**Supplemental Digital Content (SDC) for Puccio et al.**

 **SDC 1.** Additional information on the assessment of study outcomes.

Anthropometric measurements were assessed by medical investigators and body weight, length, and head circumference were measured according to standard procedures. Subject weight was measured on an electronic scale to the nearest 10 g, and body length was measured to the nearest 1 mm using a standardized length board. Head circumference was measured to the nearest 1 mm with a non-elastic plastic coated measuring tape. Z-scores for anthropometric variables were calculated using the WHO Anthro version 3.2.2 SAS macro (“%igrowup\_standard”) available at http://www.who.int/childgrowth/software/en/.

Stool characteristics (stool number and consistency), digestive tolerance (flatulence, spitting up, and vomiting), behavioral patterns (colic, restless, and night awakenings), formula intake, and illnesses and medication use were evaluated using a paper diary completed by the parent/caregiver over the 3 consecutive days prior to each post-baseline study visit.

Parents/caregivers were asked to record the number of stools per 24 hours for each of the 3 days. In addition, parents/caregivers were provided with stool images and written descriptions from the Bristol Stool scale (1=hard, 7=watery) and asked to indicate the predominant consistency of the infant’s stools during the 3 days prior to each post-baseline visit.

To assess digestive tolerance and behavioral patterns, parents were asked to respond to the following questions “Did your child suffer from flatulence during the last period?”, “Did your child spit up (1-2 teaspoons) during the last period?”, “Did your child vomit over the last three days?”, “Is your child restless and irritable?”, and “Does your child suffer from colics?” by selecting one of the response options (“Not at all”, “A bit”, or “A lot”; these response options were then converted to “never”, “sometimes”, and “often” for data analysis). Parents/caregivers also were asked “Does your child wake up during the night?” and the response options were “Never,” “Sometimes,” or “Often”.

To obtain information on formula intake, parents were provided with a grid and asked to record total ml prepared/total ml left for each meal over 3 days, along with total ml consumed for each of the 3 days. A blank space was provided for parents to record foods other than infant formula (only for the first 4 months of life).

Finally, as part of the paper diary, parents were provided with a grid to record any illness symptoms including fever or specific illnesses diagnosed by either the child’s primary care physician or the study physician (depending on which clinic the child was taken to when he/she was sick), hospitalization (reason, duration), and intake of medications since the prior visit, and the associated start and stop dates. The information recorded in the diary by the parent was reviewed and confirmed by the study physician before being recorded in the study database as reported AEs or reported medication use; these AEs were then coded and categorized by a single physician who was not involved in the study conduct using the Medical Dictionary for Regulatory Activities (MedDRA) System, Organ, and Class (SOC) categories as well as the Preferred Terms (PTs) within each SOC category. It is worth noting that during either the illness diagnosis or verification of the illness symptoms / episodes, study physicians were not provided with standard definitions for common illnesses. All diagnoses were based on the medical knowledge and clinical practice of individual study physicians.

Several PTs within the “Infections and Infestations” SOC category were identified *a priori* as being of particular interest in this study, including the PTs of upper respiratory infection, pyrexia, rhinitis, bronchitis, bronchiolitis, otitis media, pharyngitis and gastroenteritis. Additionally, **three AE clusters** were identified including upper respiratory infection (comprised of the following PTs: respiratory tract infection, acute tonsillitis, laryngitis, pharyngitis, rhinitis, tracheitis, upper respiratory tract infection, respiratory tract infection viral, viral upper respiratory tract infection, nasal obstruction, and nasopharyngitis), lower respiratory tract infection (comprised of the following PTs: bronchitis, lower respiratory tract infection, pneumonia, respiratory syncytial virus bronchiolitis, respiratory syncytial virus bronchitis, bronchiolitis, lower respiratory tract infection viral, respiratory tract infection viral), and otitis/ear infection (comprised of the following PTs: otitis media acute, ear infection, otitis media). Similarly, information on medications or other substances used by the infant were reported by caregivers and reviewed by the study investigators before being recorded as a concomitant medication in the study database; later these medications were coded and categorized into groups as appropriate, including antibiotics, antipyretics, and gastroesophageal reflux disease (GERD) medications. Data related to AEs and medication use were expressed as the proportion of infants in each group with at least 1 episode of the specific AE or medication use.