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Processes applied to the manufacture of infant formulas and foods for special medical purposes

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ABSTRACT

Breastfeeding is the gold standard in pediatric nutrition. When it is not possible, desired, or sufficient, infant formulas and foods for specific medical purposes are available, developed to meet special nutritional requirements. These products are manufactured using complex technological processes, under strict quality, hygiene, safety, and international regulations. Unlike other mass-market products (cookies, snacks), they are designed to contribute to children's nutrition. Their formulation includes adaptations in proteins, lipids, carbohydrates, vitamins, and minerals, according to the infant's needs. They are recommended in cases of prematurity, allergies, intolerances, digestive or metabolic disorders, or special conditions, and should always be recommended by a healthcare professional. Their correct use ensures the nutrients necessary for proper growth and development, as well as those essential for dietary and nutritional therapy.

Keywords: *technology; food production; infant formulas; specialized foods.*

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INTRODUCTION

Exclusive breastfeeding during the first 6 months of life and continued alongside complementary feeding until 2 years of age or beyond is the best nutritional approach during this period. When breastfeeding is not possible, or due to certain health conditions of the infant, food science and technology have developed infant formulas (IF) and foods for special medical purposes (FSMP) to provide the nutrients necessary for infant development. These foods are constantly evolving to come as close as possible to the biochemical and microbiological complexity of human milk.

The objective of this narrative review is to describe the technological processes used to obtain this type of food, the regulatory framework, and its use in pediatric populations.

FROM THE ORIGINS OF FOOD SCIENCE AND TECHNOLOGY TO OPERATIONS AND PROCESSES

Humanity needs water, oxygen, and food to grow and develop. The human being went from being a hunter-gatherer to settling down and producing their food. This gave rise to bartering and rudimentary trade, but the development that never stopped was that of production and preservation itself.

When nothing was known about food spoilage, people began experimenting by drying and salting meat, cooking fruit with honey, vegetables and meat with vinegar, and fermenting milk and vegetables. Through trial and error, they managed to mitigate the problem of food loss to some extent, as food became unpalatable or caused diseases that went untreated due to a lack of knowledge. These procedures helped to provide food in times of scarcity, preventing famines. The first modification and preservation techniques were being developed, while life expectancy was less than half what it is today, and there was a high rate of morbidity and mortality.[1] As techniques were continually refined, the results were longer shelf life, better flavors, and fewer diseases. The secret lay in the operations and processes applied to the raw material.[2] This gives rise to two concepts: operation (or unit operation) and process. In the case of food, an operation is a physical action that modifies it without chemical changes, for example, pasteurization.[3] On the other hand, a process is the application of a series of logical and orderly steps that pursue a common goal.[3] Finally, to complete and differentiate concepts, a formulation is the combination of strictly studied ingredients, which allows for a final composition designed for a specific purpose.[1]

Therefore, operations are physical actions that, in an orderly manner, constitute a process, which has been diagrammed with a detailed formulation and is monitored, tracked, and subject to exhaustive measurements and controls. From this, the concept of quality emerges: "the degree to which a set of inherent differentiating characteristics fulfills a generally established, explicit, or implied need or expectation."[2] Processes, therefore, guarantee quality and enable mass production that is accessible, safe, and of a defined composition. All of this results in a food product or formula to replace or supplement food, facilitating and ensuring effective and efficient nutritional intervention. Intermediate controls during the processes include monitoring pH, temperature, viscosity, and refractive index, among others. Any variation from the established values is corrected so that the final product meets the expected standards.[4]

When considering the composition and production of IF and FSMP, and comparing them with mass-market products such as cookies, snacks, breakfast cereals, among others, it is clear that the former have a much stricter manufacturing process, given that their operations and processes require special equipment and training, in addition to numerous intermediate and final controls and studies to verify their composition and safety.[5] The manufacturing process and final composition of IF and FSMP are key to their use for specific nutritional and therapeutic purposes.[6]

PRODUCTION AND QUALITY CONTROL OF INFANT FORMULAS AND FOODS FOR SPECIAL MEDICAL PURPOSES

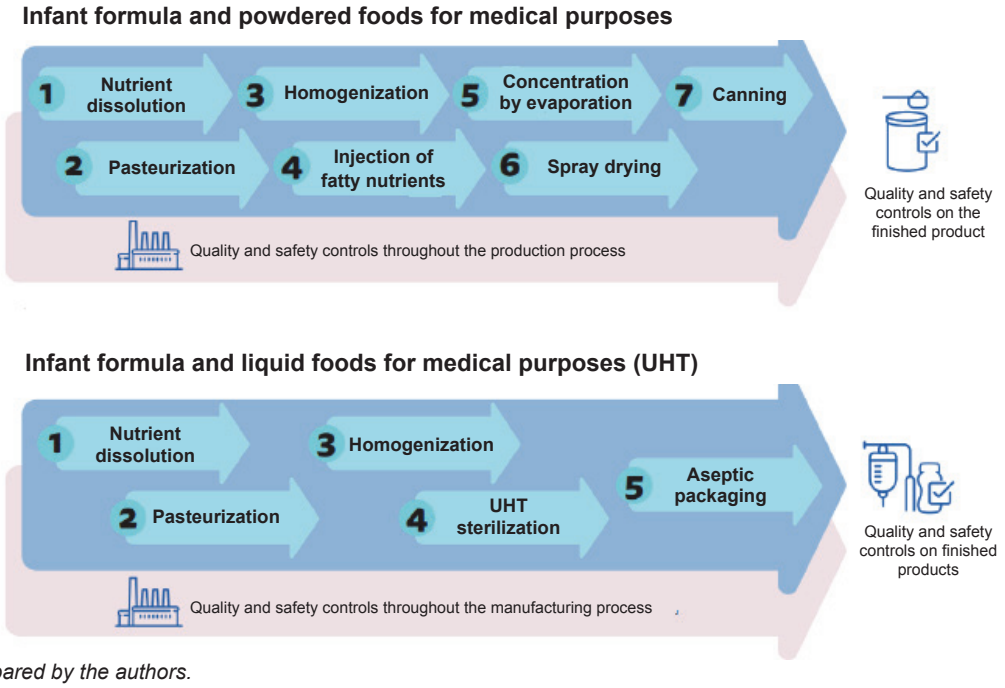
At the beginning of the 20th century, infant formulas consisted of barely modified cow's milk. Thanks to developments in infant nutrition and technological advances, they have become more sophisticated to approximate the composition of human milk. For cow's milk to be suitable for children in the early stages of their development, the protein and mineral concentration must be adjusted, the proportion of different proteins must be changed, increasing those of whey, and the Ca:P ratio must be increased from 1.2 to 2.0. Carbohydrates, fats, and vitamins must also be added.[7,8]

Powdered IF and FSMP are manufactured

using one of the following processes: "dry mixing" or "wet mixing and spray drying" of the ingredients. However, due to the microbiological challenge of maintaining safety during dry mixing, this process has been progressively replaced by wet mixing, followed by dehydration, known as spray drying, pulverization, or spraying. The process begins with the blending of water-soluble macro- and micronutrients, pasteurization to ensure the inactivation of any potentially pathogenic microorganisms, homogenization (to reduce and standardize particle size), the aseptic in-line injection of fatty nutrients (oils), and concentration by partial evaporation of water, to achieve total dehydration by spray drying. Following this, the product is packaged, and quality and safety controls are carried out.[9] In the case of liquid presentations, the process is slightly different. Macro- and micronutrients (water-soluble and fatty, such as oils) are mixed at the beginning, followed by pasteurization, homogenization (to ensure that the fatty components are dispersed in the liquid phase and distributed evenly), sterilization (UHT, ultra-high temperature), and aseptic packaging through terminal sterilization, before moving on to the quality control and safety assurance stage. Liquid products must be sterilized and pasteurized because they must be microbiologically stable at room temperature during storage and marketing. *Figure 1* illustrates the series of unit operations that take place throughout the IF and FSMP production process.

The manufacture of IF and FSMP is complex and requires effective quality control that goes beyond the classic parameters considered during the process and a final microbiological analysis. To guarantee a safe end product, various tools have been developed, such as hazard analysis and critical control points (HACCP), which facilitate the management of product food safety, and good manufacturing practices (GMP), which are a set of guidelines that establish the general requirements for effective control of the ingredients, formulas, processes, facilities, and equipment used in the production of this type of infant food. The combination of HACCP and GMP guarantees their quality and safety.[10] Routine microbiological controls include those designed to ensure the absence of *Cronobacter sakazakii*, *Salmonella enterica*, *Staphylococcus aureus*, *Bacillus cereus*, *Clostridium botulinum*, *C. difficile*, *C. perfringens*, and *Listeria monocytogenes*.

Figure 1. Unit operations and processes applied to the manufacture of infant formulas and foods for specific medical purposes



Source: prepared by the authors.
UHT: ultra-high temperature.

Among possible chemical contaminants, the absence of heavy metals, melamine, bisphenol A (BPA), and polychlorinated biphenyls (PCBs), among others, is guaranteed.[11]

NUTRITIONAL PROFILE AND REGULATORY ASPECTS OF INFANT FORMULAS AND FOODS FOR SPECIAL MEDICAL PURPOSES

Breastfeeding is the most cost-effective intervention in terms of nutrition and reducing infant morbidity and mortality.[12] IF and FSMP are foods intended to meet the special needs of infants and children. According to the Codex Alimentarius, IF or breast-milk substitutes are food products designed for the total or partial feeding of infants. Their labels must indicate the superiority of breast-milk and the recommendation that they be used only under the guidance of a health professional.[13]

IFs and FSMPs are correctly specified and defined.[13,14] According to the EFSA (European Food Safety Authority), "infant formulae are the only food products designed to meet the nutritional needs of infants during the first months of life until the introduction of appropriate complementary feeding." To protect the health of infants, it is necessary to ensure that preparations are the only products marketed as suitable for administration during that period.[15]

The Argentine Food Code (CAA, by its Spanish acronym) establishes that "the term infant formula refers to products intended to be used, when necessary, as a substitute for breast-milk to meet the nutritional needs of infants" and details the nutrient content requirements.[13]

Similarly, it defines FSMPs as formulations designed to meet the dietary needs of people with special health conditions. These products provide essential nutrients and should be used under professional guidance to improve nutritional status and contribute to patient recovery.

Among the ingredients, they contain hydrolyzed proteins, which have been technologically fragmented to reduce digestive work. Most contain maltodextrins, which are glucose oligomers derived from the hydrolysis of corn starch, which makes digestive enzymes less overloaded and allows them to be used instantly without any problems, ensuring optimal dispersion and/or solubilization. In some cases, medium-chain triglycerides are added, which do not require lipases for digestion and are absorbed directly through the portal vein. In other cases, protein hydrolysis is greater to minimize the impact on the immune system (allergies). The addition of minerals and vitamins in their chemical forms optimizes bioavailability and meets requirements in the appropriate doses. It is essential to have a thorough understanding of the regulatory framework for each product.

The microbiological quality of formulas and their ingredients is "an essential element in the protection of infants' health and must therefore be of a high standard."[13] The applicable standards recommended by the Codex Alimentarius and the Codex provisions contained in the Code of Hygienic Practice for Foods for Infants and Young Children must be met.[14] The elemental nutritional composition of FSMP and IF is specified in the CAA. In addition, Codex Alimentarius[15] and EFSA[16] include the nutritional profile of IFs. To date, there is no scientific evidence to support that the level of processing of foods and beverages involved determines the nutritional value of the final product.[17]

There is also the International Code of Marketing of Breast-milk Substitutes, which aims to protect and promote breastfeeding by ensuring the appropriate use of breast-milk substitutes through proper marketing, promotion, and distribution.

PEDIATRIC INDICATIONS FOR INFANT FORMULA AND FOODS FOR SPECIAL MEDICAL PURPOSES

Breastfeeding is the gold standard and the best option for infant growth and development; human milk is a dynamic fluid that meets their nutritional requirements.[18] However, in some special situations or maternal illnesses that contraindicate breastfeeding, or when the mother does not wish to breastfeed, appropriate substitutes are infant formulas for the first 0 to 6 months and then follow-up formulas for 6 to 12 months,[19] as they have specific modifications and processes to meet the requirements of infants. The use of cow's milk or other mammalian milk, or vegetable-based beverages (coconut, almond, rice, and oat, among others) before one year of age is not recommended.[20]

The composition of infant formulas has significantly evolved due to advances in scientific knowledge and manufacturing processes; specific formulas are now available for special situations.[21] There are FSMP for premature babies whose protein, lactose, lipid, and specific amino acid concentrations have been modified to ensure adequate growth.[22] There are also formulas with increased energy density or energy

density equal to one; others are reformulated into carbohydrates, where lactose is totally or partially replaced for situations of lactase deficiency (lactose intolerance).[23] There are IF with different degrees of protein hydrolysis. Those with a low degree of hydrolysis are indicated for use in disorders of the gut-brain axis[23] and, in the case of a high degree of hydrolysis, they are indicated for cow's milk protein allergy (CMPA).[24] As part of the treatment of CMPA, there is a period of cow's milk elimination, which consists of a maternal exclusion diet in the case of exclusive breastfeeding, or an extensively hydrolyzed formula in the case of formula or mixed feeding. In situations where symptoms persist, the indication is CMPA with free amino acids.[24]

Anti-reflux formulas are FSMP-designed to reduce regurgitation in infants with gastroesophageal reflux. These formulas contain thickeners such as carob seed gum, corn starch, or potato starch, which increase the viscosity of gastric contents, helping to keep them in the stomach. Like many FSMPs intended for nutritional support, their use improves weight gain and infant well-being.[25]

Tables 1 to 5 show the characteristics of infant and follow-up formulas for healthy infants and children, and modified milks (*Table 1*); formulas and FSMPs for infants with digestive disorders (*Table 2*); polymeric FSMPs for infants and children (*Table 3*); elemental and semi-elemental FSMPs, according to the degree of protein hydrolysis (*Table 4*); and FSMPs for rare diseases (*Table 5*). There are also formulations in which the ingredients are only one type of macronutrient, protein modules with calcium caseinate for reinforcement in high biological value proteins, carbohydrates to reinforce energy density, and medium-chain triglycerides that do not overload the biliary or pancreatic functions, among other essential functions (*Table 5*).

CONCLUSIONS

Breastfeeding is the gold standard in infant nutrition. In cases where it is not possible, desired, or sufficient, IF and FSMP should be indicated by qualified professionals.

The products discussed in this paper are developed using specific technological processes and formulations that follow strict quality and safety controls and are marketed within national and international regulatory frameworks. In addition, they provide the nutrients necessary for proper growth and development and/or are intended for nutritional therapy. Clinical studies also accompany them on safety and efficacy. ■

REFERENCES

1. Fennema O, Srinivasan D, Parkin K. ¿Qué es la química de los alimentos? En Fennema O, Srinivasan D, Parkin K. Introducción a la química de los alimentos. 4ª ed. Wisconsin: Acribia; 2021:1-16.
2. Baca Urbina G, Cruz Valderrama M, Cristóbal VM, Baca CG, Gutiérrez MJ, Pacheco EA, et al. Los procesos industriales. In: Introducción a la ingeniería industrial. 2ª ed. México: Patria; 2014:32-3.
3. Elham Alehosseini E, Mohammadi, Z, Mahdi Jafari S. Introduction to unit operations and process description in the food industry. In: Jafari SM, ed. *Engineering principles of unit operations in food processing*. London: Woodhead Publishing; 2021:1-27.
4. Lewis M. Viscosidad. En Lewis M. Propiedades físicas de los alimentos y de los sistemas de procesado. Zaragoza: Acribia; 1993:101-32.
5. Badui Dergal S. Lípidos. In: Badui Dergal S. Química de los alimentos. 5° ed. México: Pearson: 2013:279-95.
6. Klepper CM, Moore J, Gabel ME, Fleet SE, Kassel R. Pediatric formulas: categories, composition, and considerations. *Nut Clin Pract*. 2023;38(2):302-17.
7. Jiang YJ, Guo M. Processing technology for infant formula. In: Guo M, ed. *Human Milk Biochemistry and Infant Formula Manufacturing Technology*. London: Woodhead Publishing; 2014:211-29.
8. Codex Alimentarius Commission. Standard for Follow-Up Formula for Older Infants and Product for Young Children. Codex Standard 156-1987, 2023. [Accessed on: May 16, 2025]. Available at: https://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=h

Table 1. Formulas for healthy infants and children, starter and follow-on formulas, and modified milks (may include the addition of probiotics, prebiotics, and postbiotics)

Stage	Type of product	Indication
1	Infant formula	Feeding healthy full-term infants from birth to 6 months of age.
2	Follow-on formulas	Feeding healthy infants from 6 months to 12 months of age. They accompany complementary feeding.
3	Modified milks	Complement the diet of healthy children from one year of age.
4	Modified milks	Complement the diet of healthy children aged 2 to 3 years.

Adapted from Klepper et al., 2023[6], and adapted to the availability of these products in Argentina.

Table 2. Formulas and foods for specific medical purposes for infants with digestive disorders

Stage	Main characteristics	Indication
Anti-regurgitation FSMPs	Nutritionally complete formulas with protein, lactose, and long-chain fatty acids. With added thickeners, prebiotics, probiotics, and postbiotics.	Regurgitation and/or gastroesophageal reflux.
Formulas for infants from 0 to 12 months with functional digestive disorders	Nutritionally complete formulas with partially hydrolyzed proteins, maltodextrin, reduced lactose, lipids: long-chain fatty acids, beta-palmitate. With added prebiotics and probiotics.	Colic and/or constipation.
Low-lactose or lactose-free formulas for infants from 0 to 12 months	Nutritionally complete formulas with proteins, maltodextrin and lactose or maltodextrin only, lipids: long-chain fatty acids. With added probiotics.	Lactose intolerance, transient or congenital.

FSMPs: foods for special medical purposes.
Adapted from Klepper et al., 2023,[6] and adapted to the availability of these products in Argentina.

Table 3. Polymeric foods for special medical purposes for infants and children, with or without fiber

Energy density	Main characteristics	Indication
1 kcal/g	Intact molecules of carbohydrates (lactose or maltodextrin), proteins, and lipids. Energy density suitable for the age.	Malnutrition related or unrelated to disease, with normal gastrointestinal tract function, swallowing disorders, and neurological diseases.
>1 kcal/g	Intact carbohydrate molecules (lactose or maltodextrin), proteins, and lipids. High energy density for age.	Disease-related malnutrition.

Adapted from Klepper et al., 2023,[6] and adapted to the availability of these products in Argentina.

Table 4. Foods with specific medical purposes, elementary and semi-elementary, according to the degree of protein hydrolysis

Degree of protein hydrolysis	Main characteristics	Indication
Partially hydrolyzed	Formulas with partially hydrolyzed macronutrients. Carbohydrates: maltodextrin or glucose syrup; proteins: peptides; lipids: medium-chain triglycerides.	Digestive disorders with chronic diarrhea, insufficiency, intestinal resections, and transition from parenteral to enteral feeding.
Extensively hydrolyzed	Formulas with extensively hydrolyzed macronutrients. Carbohydrates: maltodextrin or glucose syrup; proteins: peptides; lipids: medium-chain triglycerides.	Cow's milk protein allergy and other food allergies.
With free amino acids	Formulas with hydrolyzed macronutrients. Carbohydrates: monosaccharides and oligosaccharides; proteins: free amino acids; lipids: medium-chain triglycerides.	Allergy to cow's milk protein and other severe food allergies, conditions that cause gastrointestinal tract disorders or malabsorption.

Adapted from Klepper et al., 2023,[6] and adapted to the availability of these products in Argentina.

ttps%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FStandards%252FCXS%2B156-1987%252FCXS_156e.pdf
9. Bakshi S, Paswan VK, Yadav SP, Bhinchhar BK, Kharkwal S, Rose H, et al. A comprehensive review on infant formula: nutritional and functional constituents, recent trends in processing and its impact on infants' gut microbiota. *Front Nut*. 2023;10:1194679.
10. Hamrin P, Hoeft B. Quality control throughout the production process of infant food. *Ann Nutr Metab*. 2012;60(3):208-10.
11. Jiang SL, Guo MR. Processing technology for infant formula. In: Mingruo G. Human Milk Biochemistry and Infant Formula Manufacturing Technology. 2nd ed. Duxford: Woodhead Publishing; 2021:223-40.
12. Gonzalez F, Carosella M, Fernandez A. Riesgos nutricionales en lactantes que no reciben lactancia materna exclusiva en los primeros seis meses de la vida. *Arch Argent Pediatr*. 2021;119(6):e582-8.
13. Código Alimentario Argentino. Alimentos de régimen o dietéticos. 2024:1-84. [Accessed on: May 16, 2025].

Table 5. Foods for special medical purposes for rare diseases and modules with a single type of macronutrient

Type	Main characteristics	Indication
FSMP with modifications depending on the pathology	With the elimination or reduction of the compound/nutrient that cannot be metabolized properly.	For congenital errors of metabolism, such as urea cycle enzyme deficiency and other enzymes, among others.
Lipid-predominant FSMP	With different ratios such as 4:1, 3:1, and 2.5:1 (g of fat: g of protein plus carbohydrates).	For ketogenic diets in the treatment of refractory epilepsy.
Carbohydrates	Maltodextrin, glucose, maltose, and other starch derivatives of starch.	Patients requiring pre-surgical carbohydrate loading, malnourished patients who need nutritional modulation.
Proteins	Calcium caseinate or whey protein.	Patients in the perioperative period and any condition requiring extra protein intake.
Lipids	Medium-chain triglycerides.	For the dietary management of conditions that require extra energy intake and/or are associated with severe malabsorption or digestive intolerance to triglycerides. For ketogenic diets in the treatment of refractory epilepsy.
Fiber	Mixture of fiber components.	For the management of constipation.

FSMP: foods for special medical purposes.

Adapted from Klepper et al., 2023[6] and adapted to the availability of these products in Argentina.

Available at: https://es.scribd.com/document/519176231/CAPITULO-XVII-codigo-alimentario-argentino

14. Olagnero G. Fórmulas infantiles. Introducción al diseño de sistemas alimentarios complejos. In: Kabbache DM, ed. *Técnica Dietoterápica Avanzada: Diseño, análisis y reformulación de sistemas alimentarios para fines especiales*. Buenos Aires: Akadia; 2019:195-204.
15. Codex Alimentarius. Norma para preparados para lactantes y preparados para usos medicinales especiales destinados a los lactantes. Codex stand 72-1981-2007. [Accessed on: May 16, 2025]. Available at: https://www.isdi.org/wpcontent/uploads/2021/02/CODEX-STAN-72-1981_ES.pdf
16. EFSA IFFO. Food for infants and young children. 2006. [Accessed on: May 16, 2025]. Available at: https://food.ec.europa.eu/food-safety/labelling-and-nutrition/specificgroups/food-infants-and-young-children_en
17. Ahrné L, Chen H, Henry CJ, Kim HS, Schneeman B, Windhab EJ. Defining the role of processing in food classification systems—the IUFoST formulation & processing approach. *NPJ Sci Food*. 2025;9(1):56.
18. World Health Organization. International code of marketing of breast-milk substitutes. 1981. [Accessed on: May 31, 2025]. Available at: https://iris.who.int/handle/10665/40382
19. García SM. Lactancia en recién nacidos prematuros. In: Sociedad Argentina de Pediatría. PRONAP. 2020;2(2):57-86.
20. Guía de práctica clínica sobre alimentación complementaria para los niños y niñas menores de 2 años. [Accessed on: May 16, 2025]. Available at: https://www.argentina.gob.ar/sites/default/files/bancos/2022-03/guia-alimentarianyn-2022.pdf
21. Setton D, Fernández A. Nutrición en Pediatría. Bases para la práctica clínica en niños y enfermos. Buenos Aires: Panamericana; 2014.
22. Embleton ND, Moltu SJ, Lapillonne A, van den Akker CHP, Carnielli V, Fusch C, et al. Enteral Nutrition in Preterm Infants (2022): A Position Paper from the ESPGHAN Committee on Nutrition and Invited Experts. *J Pediatr Gastroenterol Nutr*. 2023;76(2):248-68.
23. Toca MC, Fernández A, Orsi M, Tabacco O, Vinderola G. Intolerancia a la lactosa: mitos y verdades. Actualización. *Arch Argent Pediatr*. 2022;120(1):59-66.
24. Toca MC, Parisi C, Fernández A, Tabacco O, Zubiri C, Furnes R, et al. Tratamiento de la alergia a la proteína de la leche de vaca. Consenso interdisciplinario de expertos. *Arch Argent Pediatr*. 2024;122(5):e202410404.
25. Toca MC, Balbarrey S, Bastianelli C, Guzmán L, Leta K. Trastornos funcionales gastrointestinales. Cómo tratar sin medicar. *Arch Argent Pediatr*. 2022;120(5):346-53.