

**Best Practices  
for  
Ethical Conduct  
of  
Human Intervention  
Studies  
for**

*Novel Food/Ingredients/  
Processes/ Technology /  
Claim  
Substantiation*



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**International Life Sciences Institute India  
Knowledge Centre on Functional Foods, Immunity and Gut Health**





## **PREFACE**

There has been greater focus on building health and immunity through food based approaches in recent times. The rising incidence of non-communicable diseases and Covid-19 pandemic – its occurrence and reoccurrence- has further underlined the importance of healthy diet along with appropriate lifestyle. The concept of “Food is Medicine” is gaining ground and is popular among consumers.

ILSI India **Knowledge Centre on Functional Foods, Gut Health and Immunity (K-FFIG)** has been devoting attention to critical issues in nutrition including functional foods such as probiotics and prebiotics and nutraceuticals which require further studies, research and investigation. It has also been looking at how the benefits associated with scientific findings can be translated into strategies to improve public health at country, regional and global levels.

Clinical Trials for food and food ingredients has been identified as one important area requiring attention of scientific community as well as concerned authorities. It acquires significance as with technological advancements a number of new products with a variety of claims have been introduced in the market by the Food Business Operators (FBOs) to fulfill the aspirations of health conscious consumers. These are called by various names - Dietary Supplements, Functional Foods or Nutraceuticals. The process for substantiation of claims have yet to evolve.

K-FFIG had organized a **Seminar entitled “Clinical Evaluation/Intervention Studies for New Foods & Food Ingredients-Current Status and Way Forward” in New Delhi on May 29** to discuss the need for conducting clinical evaluation/intervention studies for new foods and food ingredients, the current process and to debate on whether separate set of Guidelines have to be developed for conducting such clinical evaluation/intervention studies. The Seminar was addressed by leading experts in this area including ILSI India Chairman Dr. B K Nandi and Dr. D Kanungo, Former Additional Director General, Ministry of Health and Family Welfare, Government of India.

It was pointed out by experts at the Seminar that while country has an effective mechanism for Clinical Trials for Drugs under “New Drugs and Clinical Trials Rules, 2019”, the fast pace at which food sector is developing and new products launched and new food ingredients used, it has now become imperative that a Standard Operating Protocol (SOP)/guidelines be laid down for conducting “Human Intervention Studies for Food and Food Ingredients” including the nutrients as such but not limited to vitamins, minerals, amino acids, botanical extracts, herbs, spices, spice oleoresins and bioactive substances. Foods are part of everyday life and Food Trials are designed closer to “real-life” situations than typical Drug Trials,

which need to be highly controlled. Therefore, “Human Intervention Studies for Food and Food Ingredients including Nutrients” must be designed to capture their multifunctionality.

Number of suggestions were made by the experts and it was recommended that K-FFIG should prepare a Concept Paper. The Concept Paper has been prepared and has been reviewed several times by the experts. I am grateful to all of them for their inputs on the draft of the Concept Paper authored by me.

I would like to mention that the issue of what should be the nomenclature for Food Trials i.e. whether it should be Clinical Trials or Human Intervention Studies was debated intensely and majority of experts recommended that since “Food Trials” are quite different, in a number of ways, from Drugs Trials a different approach and nomenclature has to be adopted, hence the nomenclature “Human Intervention Studies” has been used.

It is hoped that Concept Paper will be useful to the stakeholders and the concerned authorities will take steps to come out with Guidelines (Best Practices) for Ethical Conduct of Human Intervention Studies for Novel Food / Ingredients / Processes / Technology / Claim Substantiation.



**Dr. B. Sesikeran**  
**Chairman, K-FFIG**

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## **PREAMBLE**



The National Institute of Health's (NIH)-definition of **Clinical Trials** is - A research study in which one or more human participants are prospectively assigned to one or more interventions (which may include a Placebo or other Control) to evaluate the effects of those interventions on health -related biomedical or behavioral outcomes.

**“National Ethical Guidelines for Biomedical and Health Research involving Human Participants” published by Indian Council of Medical Research (ICMR) in 2017 mentions the scope as follows:**

“The purpose of such research should be:

- i. directed towards enhancing knowledge about the human condition while maintaining sensitivity to the Indian cultural, social and natural environment;
- ii. conducted under conditions such that no person or persons become mere means for the betterment of others and that human beings who are participating in any biomedical and/or health research or scientific experimentation are dealt with in a manner conducive to and consistent with their dignity and well-being, under conditions of professional fair treatment and transparency; and
- iii. subjected to a regime of evaluation at all stages of the research, such as design, conduct and reporting of the results thereof.”

**New Drugs and Clinical Trials Rules (NDCT), 2019 was notified by the Central Drugs Standard Control Organization, Ministry of Health and Family Welfare (CDSCO, MoHFW). These rules and regulations were intended and applicable to research as well as regulatory studies where the test material is a DRUG as defined in the Drugs and Cosmetics Act, 1940.**

**“[(b) —As per Drugs and Cosmetics Act (DCA), Drug includes:**

- (i) all medicines for internal or external use of human beings or animals and all substances intended to be used for or in the diagnosis, treatment, mitigation or prevention of any disease or disorder in human beings or animals, including preparations applied on human body for the purpose of repelling insects like mosquitoes];
- (ii) such substances (other than food) intended to affect the structure or any function of the human body or intended to be used for the destruction of [vermin] or insects which cause disease in human beings or animals, as may be specified from time to time by the Central Government by notification in the Official Gazette];
- (iii) all substances intended for use as components of a drug including empty gelatine capsules;] and

(iv) such devices\* intended for internal or external use in the diagnosis, treatment, mitigation or prevention of disease or disorder in human beings or animals, as may be specified from time to time by the Central Government by notification in the Official Gazette, after consultation with the Board]”

**By these definitions, a Food shall be anything that does not fall within the above definition of a Drug.** Furthermore, the categories of foods that are defined as Foods for Special Medical Purposes and Foods for Special Dietary Uses (FSMP and FSDU) also do not fall under the definition of a Drug.

**The Food Safety and Standards Authority of India's (FSSAI) definitions of Food and Food Additives as given in Food Safety and Standards Act, 2006:**

**(j) “Food”** means any substance, whether processed, partially processed or unprocessed, which is intended for human consumption and includes primary food to the extent defined in clause (zk), genetically modified or engineered food or food containing such ingredients, infant food, packaged drinking water, alcoholic drink, chewing gum, and any substance, including water used into the food during its manufacture, preparation or treatment but does not include any animal feed, live animals unless they are prepared or processed for placing on the market for human consumption, plants, prior to harvesting, drugs and medicinal products, cosmetics, narcotic or psychotropic substances:

Provided that the Central Government may declare, by notification in the Official Gazette, any other article as food for the purposes of this Act having regards to its use, nature, substance or quality;

**(k) “Food Additive”** means any substance not normally consumed as a food by itself or used as a typical ingredient of the food, whether or not it has nutritive value, the intentional addition of which to food for a technological (including organoleptic) purpose in the manufacture, processing, preparation, treatment, packing, packaging, transport or holding of such food results, or may be reasonably expected to result (directly or indirectly), in it or its by-products becoming a component of or otherwise affecting the characteristics of such food but does not include “contaminants” or substances added to food for maintaining or improving nutritional qualities.

**The scope of this CONCEPT PAPER is to consolidate the validated approach for conducting Human Intervention Studies {though technically they are also Clinical Trials (CT), considering that CT is a term most often denoting drug trials and since FOOD and DRUG are differentiated in both the Drug as well as the Food Acts , this document uses the terminology HUMAN INTERVENTION STUDIES} using food and the potential guidance / scientific inputs needed for conducting such studies.**

## I - INTRODUCTION

ILSI India has been discussing this issue in its Scientific Advisory Committee; and K-FFIG (Knowledge Center on Functional Foods, Immunity and Gut Health) Governing Council has been deliberating on the need for preparing guidelines for conducting “**Human Intervention Studies for Food and/or Food Ingredient**” as the case may be. The need arises, due to technological advancements besides discovery and designing of new food matrix. Now a days many products are available in the markets with various claims about their health benefits for health-conscious consumers. It is recognized that there should be a system for:

- Validating claimed benefits at the recommended consumption frequency of the food and/or food ingredient,
- How food, food ingredient impacts the health including both benefits and risks to human health,
- What type of claims can be made; and
- How these claims should be substantiated?

In view of the fast progress in food sector it has now become imperative that a **Standard Operating Protocol (SOP)/Guidelines** be laid down for conducting **Human Intervention Studies** for food and food ingredients including the nutrients as such but not limited to vitamins, minerals, amino acids, botanical extracts, herbs, spices, spice oleoresins and bioactive substances. Foods are part of everyday life and food trials are designed closer to “real-life” situations than typical drug trials, which need to be highly controlled. Therefore, **Human Intervention Studies** for food and food ingredients including nutrients must be designed to capture their multifunctionality.

### Figure 1

#### *Possible Indications to conduct Human Intervention Studies on foods and food ingredients*

- FBO (Food Business Operator) intends to market food or food ingredient with claimed benefits and seeks regulatory approval from authorities.
- The Food or Food Ingredient with history of proven efficacy over 30 years but in another country.
- A Novel Food or ingredient with evidence of safety and efficacy mentioned in traditional literature but may not be applicable to the benefits claimed. For example, Brahmi (*Bacopa monneiri*) may qualify for cognition and memory related benefits as per Ayurvedic scriptures, but any benefit not mentioned there would warrant an independent human intervention study.
- FSDU or FSMP for efficacy or claim.



### Figure 2

#### *Conditions where no Human Intervention Studies may be needed*

- A Food and/or Food Ingredients with history of safe use of at least 15 years in India and no product efficacy claim being made.
- A Food and/or Food Ingredients with sufficient data available in traditional literature and prepared as per traditional methods.
- A Food and/or Food Ingredient where only the content claim is being made where relevant adequate scientific publications are available for substantiation.

**The existing FSSAI Regulations require data on Safety and Efficacy as well as Claims made on Product or Ingredients or Nutrients.**

- 1. Food Safety and Standards (Approval for Non-Specified Foods and Food Ingredients) Regulation 2017**, wherein the manufacturer or importer of Non-Specified food has to submit an application in Form I. Information on the target population, data on safety and efficacy from human studies, Toxicology as well as allergenicity data is required. This applies to novel foods, ingredients/additives, technology, processing methods like new enzymes.
- 2. Food Safety and Standards (Advertisements and Claims) Regulations 2018**, where a claimed benefit is attributed directly to the product or used on labels, advertisement or any other mode of communication, the regulation requires scientifically generated data using well-designed scientifically acceptable methods, conducted by or under guidance of a reputed or well established research institution etc.

**Data on properly conducted studies published in peer reviewed journals are necessary to ensure compliance with regulations.** There is lack of guidance to carry out such studies. It is imperative that Guidelines for conducting **Human Intervention Studies on Food and Food Ingredients** be developed. FSSAI may provide Guidelines similar to New Drugs and Clinical Trials (NDCT) Guidelines of Central Drugs Standard Control Organization (CDSCO). However, there are differences between drugs and foods as given in Table 1.



**Table 1**  
**Differences between Clinical Trials for Foods and Drugs**

<b>Food Human Intervention Studies</b>	<b>Drug Clinical Trials</b>
Designed to evaluate specific marketing claims.	Document the safety and efficacy of a specific drug for a specific intended use .
Tend to be more pragmatic and exploratory as they document human experiences with specific foods in the context of the human diet.	Tend to be more explanatory as they document specific drug doses and schedules for response in and specific diseases.
Typically enroll healthy individuals. Food trials may not have a standard of care group like for drugs.	Only in phase I healthy individuals are enrolled. In case of toxic drugs patients with a specific disease type potentially needing research / treatment are enrolled.
Foods are complex mixtures of ingredients (e.g., plant parts, meats, eggs, chemicals, beverages, whole meals, etc.) designed to be palatable and which may have the general health effect under investigation.	Drugs are synthetic or herb based highly purified products and designed to have specific effects on a disease.
Food studies may find it difficult to use placebos due to taste and flavour .	Placebos or standard of care or another drug or dose need to be used as reference group or comparator.
Human studies with foods most often have a very small risk (Less than minimal) compared with drug trials.	
Human studies on bioactive substances will be very similar to drug trials.	

**A Guidance Document containing the Standard Operating Procedures, that clearly lays down the processes, pre requisites, design, statistics as well as limitations, quality control etc. would be beneficial to the following stake holders:**

- Food Business Operators (FBO)
- Contact Research Organization (CRO)
- Participant: Volunteers who take part in the Human Intervention studies.
- Investigators: A researcher who helps conduct the Human Intervention Studies — A researcher could be a qualified professional from any field but one of the investigators should be a qualified health care professional, another a nutritionist and a statistician.
- Study Coordinator: Works with investigator to manage the human intervention studies —such as a nurse, nutritionist, food technology expert, junior researcher, or clinical research coordinator, employed for the purpose.
- Ethics Committees
- Sponsors
- Regulatory Agencies
- Consumer Advocacy Groups
- Public

## II- SUGGESTED GUIDELINES

**The Guidelines for conducting Human Intervention Studies are being suggested against the following background:**

1. Foods or ingredients that are not yet included in the approved standards and are novel need to follow the FSSAI regulations for Non Specified Food (NSF), 2017 .
2. FSMP and FSDU categories of NSF category shall follow the appropriate regulations and guidance documents notified by the FSSAI subsequent to the above.
3. All Guidelines notified under Nutraceutical, Advertisement and Claims Regulations should be followed and complied with (Food Safety and Standards (Health Supplements, Nutraceuticals, Food for Special Dietary Use, Food for Special Medical Purpose, Functional Food and Novel Food) Regulations, 2016 and Food Safety and Standards (Advertising and Claims) Regulation, 2018).
4. Prior approval to conduct a study from the regulatory authority may not be made mandatory for all studies, however, FSSAI may makes it a prerequisite on case to case basis taking into consideration chemistry, mode of action vis-vis the proposed claim and develop suitable guidelines and exemptions.

### **Why Conduct Human Intervention Studies?**

**There are several reasons for the conducting Human Intervention Studies including the following:**

- New Ingredient or Food coming under NSF category,
- An approved Food or Ingredient falling under FSMP or FSDU category to demonstrate the efficacy and safety,
- An approved Food or Ingredient using a new process or processing aid,
- A traditional Food using a Novel Non-Traditional method for purpose of safety and /or efficacy,
- Any Food or Ingredient or nutrient approved by the FSSAI or in the existing standards/schedules but with intent of generating efficacy data to make a novel label claim.

**It may be noted that,** research studies on approved products intended for purposes of advancement of knowledge with no regulatory intent like a label claim etc. may not require FSSAI approvals but shall follow procedures as per standard research studies with due approvals from the respective Ethics Committees and other research management procedures as per ICMR/DHR guidelines as applicable.

Evidence generated through such research studies and published in standard peer reviewed journals could be submitted subsequently if the FBO wants to make a label claim through appropriate procedures to the FSSAI. A claim cannot be made based on published research

studies without the acceptance of the data and approval of the claim by FSSAI. The distinct advantage of a pre-approval is the same as followed by CDSCO where the entire study protocol, its progress and the final report are guided by the regulator and hence monitored. All novel products and novel ingredients must seek approval of the FSSAI with adequate pre-clinical safety data as well as human data if available from other countries before getting approval to conduct a **Human Intervention Trial**.

### **Protocol for Conducting Human Intervention Studies**

**It is important to develop a protocol for conducting Human Intervention Studies.** The following components need to be spelt out.

1. Study Design
2. Procedure for Selection of Participants (Sampling)
3. Approval of the Ethics Committee
4. Approval of Heads of Participating Institutions
5. Registration in the Clinical Trial Registry
6. Protocol for Data Management and Analysis

**The types of Human Studies include:**

- Proof of Concept / Pilot Studies
- Non-Inferiority Study
- Bioequivalence/ Bioavailability Study
- Case Control
- Cross-sectional Studies
- Randomized or Non-Randomized Trials
- Blinded or open Label Trials

Declaration of “No Conflict of Interest” by the investigators and the CRO / FBO is important to ensure independence of the conduct of the study.

**Note:** Though FSSAI or the reviewers or all those who have access to the study protocol shall declare their confidentiality agreements, the trial information will be in public domain through the registry. While product formulations may be unique to the developer, the study protocols may be generic or standard methods.

### **Important Considerations for Conducting Human Intervention Studies**

#### **• Pre-Clinical Data:**

- I. Data from pre-clinical studies conducted in any GLP accredited laboratory as per New Drugs and Clinical Trial Rules (2023) India / Organisation for Economic Cooperation and Development (OECD) Guidelines in any country will be acceptable and need not be repeated in India unless the outcomes are not relevant to the application.

- II. If studies are done in India it should have been carried out in a GLP accredited facility as per OECD guidelines and all analytical methods should be acceptable if approved by Association of Analytical Chemists (AOAC) or published in any reputed journal or done by FSSAI-NABL approved or accredited laboratories.
- III. Compositional equivalence / Bio equivalence / Bioavailability / Comparative trials with effective markers or proof of concept in vitro / in vivo or human volunteer studies should also follow above mentioned norms for acceptance of data by the FSSAI. **Human Intervention Studies** need to be done by accredited CROs or any hospital/research facility that follow **Good Clinical Practices (GCP)** as well as ICMR Ethical Guidelines or facilities acceptable to the CDSCO Guidelines.

**\* Personalised Nutrition:**

In recent years there is a lot of interest in developing foods and combination of nutrients for individuals based on their genetic/ metabolic profiles. Such studies or claims thereof shall not be regulated by the FSSAI so long as the components of such diets have been already approved by the regulator.

**\* Extension of An Approved Claim for Another Formulation/ Product:**

A claim approved for a specific product formulation that was used for the **Human Intervention Studies** will be applicable as a label claim ONLY for the product that continues to have the same formulation. When changes are made to the formulation, the FBO should reapply to the FSSAI providing all information on the changes and justifying the need to continue using the same claim that was approved earlier on a different formulation now.

**\* Post Marketing Studies :**

FSSAI may decide the need to carry out post approval studies for marketing a novel ingredient or food in case either history of safe use is not available from any other country or there is adequate reason to believe that some individuals could be allergic or intolerant to the ingredient.

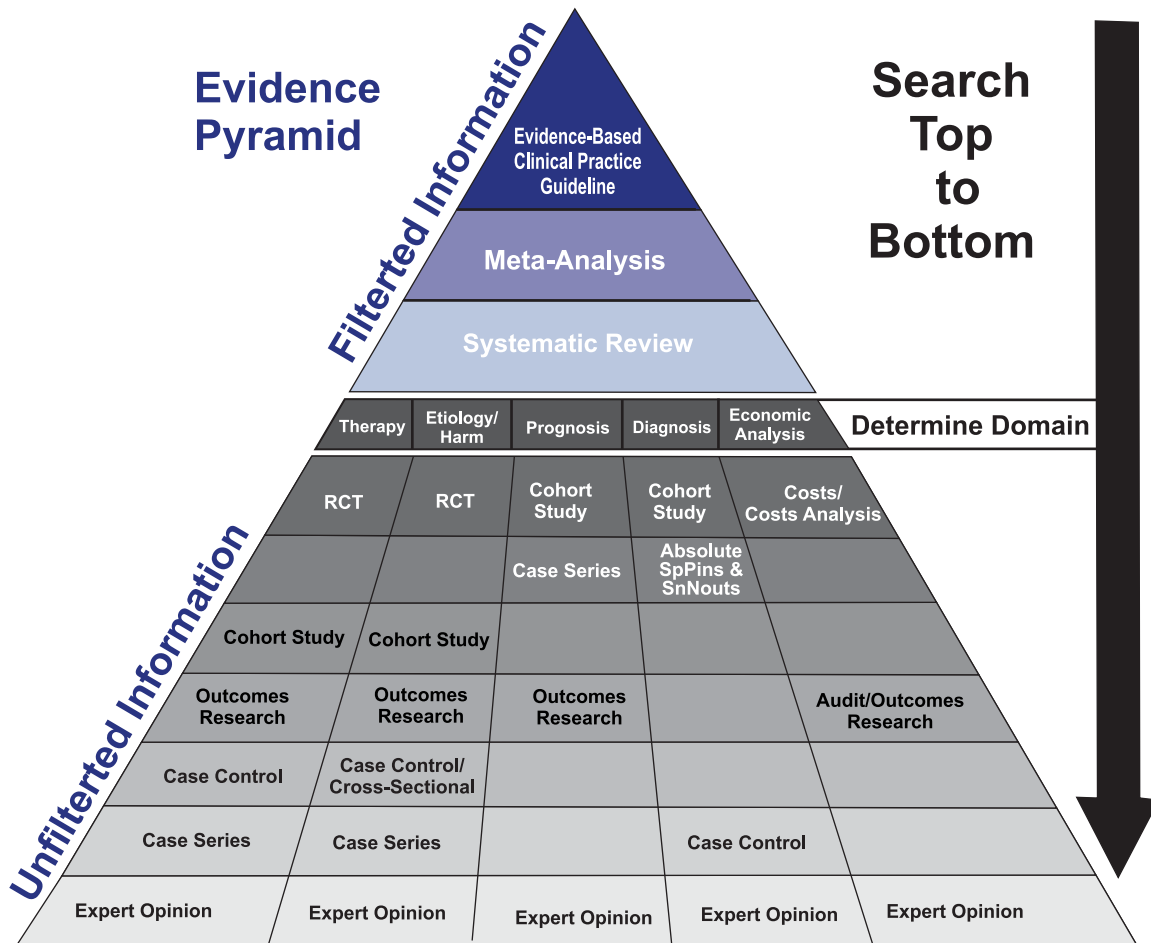
**\* Published Research Articles as Evidence for Claims:**

Published information from reputed and internationally or nationally accepted Journals or traditional texts can be used as evidence for either making an ingredient or content claim or a product claim. FSSAI shall review the data through a panel of experts and either approve / disapprove / allow a modified claim. If the FBO intends to further strengthen the claim through a well-planned study, they may do so following the procedures laid down for the conduct of a **Human Intervention Studies**.

**\* Other Sources of Evidence for Safety as well as Claims:**

Systematic Reviews, Meta-Analysis, Cochrane Reviews and Commissioned Reviews by FSSAI / FBO could be used as scientific evidence other than published outcomes of **Human Intervention Studies**. The best evidence of history of safe use can be from WHO/FAO/JECFA/ CODEX and such international agencies which review and evaluate safety and efficacy data based on international best practices and published peer reviewed data. Such data are also updated from time to time and can circumvent the need to redo **Human Intervention Studies**. Figure 3 depicts how Systematic Reviews and Meta-Analysis are considered to be at the top of the evidence pyramid providing data with the least risk of bias.

Figure 3 : Levels of Evidence



Source: Level of Evidence, Evidence based practice toolkit- Research Hub at Winona State University. <https://libguides.winona.edu/ebptoolkit/Levels-Evidence>



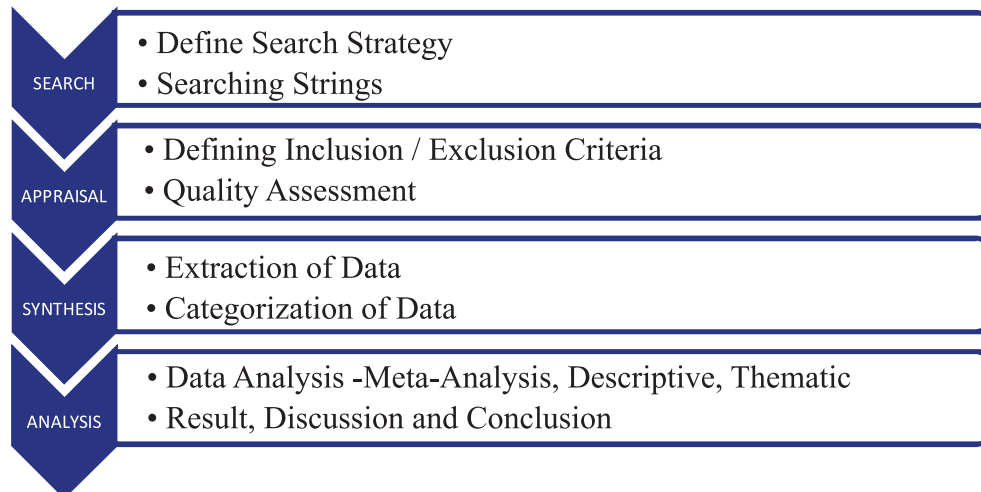
## Types of Frameworks and Formats for Systematic Reviews:

- PRISMA is a minimum set of items which primarily focuses on the reporting of reviews evaluating the effects of interventions, but can also be used as a basis for reporting Systematic Reviews with objectives other than evaluating interventions (e.g. evaluating aetiology, prevalence, diagnosis or prognosis).
- The PICO (Population, Intervention, Comparison and Outcomes) format is commonly used in evidence-based clinical practice. This format creates a "well-built" question that identifies four concepts: (1) the Patient problem or Population, (2) the Intervention, (3) the Comparison (if there is one), and (4) the Outcome(s).

The PICO tool focuses on the Population, Intervention, Comparison and Outcomes of a (usually quantitative) article. It is commonly used to identify components of clinical evidence for systematic reviews in evidence based medicine and is endorsed by the Cochrane Collaboration.

- PEO (Population, Exposure, Outcome) is also used in health research to help identify the key concepts of a topic and structure the literature.
- Figure 4 presents the SALSA framework which is often used for conducting the review of literature.

**Figure 4: SALSA Framework**



Source: Maria J. Grant and Andrew Booth. A Typology Of Reviews:

An Analysis Of 14 Review Types And Associated Methodologies. Health Information And Libraries Journal, Volume26, Issue2, June 2009, Pages 91-108. <https://doi.org/10.1111/j.1471-1842.2009.00848.x>

### \* **Cochrane Reviews:**

- Systematic Reviews seek to collate evidence that fits pre-specified eligibility criteria in order to answer a specific research question. They aim to minimize bias by using explicit, systematic methods documented in advance with a protocol.

- Cochrane prepares, maintains and promotes Systematic Reviews (Cochrane Reviews) to inform decisions about health and social care.
- Cochrane Reviews are published in the Cochrane Database of Systematic Reviews in the Cochrane Library.
- The Cochrane Handbook for Systematic Reviews of Interventions contains methodological guidance for the preparation and maintenance of Cochrane Reviews on the effects of interventions.

\* **Databases to Search:**

- Google Scholar
- Science Direct
- Scopus
- Ovid Medline,
- Embase
- Cochrane CENTRAL
- Cochrane Database of Systematic Reviews
- PROSPERO for Prospective Reviews

### **III- CONCLUSIONS AND WAY FORWARD**

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1. **FSSAI** with help of experts from Food and Nutrition sectors shall notify a **broad set of guidelines** to be followed by applicants who intend conducting a Human Intervention Study on a novel food or ingredient or an approved or standardised food to make a product or ingredient claim. May be called **FSSAI guidelines for ethical conduct of Human Intervention Studies for Novel Food / Ingredients / Processes / Technology / Claim Substantiation**.
2. **Templates for such applications** that include the background of test material, reason for doing the study, detailed protocol; etc. to be prepared.  
  
Templates for data submission may also be prepared for purposes of data review to approve a claim without actually conducting a trial.
3. **For facilitation of FBOs for preparation of application as well as experts in FSSAI to take appropriate decision**, a decision tree approach may be devised. This will exhibit transparency in the ecosystem.
4. **A Committee** to oversee the applications, discuss and approve the protocol with the FBO, review the data and recommend a claim or give approval for a new food through the respective scientific panels.
5. **Subject experts** in Ayurveda, Food Science, Nutrition & Dietary Principles, Basic scientists , Risk Assessment experts, Information technologists when Artificial Intelligence (AI) is being used, statisticians or any clinical speciality may be co -opted into the Committee .
6. **Accreditation of CROs / FBOs equipped with** for human intervention studies to be initiated with GCP, GLP, NABL, ICMR linkages.
7. **CTRI** can create a separate sub registry for Food regulatory studies.
8. **Training programs** for all stakeholders through FSSAI for Human Intervention Studies using Food / Food Ingredient.
9. **Study monitors** to be trained and accredited by FSSAI or can be undertaken through NABH assessors.



## GLOSSARY

- **Clinical Trail:** According to Central Drugs Standard Control Organization, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India a “clinical trial” in relation to a new drug or investigational new drug means any systematic study of such new drug or investigational new drug in human subjects to generate data for discovering or verifying its,

  - (i) clinical or;
  - (ii) pharmacological including pharmacodynamics, pharmacokinetics or;
  - (iii) adverse effects,

with the objective of determining the safety, efficacy or tolerance of such new drug or investigational new drug.

*Reference: Central Drugs Standard Control Organization, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India, [https://cdsco.gov.in/opencms/reReferences/UploadCDSCOWeb/2018/UploadPublic\\_NoticesFiles/faqnd.pdf](https://cdsco.gov.in/opencms/reReferences/UploadCDSCOWeb/2018/UploadPublic_NoticesFiles/faqnd.pdf)*
- **According to US FDA Clinical Trials,** also known as clinical studies, test potential treatments in human volunteers to see whether they should be approved for wider use in the general population. A treatment could be a drug, medical device, or biologic, such as a vaccine, blood product, or gene therapy. Potential treatments, however, must be studied in laboratory animals first to determine potential toxicity before they can be tried in people. Treatments having acceptable safety profiles and showing the most promise are then moved into clinical trials.

*Reference: U.S. Food and Drug Administration, <https://www.fda.gov/drugs/information-consumers-and-patients-drugs/inside-clinical-trials-testing-medical-products-people>*
- **What is Clinical Research / Study / Trial?**  
According to Indian Council of Medical Research Clinical Research/ Study/ Trial can be defined as:

  - o Clinical research/study/trial test capability of treatments in human volunteers or patients to see whether they should be further investigated or commercially used in general population.
  - o A treatment could be a drug (medicine), medical device, or a stem cells, vaccine, blood product, or gene therapy.

It must be noted that participants of a clinical trials can't be charged for the trial treatment they are getting.

*Reference: Indian Council of Medical Research, [https://main.icmr.nic.in/sites/default/files/upload\\_documents/clinical\\_eng.pdf](https://main.icmr.nic.in/sites/default/files/upload_documents/clinical_eng.pdf)*
- **Food:** Food is defined under the Food Safety and Standards Act, 2006 (34 of 2006) and Regulations. “Food” means any substance, whether processed, partially processed or unprocessed, which is intended for human consumption and includes primary food to the extent defined in clause (zk), genetically modified or engineered food or food containing such ingredients, infant food, packaged drinking water, alcoholic drink, chewing gum, and any substance, including water used into the food during its manufacture, preparation or treatment but does not include any animal feed, live animals unless they are prepared or processed for placing on the market for human consumption, plants, prior to harvesting, drugs and medicinal products, cosmetics, narcotic or psychotropic substances.

*Reference: Food Safety and Standards Act, 2006, <https://fssai.gov.in/cms/food-safety-and-standards-act-2006.php>*
- **Ingredients:** “Ingredient” means any substance, including a food additive used in the manufacture or preparation of food and present in the final product, possibly in a modified form.

*Reference: Food Safety and Standards Act, 2006, <https://fssai.gov.in/cms/food-safety-and-standards-act-2006.php>*
- **Nutrient Bioavailability:** Nutrient bioavailability is defined as the fraction of a nutrient in a food that is absorbed and utilized.

*Reference: Encyclopedia of Human Nutrition (Second Edition), 2005, Science Direct. <https://www.sciencedirect.com/topics/medicine-and-dentistry/nutrient-bioavailability>*

- **Bioequivalence (BE)** is a term used in pharmacokinetics when there are two or more medicinal products (proprietary preparations of a drug), containing the same active substance that need to be compared in vivo for biological equivalence. These comparative studies are used to assess if the new version (generic) produces the same concentration in the systemic circulation when given to human participants. If two products are said to be bioequivalent it means that they would be expected to be, for all intents and purposes, the same.

BE studies are used as surrogates for clinical effectiveness data for generic drugs where no clinical difference is anticipated between the two products. **It may be applicable when bioactive molecules in foods are being compared for efficacy.**

*Reference: Indian Council of Medical Research National Ethical Guidelines for Biomedical and Health Research Involving Human Participants.*

[https://ethics.ncdirindia.org/asset/pdf/ICMR\\_National\\_Ethical\\_Guidelines.pdf](https://ethics.ncdirindia.org/asset/pdf/ICMR_National_Ethical_Guidelines.pdf)

- **Traditional Food:** Traditional foods include a gamut of food preparations or raw food commodities, whose use is deep rooted in traditional practices. Traditional foods are best described as foods that people have eaten for ages. These foods have become part of traditions and cultures. Traditional foods are generally perceived as foods with beneficial properties due to genuineness, local production, propagation and minimal or no industrial processing (Bhaskarachary et al, 2016).

*Reference: Bhaskarachary et al, 2016, Review Article on Traditional Foods, Functional Foods and Nutraceuticals. Proc Indian Natn Sci Acad 82 No. 5 December 2016 pp. 1565-1577. DOI: 10.16943/ptinsa/2016/48888*

**According to FAO (2008)**, traditional food products represent an expression of culture and lifestyle resulting from the local climatic, agricultural and economic conditions that determine production and processing practices. As a consequence, the traditional nature of a product is based on collective heritage and is linked to a specific territory although it is transmitted by migration of individuals or populations.

*Reference: FAO (2008) Promotion of Traditional Regional Agricultural and Food Products: A Further Step Towards Sustainable Rural Development. <https://www.fao.org/3/k2473e/k2473e.pdf>*

**The European Food Information Reference Network** project defines traditional foods as those with specific features that distinguish them clearly from other similar products of the same category in terms of use of traditional raw materials/primary products/traditional composition/ traditional production and/or processing methods.

*Reference: Bhaskarachary et al, 2016, Review Article on Traditional Foods, Functional Foods and Nutraceuticals. Proc Indian Natn Sci Acad 82 No. 5 December 2016 pp. 1565-1577. DOI: 10.16943/ptinsa/2016/4888*

- **Food for Special Dietary Use (FSDU):** According to Food Safety and Standard Authority of India, Foods for Special Dietary Uses are foods specially processed or formulated to satisfy particular dietary requirements for certain physiological or specific health conditions.

*Reference: Food Safety and Standard Authority of India,*

[https://www.fssai.gov.in/upload/uploadfiles/files/Guidance\\_Note\\_FSMP\\_28\\_08\\_2020.pdf](https://www.fssai.gov.in/upload/uploadfiles/files/Guidance_Note_FSMP_28_08_2020.pdf)

- **Food for Special Medical Purpose (FSMP):** According to Food Safety and Standard Authority of India the food for special medical purpose” means food intended for:

- I. particular dietary use specially processed or formulated;
- II. the dietary management of persons and used only under medical advice;
- III. the exclusive or partial feeding of persons with a limited, impaired or disturbed capacity to take, digest, absorb, metabolize or excrete ordinary foodstuffs or certain nutrients contained therein or metabolites; or
- IV. other medically determined nutrient requirements, whose dietary management cannot be achieved only by modification of the normal diet, by food for specific nutritional use, or a combination of them

*Reference: Food Safety and Standard Authority of India,*

[https://www.fssai.gov.in/upload/uploadfiles/files/Compendium\\_Nutra\\_29\\_09\\_2021.pdf](https://www.fssai.gov.in/upload/uploadfiles/files/Compendium_Nutra_29_09_2021.pdf)

- **Human Intervention Studies:** Human Intervention Study means a research study involving human participants.

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## **LIST OF ABBREVIATIONS**



<b>AOAC</b>	<b>Association of Analytical Chemists</b>
<b>CDSCO</b>	<b>Central Drugs Standard Control Organization</b>
<b>CODEX</b>	<b>Codex Alimentarius</b>
<b>CRO</b>	<b>Contact Research Organization</b>
<b>CSIR</b>	<b>Council of Scientific &amp; Industrial Research</b>
<b>CSR</b>	<b>Clinical Study Report</b>
<b>CTRI</b>	<b>Clinical Trials Registry India</b>
<b>DCA</b>	<b>Drugs and Cosmetics Act</b>
<b>DCT</b>	<b>Drug Clinical Trial</b>
<b>DHR</b>	<b>Department of Health Research</b>
<b>FAO</b>	<b>Food and Agriculture Organization</b>
<b>FBO</b>	<b>Food Business Operators</b>
<b>FSDU</b>	<b>Foods for Special Dietary Uses</b>
<b>FSMP</b>	<b>Foods for Special Medical Purposes</b>
<b>FSSAI</b>	<b>Food Safety and Standard Authority of India</b>
<b>GCP</b>	<b>Good Clinical Practice</b>
<b>GLP</b>	<b>Good Laboratory Practice</b>
<b>ICMR</b>	<b>Indian Council of Medical Research</b>
<b>JECFA</b>	<b>Joint FAO/WHO Expert Committee on Food Additives</b>
<b>K-FFIG</b>	<b>Knowledge Center on Functional Foods, Immunity and Gut Health</b>
<b>MOHFW</b>	<b>Ministry of Health and Family Welfare</b>
<b>NABH</b>	<b>National Accreditation Board of Hospitals and Healthcare Providers</b>
<b>NABL</b>	<b>National Accreditation Board for Testing and Calibration Laboratories</b>
<b>NDCT</b>	<b>New Drugs and Clinical Trials</b>
<b>NIH</b>	<b>National Institute of Health (US)</b>
<b>NSF</b>	<b>Non Specified Food</b>
<b>OECD</b>	<b>Organization for Economic Cooperation and Development</b>
<b>SOP</b>	<b>Standard Operating Protocol</b>
<b>WHO</b>	<b>World Health Organization</b>

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**Rekha Sinha**  
Executive Director  
ILSI India

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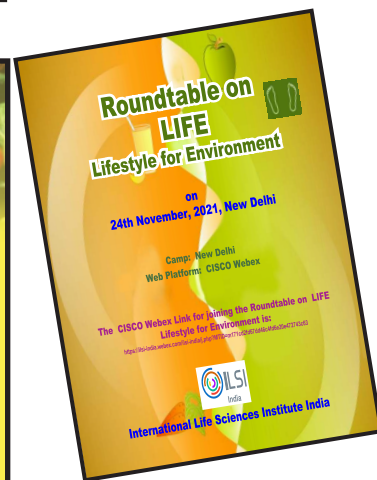
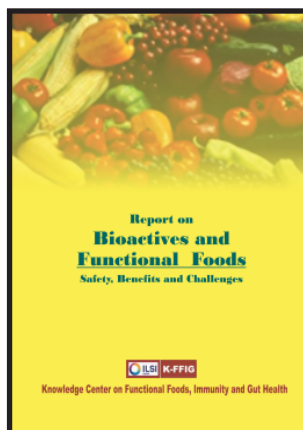
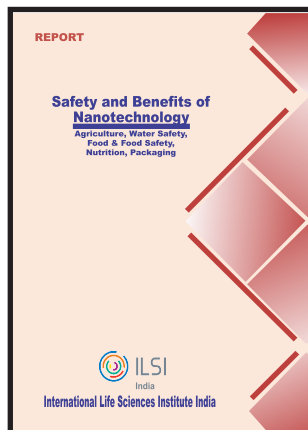
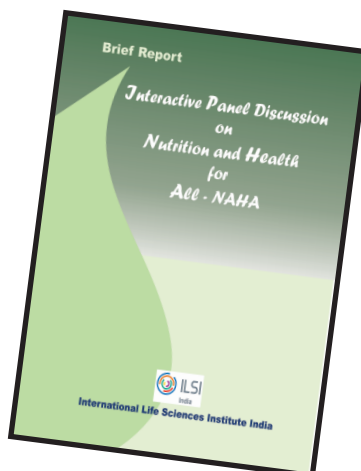
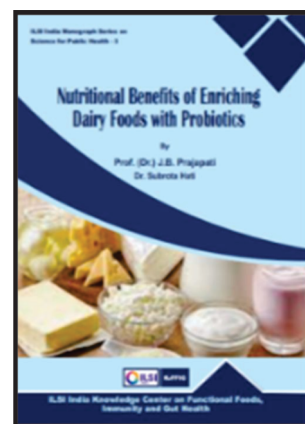
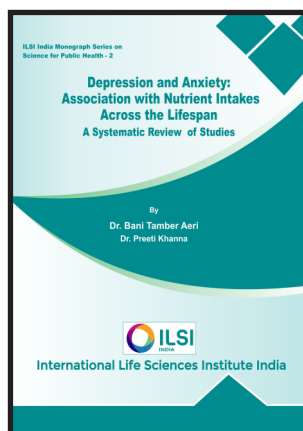
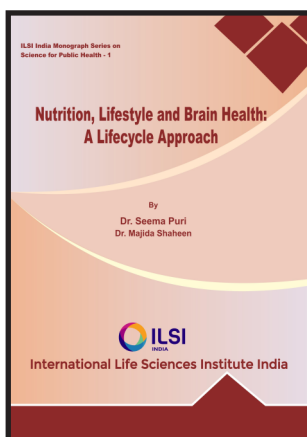
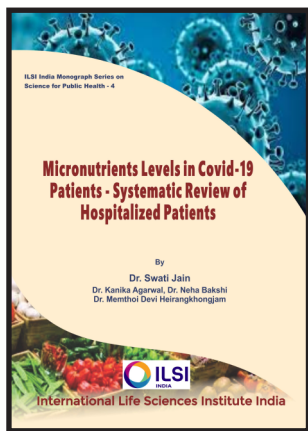
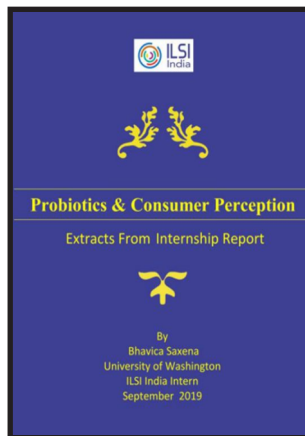
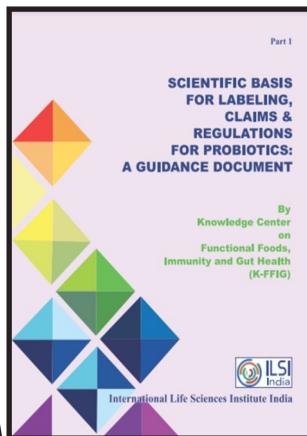
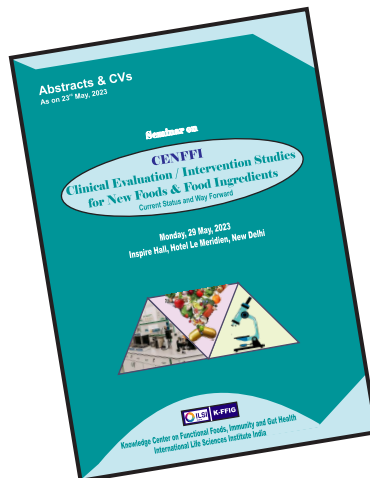
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