

JAMA. 2012;307(18):1959-1969

**General public health
recommendations**

≠

**Commercial promotion of a
brand/proprietary strain
through claims**

www.jama.com

By Ambroise Marin



PROPOSALS TO CIRCUNVENT THE PROBLEM FROM (SOME) STAKEHOLDERS


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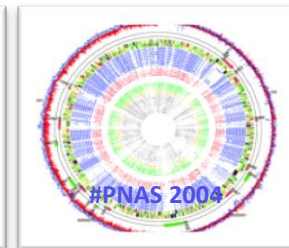
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NEW GUIDANCE ON GUT-IMMUNE-PATHOGEN CLAIMS

- 
- **Improve dialogue** via several public consultations:
 - Discussion paper (Jun-Sept 2014)
 - Guidance Draft (Feb-March 2015)
 - Claims with favorable opinions are used to provide **scientific advice**, while those with unfavorable opinions illustrate shortcomings.
 - **Update** EFSA principles:
 - General scientific guidance for stakeholders on [health claim applications](#). EFSA Journal 2016;14(1):4367
 - Guidance on the scientific requirements for health claims related to the [immune system, the gastrointestinal tract and defence against pathogenic](#) microorganisms. EFSA Journal 2016;14(1):4369

WHAT IS NEW IN THE GUIDANCE UPDATE?

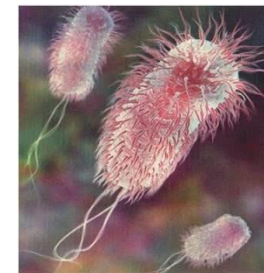
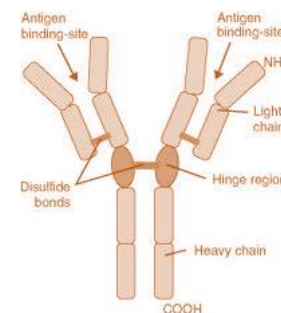
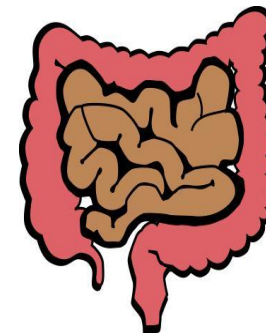
Characterization



- Move to the **general guidance** on claims
- New **molecular tools added** according to the state-of-art (multilocus sequence typing, optical mapping, whole-genome sequencing, etc.). **Open list** to others.
- **Indigenous human bacteria** (called “next generation probiotics”) can be considered **novel foods** (Regulation EU 2015/2283). Section 9 of EFSA guidance **relates to taxonomic and safety evaluation** (under revision).

WHAT IS NEW IN THE GUIDANCE UPDATE?

1. Outcome variables
2. Validation of questionnaires
3. Duration of interventions
4. Biological plausibility-mechanism
4. Appropriate study population
5. Risk factors



WHAT IS NEW? CLAIMS OF GI FUNCTION

Claims on maintenance of normal defecation

- **Outcomes variables:**

Several outcome variables provide information about the function and the underlying mechanism of action (e.g. **stool frequency**, **stool consistency**, **sensation of complete/incomplete evacuation**, **faecal bulk**, **transit time**)

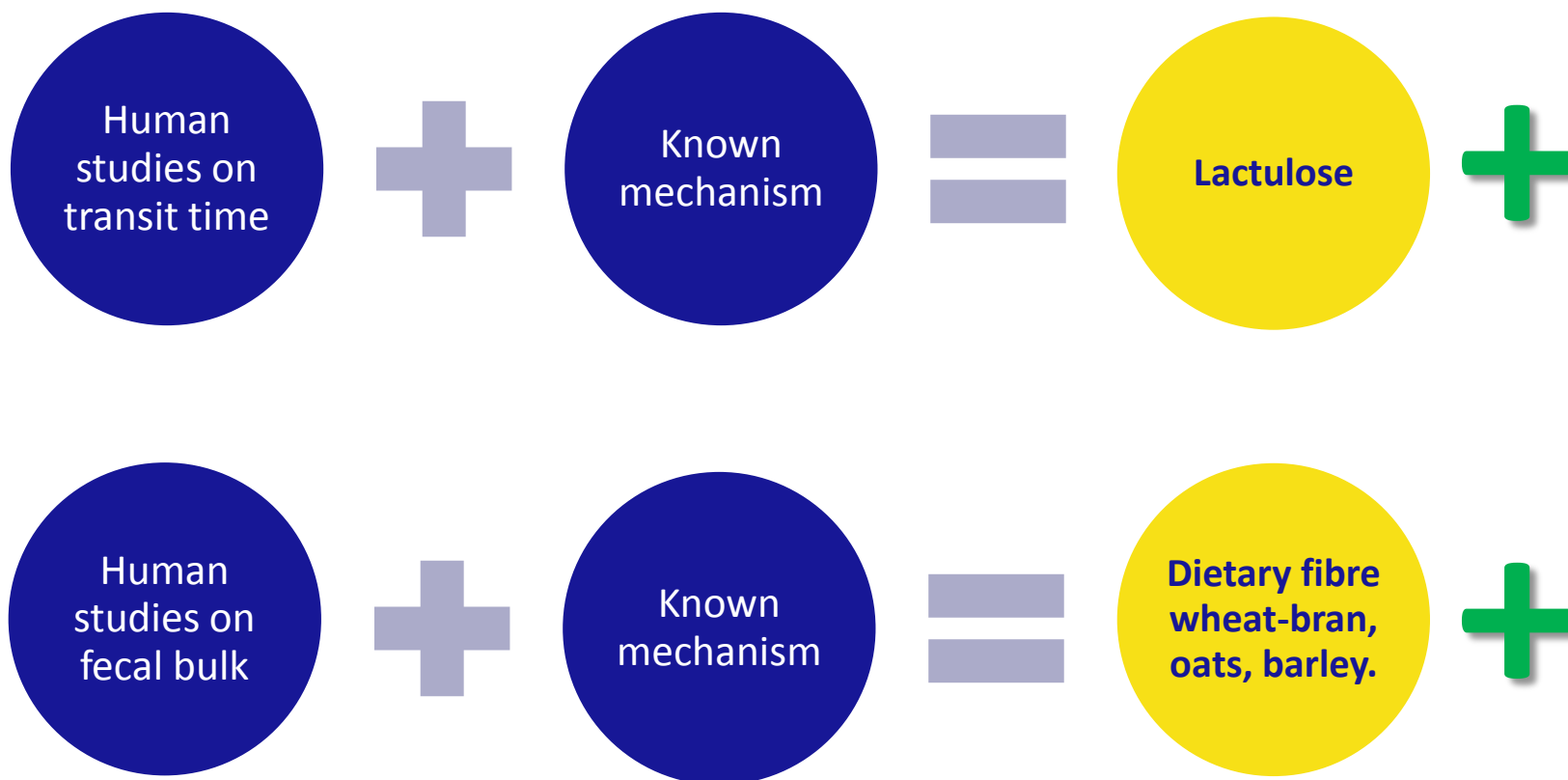
- **Duration.** **Exclude adaptation** and **chance findings** owing to **fluctuation** of outcome measures (e.g. 4–8 weeks).

- **Consistency of effects + mechanism of action**



WHAT IS NEW? CLAIMS OF GI FUNCTION

Claims on maintenance of normal defecation



WHAT IS NEW? PATHOGENS –REDUCTION OF RISK

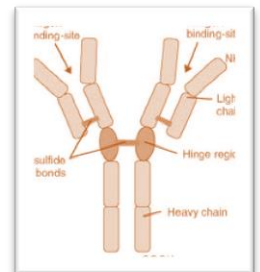
(Immune) Defences against pathogens

- **Study population:** subjects without an infection at baseline
- **Outcome variables:**
 - Clinical outcomes alone are sufficient
 - Immune markers may explain the mechanism

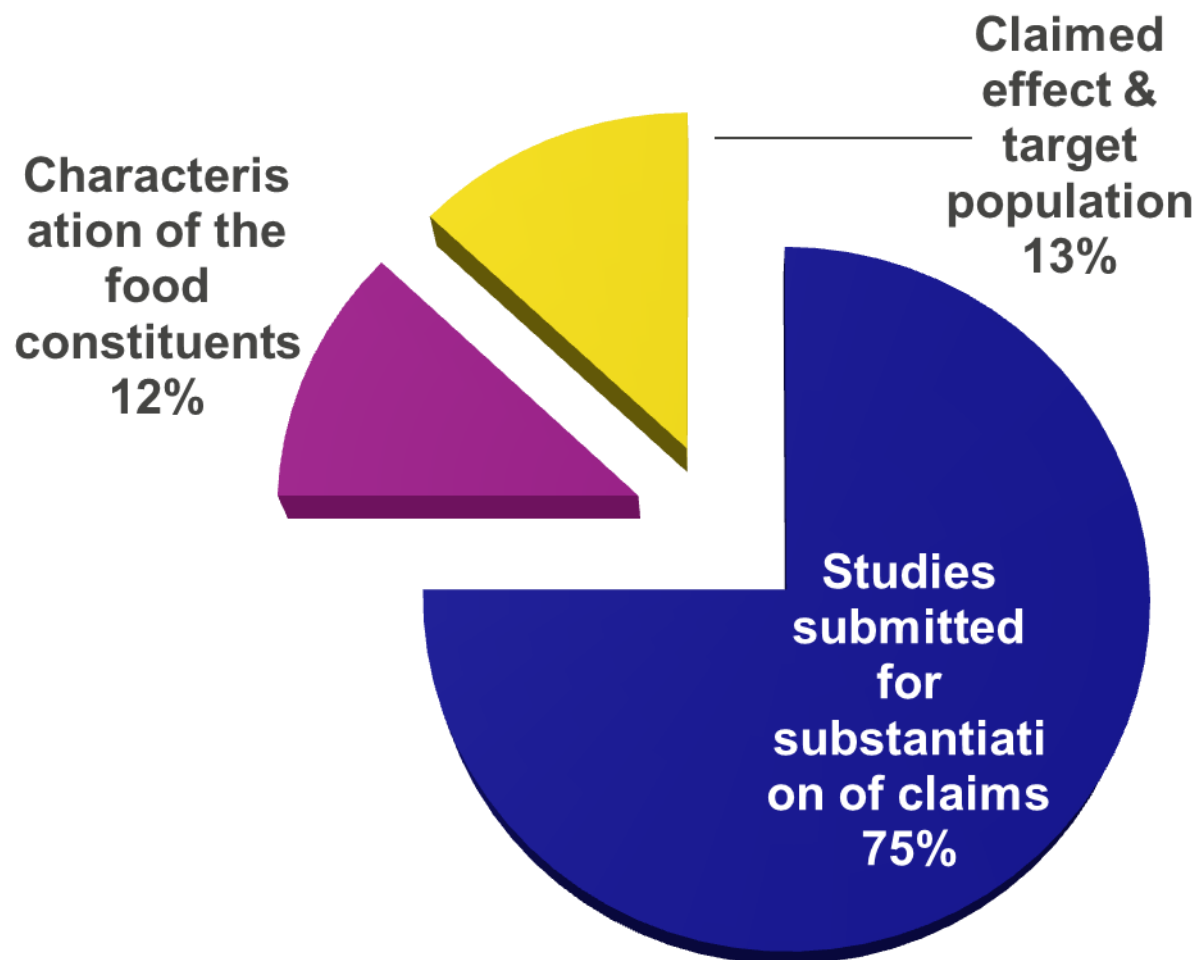


Reduction of a risk factor for infection

- **Risk factors well-established**
 - **Outcome: risk factor** (e.g. toxigenic *Clostridium difficile*/ toxins)
- **Less-well established risk factors**
 - IgA↓ and risk of respiratory tract infections
 - **Outcome: clinical + risk factor**

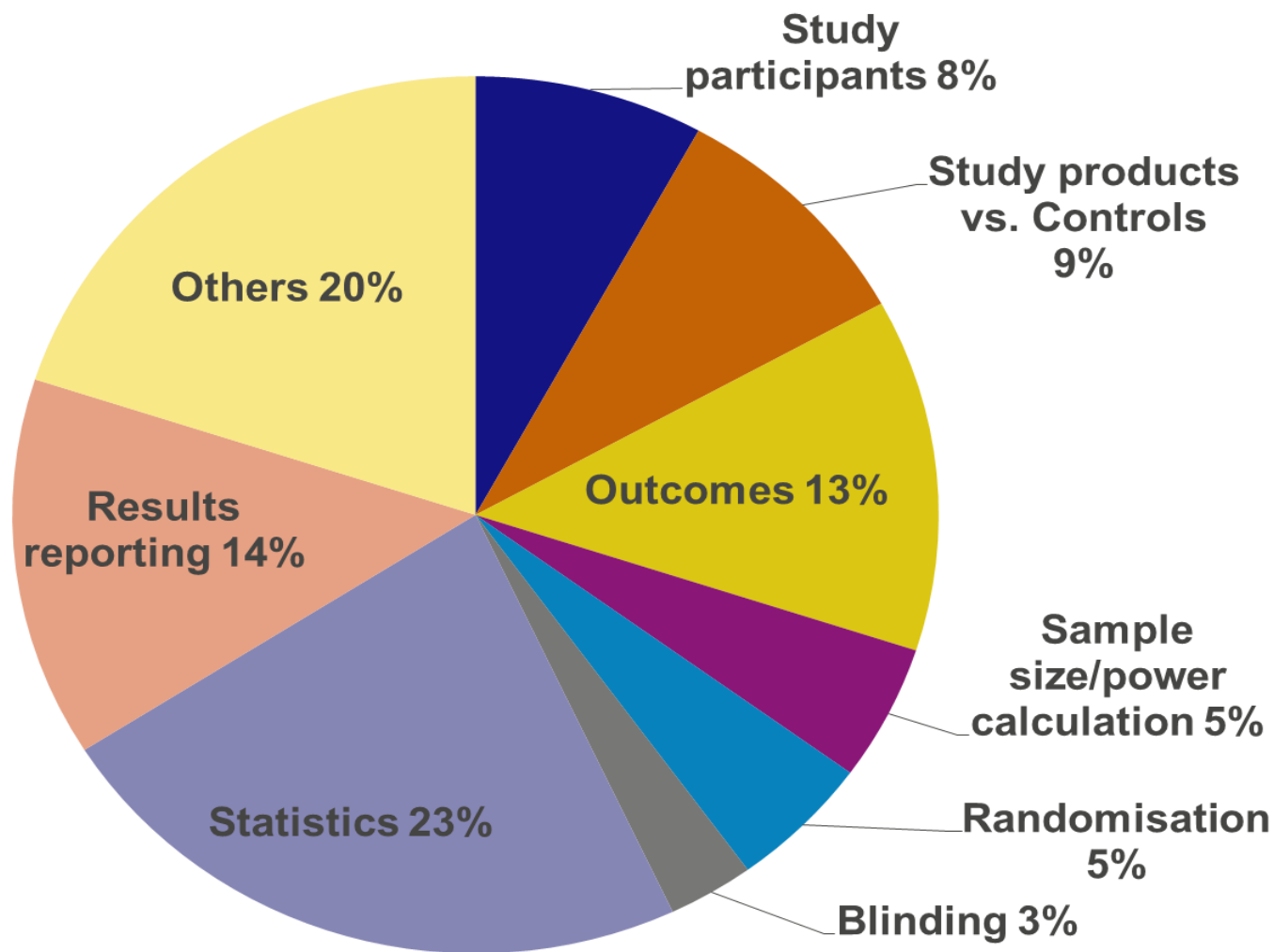


REASONS FOR CLOCK STOP=MAIN WEAKNESSES





QUESTIONS ON STUDIES SUBMITTED FOR SUBSTANTIATION



In summary

- EFSA guidance documents and scientific opinions on previous evaluations provide **scientific advice** and **illustrate shortcomings**.
- Each claim is unique. **Impossible to anticipate all possibilities** (claim effects, outcomes, methods) and **unfair to introduce constraints**.
- More important **understanding the rationale** of the principles applied than seeking for magic recipes.





Thank you!