Regulatory Challenges in the Development of Foods for Gut Health

*Regulatory Body Perspective*

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1. Introduction

2. Regulation on Probiotic

3. Premarket evaluation and post market control on probiotics in Indonesia

4. Opportunity and Challenge for Probiotic Development

5. Conclusion and recommendation
Introduction
Probiotics are live microorganisms, which when administered in adequate amounts confer a health benefit on the host.

FAO/WHO (2001)
PREREQUISITES OF A PROBIOTIC

• A probiotic must be alive when administered.
• A probiotic must have undergone controlled evaluation to document health benefits in the target host.
• A probiotic must be a taxonomically defined microbe or combination of microbes (genus, species and strain level)
• A probiotic must be safe for its intended use

a non-viable food component that confers a health benefit on the host associated with modulation of the microbiota

How to evaluate and substantiate that a product is a prebiotic

4.1. Product specification/characteristics of the prebiotic

4.2. Functionality

Substantiation of a claim should be based on studies with the final product type, tested in the target host.

4.3. Qualifications

Bifidogenic effects are not sufficient without demonstrated physiological health benefits

4.4. Safety

WORLD PROBIOTIC MARKET

- Functional food (56%)
- Food supplement (37%)
- Pharmacy (7%)

Source: UBIC Consulting (2009)
Consumer Buying Habits Change as Indonesia Welcomes a New Era
April 21, 2011
Venu Madhav, Executive Director of Client Leadership, Nielsen Indonesia

Nielsen observed three categories that experienced growth by answering the needs of the upper class: lifestyle, health and convenience.

Hair conditioners: By offering convenience with their leave-on product, manufacturers of hair conditioners saw value sales grow 68 percent in 2010. The “Leave On” variant offers practicality, though the price is more than twice of regular hair conditioner.

Liquid Milk: Sales grew 18 percent, with brands promoting health-related benefits such as low/non-fat, added calcium, probiotic qualities and kids nutrition.

Toothpaste: Although it is already purchased by nearly all households in Indonesia, the sales value for this category still recorded 10 percent growth, driven mainly by medicated segments which grew 17 percent in 2010. The new variants promise stronger teeth, sensitivity reduction, calcium, antibacterial, natural and herbal.

Nielsen Indonesia (2011)
In Brazil, 29.05% people defined probiotic foods correctly (n: 420 respondents)
R&D OF PROBIOTICS AND INDUSTRY INTERESTS

April 2011 – AHRQ Report released. Robust systematic review of randomized controlled trials (RCTs), specifically focused on the safety of probiotic interventions.

The report reviewed over 11,981 articles identified and 622 studies included on probiotics.

**CONCLUSION**

- Lack of assessment and systematic reporting of adverse events in probiotic intervention studies
- RCTs does not indicate an increased risk, but rare adverse events are difficult to assess.
Probiotic microorganisms for use in food should not only be capable of surviving passage through the digestive tract, but also have the capability to proliferate in the gut.

They must be resistant to gastric juices and be able to grow in the presence of bile under conditions in the intestines, or be consumed in a food vehicle that allows them to survive passage through the stomach and exposure to bile.

They are Gram positive bacteria and are included primarily in two genera, *Lactobacillus* and *Bifidobacterium* (Holzapfel et al., 1998; Klein et al., 1998).

The functionality test of probiotic microorganisms in the intestine to select the probiotic strains for human use.

Classification and identification of individual strains.

Defining and measuring the health benefits of probiotics. Examples of possible probiotic mechanisms of action, in the control of intestinal pathogens include: antimicrobial substance production; competitive exclusion of pathogen binding; competition for nutrients; modulation of the immune system. Appropriate experiments including genetic analysis to elucidate the mechanism of actions should be performed.

Safety consideration: Bacteria, which contain transmissible drug resistance genes, should not be used in foods.

2 REGULATION ON PROBIOTICS
Consumer Protection
- to ensure safety and efficacy
- to ensure that consumers are not misled by false, ambiguous, or misleading claims
- consumers could have clear and accurate information on food labels
  - enabling them to choose food properly

Ensure fair and responsible trade

Regulation Needed
Good Regulatory Practices

- Transparancy
- Having relevancy with science and technology development
- Alignment with international standards wherever possible

Considers also:
- the readiness of the government capacity, businesses, research institutes / conformity assessment bodies, consumer awareness and also effectively communicated
GLOBAL REGULATION

EU

• Food industry in EU made extensive use of probiotic microorganisms in the absence of regulations until 2005, except France and Denmark had regulation earlier.
• The EFSA adopted a generic approach to the safety assessment of microorganisms used in food/feed and the production of food/feed additives (The EFSA Journal. 2005. 226, 1-12).
• To date, none of the 164 claims of the benefits of probiotic or prebiotic products submitted to EFSA and reviewed by the Panel on Dietetic Products, Nutrition, and Allergies (NDA) have been accepted (British Journal of Nutrition, 2011).

USA

• Several of the bacteria used in the USA as probiotics are listed by the FDA on its "Partial List of Microorganisms and Microbial derived ingredients that are used in Foods".
• The usual approach for safety assessment for marketing probiotic bacteria in the USA is presumption of safety, reasoned by a long history of safety in fermented dairy products.

JAPAN

In Japan the FOSHU (Foods for Specified Health Use) category includes such nutraceutical ingredients as oligosaccharides, and lactic acid bacteria. Japan is the first country to introduce government-approved health claims.

The regulation strictness on probiotics: EU > USA > JAPAN
• Government regulations regarding safety assessment differ among countries, and the status of probiotics as a component in food is currently not established on an international basis

• Record and analyze adverse events associated with probiotics in food and monitor long-term health benefits?
Can I claim for probiotic food in Indonesia?

1. Yes you can, as long as following the FAO/WHO Guidelines for the Evaluation of Probiotics in Food (2002).
2. It will be assessed case by case basis
Industry can submit a proposal on probiotic claim to BPOM

Refer to: Guideline on EVALUATION OF PROBIOTIC IN FOOD PRODUCT

In the process of establishing of NADFC Head Decree
The Product shall fulfill the requirements:

- Genus, species and strain designation.
- Strain designation should not mislead consumers about the functionality of the strain.
- Minimum viable numbers of each probiotic strain at the end of the shelf-life.
- The suggested serving size must deliver the effective dose of probiotics related to the health claim.
- Health claim(s).
- Proper storage conditions.
- Corporate contact details for consumer information.
- Clinical trial of Indonesian people.
Final Draft Guideline EVALUATION OF PROBIOTIC IN FOOD PRODUCT

INDONESIA

NEW

Strain Specific Probiotic Identification

Functionality Characterization

Safety and Efficacy Evaluation
• Strain specific must survive the passage through the digestive tract and proliferate in the gut
• Labelling shall include the microbial species or strain and its viable concentration,
• Claims would have to be substantiated
• Named according to the International Code of Nomenclature; be deposited in an internationally recognised culture collection;
• Strain identification shall be performed by phenotypic tests followed by genetic identification
• Stock cultures shall be maintained under appropriate conditions and be checked periodically for strain identity and probiotic properties
• Efficacy shall be determined by clinical trials with accepted standards of scientific quality (well designed trials).

• Evidence based + confirmation in Indonesian Population

• Beneficial effects must be related to dosage regimens and duration of use of each individual product or strain;

• Safety considerations shall include transmission of antibiotic or drug resistance inherent in some probiotic microorganisms; the exclusion of Enterococcus strains as probiotic
**Final Draft Guideline EVALUATION OF PROBIOTIC IN FOOD PRODUCT**

**INDONESIA**

- **Strain identification and deposit strain in international culture collection**
- **Functional characterization**
  - in vitro
  - Animal study
- **Safety assessment**
  - in vitro/ animal study
  - Clinical trial Phase 1
- **Double blind, randomized, placebo-controlled (DBPC)**
  - phase 2 human trial or other appropriate design with sample size and primary outcome appropriate to determine if strain/product is efficacious
- **Second independent DBPC study to confirm results**
  - (evidence from other country)
- **Second independent DBPC study to confirm results**
  - (Indonesian population)
- **Phase 3, effectiveness trial is appropriate to compare probiotics with standard treatment of a specific condition**
  - (Indonesian population preferred)

**PROBIOTIC FOOD**

**Labeling**
- Contents – genus, species, strain designation;
- Minimum numbers of viable bacteria at end of shelf-life;
- Proper storage conditions;
- Corporate contact details for consumer information.

**Scheme for evaluation of PROBIOTIC IN FOOD PRODUCT**

3 Premarket evaluation and post market control on probiotics in Indonesia
Application by food producer / importer / distributor

Registration approval

PRE MARKET EVALUATION

YES  NO

REJECTION / SUSPENSION DUE TO:

- Lack of scientific evidence on human study.
- Substantiation of a claim should be based on studies with the final product type.
- Inappropriate scientific evidence as proposed claim, e.g. the study was not carried out in the target group claim.
- Multi-strain probiotics: Lack of data on the assessment of safety, interaction, and efficacy.
- Probiotic information of genus, species and strain is lacking, Live microorganism (spore??tyndallization
- No instruction how to store the product
- inappropriate label, etc.

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LAB-BASED FOODS

DATA OF REGISTERED LACTIC ACID BACTERIA-BASED FOODS AND PROBIOTIC FOODS IN INDONESIA*

- LAB-based foods are dominated by yogurt and only ± 10% probiotic food.
- Probiotic foods are dominated by Growing Up Milks.
- Food products produced in Indonesia (MD) are not necessarily national company.
POST MARKET CONTROL

- Food sampling and testing in distribution channels
- Inspection in production and distribution channels

FOOD SAFETY, QUALITY, EFFICACY AND LABEL CONTROL

TRADITIONAL MARKET

RETAILER

DISTRIBUTOR FACILITY

MODERN MARKET

PRODUCTION FACILITY (MD)
POST MARKET FINDINGS NOT COMPLYING WITH REGULATION

• Some producers did not maintain Good Manufacturing Practices (GMP)
• Poor handling practices during storage and retailing
• Over health claim labels
• Different labels with the registration approval documents
• Inappropriate advertisement
• Expired food products
• Broken / damaged / spoiled products
4 Opportunity and Challenge for Probiotic Development
• SEA as one of the mega biodiversity regions, rich in genetic resources and traditional fermented foods should have a great opportunity to develop probiotics through innovation.

• Only a few companies have the capacity to develop probiotics, such as the ability to reach functionality and probiotic stability.

• Call for probiotic innovation via strong collaboration between Industry, academician and regulator.
1. Strengthen ABG (Acadimician, Business and Governemnet) partnership to develop probiotic product innovation in Indonesia.
2. Remember the definition of probiotics as live microorganisms which when administered in adequate amounts confer a health benefit on the host. Call for development of methods (in vitro and in vivo) to evaluate the functionality and safety of probiotics.
3. Follow the guidelines provided as a prerequisite for the development of strain probiotics.
4. Follow regulatory framework to allow specific health claims on probiotic food labels in cases where scientific evidence exists.
5. Good manufacturing practices (GMP) must be applied in the manufacture of probiotic foods with quality assurance, and shelf-life conditions established.
6. Trial guidelines for GLP, GCP and GMP should be in place when developing probiotics for therapeutic use and health claim.
5 CONCLUSION AND RECOMMENDATION
**CONCLUSION**

1. Probiotics have received extensive attention from public, business and research communities due to potential benefits in health sectors.

2. National Agency for Drug and Food Control (NADFC /Badan POM) provides attention to safeguard the safety, quality, efficacy and label of the probiotic products marketed in Indonesia.

3. Probiotic Foods marketed in Indonesia are mostly manufactured in Indonesia (MD), but they are produced under international licensed, probiotic strains / technology from the mother company.
Academician, Business and Government (ABG) should strengthen interactive communication for the development of probiotics in Indonesia.

Growing public interest in probiotics calls for appropriate regulatory and policy action. BPOM / NADFC welcomes academician, business, and public community to discuss regarding the development of probiotics and novel function of lactic acid bacteria in Indonesia.

Academician and business communities should follow regulation and its guidance in early stage of development of probiotics in Indonesia to meet the requirement for product safety, quality, efficacy, and label claim.
The discussion of probiotic development should cover science, medical, consumer, commercial, and regulatory communities on how such benefits can be identified, substantiated, and effectively communicated.
Terima Kasih

Thank You