Adverse Event Data Programming for Infant Nutrition Trials

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ABSTARCT

Many times in infant nutrition trials, the effect of the study product (e.g. supplementary formula feeding) is considered to have its effect on the safety profile only on the day it was consumed. Thus, it is important to present the safety data by the study product consumption pattern such as fully on study product, study product as well as breast feeding or other complementary feeding, or no study product. This unique way of presenting the safety data adds complexity in the programming as subjects frequently switch from one consumption pattern to other during the trial period. However, such presentation of safety data is very helpful for the interpretation of the study product safety profile under real life scenarios.

This paper describes a report layout for reporting adverse events by study consumption pattern and explains its programming aspects.

INTRODUCTION

This paper deals with a randomized, controlled, parallel group comparison trial, for infant nutrition. Each subject is randomized to either study product (SP) 'A' or 'B' or reference group 'No SP'. Subjects randomized to study product 'A' or 'B' consume SP on daily basis. Subjects in reference group 'No SP' are purely breast fed (BF) or may take complementary food (CF).

The adverse events (AEs) presentation in different state is crucial in infant trials. Though infant formula is being given on a daily basis, it is not restricted to have only study formula. World health organisation (WHO) recommends that a baby should be BF for at least 6 months [1]. And moreover, the mother is free to feed the infant any CF. So any AE occurring during infant nutrition trial cannot be directly attributed to the study formula. So there is a requirement of classifying AEs to a particular state. Based on onset time of AE; an AE can occur during BF/CF with no SP consumption or an AE can occur when the subject is only on SP and no BF/CF has been given. The classification of AEs according to these states has been explained below.

The paper begins with a report layout showing AE reporting style, followed by the structure of ADAE data set based on the layout, and then concludes with the process of counting AEs across states and SAS code excerpts. This paper assumes that the programmer has basic understanding about the AE data set structure, subject visit data and base SAS REPORT procedure along with ODS RTF.

THE AE REPORT LAYOUT

The layout of Table I below presents SP 'A', 'B' and 'No SP'. Further, SP 'A' and 'B' are classified into two states each, representing subjects purely on SP, i.e. no BF/CF and subjects on SP along with BF/CF. 'No SP' is the reference group where a subject is either fully on BF/CF or mixed feeding, with no SP.

Table
Frequency of Adverse Events by feeding pattern, per Visit
Population: All Subjects Treated

	A - no BF/CF		A + BF/CF		B - no BF/CF		B + BF/CF		No SP	
SYSTEM ORGAN CLASS Preferred Term	n (%)	nAE (%)	n (%)	nAE (%)	n (%)	nAE (%)	n (%)	nAE (%)	n (%)	nAE (%)
Visit 1										
N	xx		xx		xx		xx		xx	
Subjects with >= one AE	xx (x.xx)		xx (x.xx)		xx (x.xx)		xx (x.xx)		xx (x.xx)	
Subjects with no AE	xx (x.xx)		xx (x.xx)		xx (x.xx)		xx (x.xx)		xx (x.xx)	
nAE		xx		xx		xx		xx		xx
SYSTEM ORGAN CLASS 1	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)
Preferred Term 1	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)
Preferred Term 2	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)
Preferred Term 3	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)
SYSTEM ORGAN CLASS 2	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)
Preferred Term 1	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)
SYSTEM ORGAN CLASS 3	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)
Preferred Term 1	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)
Preferred Term 2	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)	xx (x.xx)

n (%) = Number (percent) of subjects, nAE = Number of adverse events, BF=Breast-feeding, CF=Complementary foods, SP = Study product
AEs are allocated to the state where the subject was at time of AE occurrence.

Table I: AE mock layout

PREPARING THE ANALYSIS DATA SET

Daily diary data for subjects has been collected to capture feeding details of the SP given, its quantity, if BF was done or not, CF was given or not. Using this information the state of the subject during an AE can be determined. For this, the analysis data set ADAE needs to have visit information, for which we added a variable AVISIT to this data set as indicated in the ADAE data structure guideline [2] section 4.1.4. AEs are mapped to a particular visit, if the onset date of AE is on or before that visit date. The state has been denoted by a flag variable BFCFFL. The value range for BFCFFL is – 'Y' to indicate SP + BF/CF, 'N' to indicate SP – no BF/CF or null to indicate 'No SP'. The state of a subject was defined at the Visit level, in the Visit data set, to be used as a denominator of percentage calculations. This is achieved by comparing the visit dates, with diary dates and checking the feeding types at that instance. Various scenarios for that were explored are discussed below.

SCENARIO 1: Subjects randomized but have not started study product

USUBJID	AEBODSYS	AEDECOD	ASTDT	TRTSDT	TRT01A	TRTA	AVISIT
AOO-105	GASTROINTESTINAL DISORDERS	Abdominal Pain	22-Aug-12	29-Mar-13	A	No SP	Visit 1
AOO-105	INJURY, POISONING AND PROCEDURAL COMPLICATIONS	Post Vaccination Syndrome	01-Oct-12	29-Mar-13	A	No SP	Visit 1
AOO-105	RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	Cough	26-Nov-12	29-Mar-13	A	No SP	Visit 1
AOO-105	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Pyrexia	27-Jun-13	29-Mar-13	A	A	Visit 1
AOO-105	GASTROINTESTINAL DISORDERS	Constipation	03-Jul-13	29-Mar-13	A	A	Visit 1

Data Set I: Highlighted dates and resulting treatment group

The state of the AE is determined considering the onset date, relative to the SP start date. Hence for all subjects that were randomized, but did not start SP, the state would be 'No SP' as illustrated above in Data Set I.

In the above illustration, it must be noted that TRT01A would not be consistent with TRTA and this needs to be recorded in the metadata. There appears to be an alternative of using the Pre-treatment flag (PREFL) in this case, but since the subjects under consideration are the reference group subjects with 'No SP', the use of PREFL has been avoided here.

SCENARIO 2: Identifying state of an AE

Though the layout looks straight forward, counting an AE in a particular state is not so simple. The subject needs to consume SP every day, and there is a high possibility that along with the SP, the subject consumes CF or BF. The initial logic is to compare the AE start date and the diary date. If the AE occurs while consumption of SP is going on and at the same time there is an indication of BF or CF, then the AE needs to be flagged under SP + BF/CF. On the other hand, if the AE occurs when the subject was purely taking SP only (with no BF/CF) then the AE needs to be flagged under SP – no BF/CF.

All possible illustrations that simulate what state a subject's AE records would fall under are discussed below:

a) AE records that need to be counted under SP – no BF/CF, would be the ones where AE onset date is before the start of any CF or BF, but after the subject has started SP. Note that the BF/CF dates would be captured only when there is BF/CF. In the absence of these dates, it is safe to consider the AE under SP – no BF/CF group. Refer to Data Set II for an example.

USUBJID	AEBODSYS	AEDECOD	ASTDT	TRTSDT	AVISIT	TRT01A	TRTA	BFCFFL
AOO-011	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Pyrexia	31-Jul-13	7-May-13	Visit 1	No SP	No SP	
AOO-012	GASTROINTESTINAL DISORDERS	Abdominal Pain	24-Jun-13	14-Jun-13	Visit 1	A	A	N
AOO-012	GASTROINTESTINAL DISORDERS	Regurgitation	31-Aug-13	14-Jun-13	Visit 1	A	A	N
AOO-012	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Pyrexia	19-Sep-13	14-Jun-13	Visit 1	A	A	N
AOO-013	INFECTIONS AND INFESTATIONS	Otitis Externa	06-Dec-12	19-Sep-12	Visit 1	No SP	No SP	
AOO-013	NERVOUS SYSTEM DISORDERS	Exaggerated Startle Response	08-Dec-12	19-Sep-12	Visit 1	No SP	No SP	

Data Set II: Highlighted records under A – no BF/CF

b) For a particular subject, for the same visit, there can be a possibility of counting AEs in different states. This happens when the onset date falls during a period/day when the diary indicates that the subject was taking CF or BF along with SP. At the same time, for other diary periods/days, the subject may be off BF or CF and would be solely taking SP only, this case the AE needs to be considered in SP – no BF/CF state. Check the values of BFCFFL to indicate the above cases in Data Set III below.

USUBJID	AEBODSYS	AEDECOD	ASTDT	TRTSDT	AVISIT	TRT01A	TRTA	BFCFFL
AOO-033	METABOLISM AND NUTRITION DISORDERS	Decreased Appetite	24-Aug-13	16-Apr-13	Visit 1	No SP	No SP	
AOO-034	PREGNANCY, PUERPERIUM AND PERINATAL CONDITIONS	Jaundice Neonatal	08-Sep-12	8-Sep-12	Visit 1	A	A	Y
AOO-034	NERVOUS SYSTEM DISORDERS	Fontanelle Bulging	19-Dec-12	8-Sep-12	Visit 1	A	A	N
AOO-034	GASTROINTESTINAL DISORDERS	Diarrhoea	20-May-13	8-Sep-12	Visit 1	A	A	N
AOO-034	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Pyrexia	15-Aug-13	8-Sep-12	Visit 1	A	A	Y
AOO-034	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Pyrexia	27-Aug-13	8-Sep-12	Visit 1	A	A	Y
AOO-036	INFECTIONS AND INFESTATIONS	Gastroenteritis	27-Aug-12	28-Jul-12	Visit 1	No SP	No SP	
AOO-036	INFECTIONS AND INFESTATIONS	Viral Infection	26-Sep-12	28-Jul-12	Visit 1	No SP	No SP	

Data Set III: Highlighted records under A – no BF/CF and A – BF/CF

c) A particular subject's AE records for a visit, may be counted under No SP and also SP + BF/CF OR SP – no BF/CF. As discussed in SCENARIO 1 above, if the onset of AE is before SP start date, then that AE would be under 'No SP'. But when the onset date falls during a period/day when the diary indicates that the subject was taking CF or BF along with SP, the these AEs would be under SP + BF/CF. The example for the above points are indicated in Data Set IV. There could also be a situation where AE records for a subject, for a visit would be counted under 'No SP' and SP – no BF/CF.

USUBJID	AEBODSYS	AEDECOD	ASTDT	TRTSDT	AVISIT	TRT01A	TRTA	BFCFFL
AOO-105	GASTROINTESTINAL DISORDERS	Abdominal Pain	22-Aug-12	29-Mar-13	Visit 1	A	No SP	
AOO-105	INJURY, POISONING AND PROCEDURAL COMPLICATIONS	Post Vaccination Syndrome	01-Oct-12	29-Mar-13	Visit 1	A	No SP	
AOO-105	RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	Cough	26-Nov-12	29-Mar-13	Visit 1	A	No SP	
AOO-105	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Pyrexia	27-Jun-13	29-Mar-13	Visit 1	A	A	Y
AOO-105	GASTROINTESTINAL DISORDERS	Constipation	03-Jul-13	29-Mar-13	Visit 1	A	A	Y

Data Set IV: Highlighted records under No SP and A – BF/CF

d) A particular subject's AE records for a visit may be counted under No SP, SP + BF/CF and also SP – no BF/CF. Proceeding with the same situations listed in SCENARIO I and Cases a), b) and c) above, it can be understood that situation depicted in Data Set V can also be possible.

USUBJID	AEBODSYS	AEDECOD	ASTDT	TRTSDT	AVISIT	TRT01A	TRTA	BFCFFL
AOO-094	MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	Muscle Spasms	05-Jun-13	15-Jun-13	Visit 1	B	No SP	
AOO-094	RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	Rhinorrhoea	05-Jun-13	15-Jun-13	Visit 1	B	No SP	
AOO-094	RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	Rhinorrhoea	15-Jun-13	15-Jun-13	Visit 1	B	B	Y
AOO-094	MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	Muscle Spasms	18-Jun-13	15-Jun-13	Visit 1	B	B	Y
AOO-094	MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	Muscle Spasms	27-Jun-13	15-Jun-13	Visit 1	B	B	Y
AOO-094	RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	Rhinorrhoea	12-Aug-13	15-Jun-13	Visit 1	B	B	N

Data Set V: Highlighted records under No SP, B – BF/CF and B – no BF/CF

FORMATTING

Once we have the AE states in place at the analysis data set level, the task of counting number of subjects and number of AEs is not so difficult. The paper refrains from discussing DATA/PROC steps to get count and percentages but would emphasise on dealing with some RTF report level situations in SAS.

a) Adding '(Continue…)' word on next page when list of Preferred Term (PT) of same System Organ Class (SOC) continues to next page. This needs to be tweaked at the report ready data set level. In the first place get the page number variable in report ready SAS data set and then determine which PTs are on next page for same SOC.

	AVISIT	COL_1	AEBODSYS	AEDECOD	A_1	
1	Visit 1	Visit 1				
2	Visit 1	N			61	
3	Visit 1	Subjects with >= one AE			41 (67.2)	
4	Visit 1	Subjects with no AE			20 (32.8)	
5	Visit 1	nAE				
6	Visit 1	EYE DISORDERS	EYE DISORDERS		2 (3.3)	
7	Visit 1	\li300 Conjunctivitis	EYE DISORDERS	Conjunctivitis	1 (1.6)	
8	Visit 1	\li300 Dacryostenosis Congenital	EYE DISORDERS	Dacryostenosis Congenital	1 (1.6)	
9	Visit 1	\li300 Eye Discharge	EYE DISORDERS	Eye Discharge	0	
10	Visit 1	\li300 Lacrimation Increased	EYE DISORDERS	Lacrimation Increased	0	
11	Visit 1	GASTROINTESTINAL DISORDERS	GASTROINTESTINAL DISORDERS		17 (27.9)	
12	Visit 1	\li300 Abdominal Distension	GASTROINTESTINAL DISORDERS	Abdominal Distension	0	
13	Visit 1	\li300 Abdominal Pain	GASTROINTESTINAL DISORDERS	Abdominal Pain	3 (4.9)	
14	Visit 1	\li300 Acetonaemic Vomiting	GASTROINTESTINAL DISORDERS	Acetonaemic Vomiting	0	
15	Visit 1	\li300 Constipation	GASTROINTESTINAL DISORDERS	Constipation	3 (4.9)	

Data Set VI: Input data set before having page number variable

```
%let NOB = 13;

data RptReady01;
  set final01;
  by AVISIT ;
  /* Page no. */
  retain PgBy 0;
  NOB + 1;
  if first.AVISIT or NOB eq &NOB + 1 then do;
    NOB = 1;
    PgBy + 1;
  end;
  SRT = _n_;
run;

data addrow ;
  set RptReady01 ;
  by PgBy ;
  if first.PgBy ;
  if AEBODSYS ne '' and AEBODSYS ne COL_1 ;
  COL_1 = strip (AEBODSYS) ||" (Continue...)";
  keep COL_1 SRT PgBy;
run;

data RptReady02 ;
  set addrow RptReady01 ;
  by SRT PgBy;
run;
```

In above SAS code 'RptReady01' data set created with PgBy variable by taking number of observations to be printed in NOB macro variable. When number of observations to print on one page reaches the macro variable value or there is a new visit in AVISIT variable then PgBy is increased by one. The 'addrow' data set extracts only the first record of each page, and checks to see if there is consistency between AEBODSYS and COL_1. If there is a mismatch, then this is a case for addition of (Continue…) record, which would be appended to original data, in the next step.

In Data Set VII below, the highlighted record shows '(Continue…)' word on page number 2 for same SOC continuing from page 1. This PgBy variable is used in BY statement of PROC REPORT to generate RTF output.

	SRT	NOB	PgBy	AVISIT	COL_1	AEBODSYS	AEDECOD	A_1
1	1	1	1	Visit 1	Visit 1			
2	2	2	1	Visit 1	N			61
3	3	3	1	Visit 1	Subjects with >= one AE			41 (67.2)
4	4	4	1	Visit 1	Subjects with no AE			20 (32.8)
5	5	5	1	Visit 1	nAE			
6	6	6	1	Visit 1	EYE DISORDERS	EYE DISORDERS		2 (3.3)
7	7	7	1	Visit 1	\li300 Conjunctivitis	EYE DISORDERS	Conjunctivitis	1 (1.6)
8	8	8	1	Visit 1	\li300 Dacryostenosis Congenital	EYE DISORDERS	Dacryostenosis Congenital	1 (1.6)
9	9	9	1	Visit 1	\li300 Eye Discharge	EYE DISORDERS	Eye Discharge	0
10	10	10	1	Visit 1	\li300 Lacrimation Increased	EYE DISORDERS	Lacrimation Increased	0
11	11	11	1	Visit 1	GASTROINTESTINAL DISORDERS	GASTROINTESTINAL DISORDERS		17 (27.9)
12	12	12	1	Visit 1	\li300 Abdominal Distension	GASTROINTESTINAL DISORDERS	Abdominal Distension	0
13	13	13	1	Visit 1	\li300 Abdominal Pain	GASTROINTESTINAL DISORDERS	Abdominal Pain	3 (4.9)
14	14	.	2		GASTROINTESTINAL DISORDERS (Continue...)			
15	14	1	2	Visit 1	\li300 Acetonaemic Vomiting	GASTROINTESTINAL DISORDERS	Acetonaemic Vomiting	0
16	15	2	2	Visit 1	\li300 Constipation	GASTROINTESTINAL DISORDERS	Constipation	3 (4.9)

Data Set VII: Output data set after having page number with SOC term added '(Continue…)' word

b) Adding and splitting line to spanning header using keyword '\brdrb\brdrs\li50', where '\brdrb' - border bottom, '\brdrs' - single thickness and '\li50' - indent from left side will give space between neighbouring two bottom lines. For header we have to bold-face'System Organ Class' and normal-face 'Preferred Term'. Using '\b' gives bold font and '\b0' removes effect of bold. These two keywords are used in header label. Statements in PROC REPORT:

```
PROC REPORT data = RptReady03  headline nowd split = '~'  style ( report )=
[frame=hsides rules=groups outputwidth = 10in background = white ]  style ( header
) = [protectspecialchars = off ] nowindows ;
by PgBy ;

COLUMN COL_1 ( "A- no BF/CF \brdrb\brdrs\li150" A_2 NAEA_2 ) ( "A + BF/CF
\brdrb\brdrs\li150"  A_1 NAEA_1  )                ( "B- no BF/CF
\brdrb\brdrs\li150" B_2 NAEB_2 ) ( "B + BF/CF \brdrb\brdrs\li150"  B_1 NAEB_1  )
( "No SP \brdrb\brdrs\li150"  NOSP NAENOSP );

DEFINE COL_1 / display "\b SYSTEM ORGAN CLASS ~\b0\    Preferred Term " style =
[just = left cellwidth = 2in protectspecialchars = off background = white] style
(header) = [just = left];

DEFINE A_1 / display "n (%)" style = [just = center cellwidth = 0.6in
protectspecialchars = off background = white] style (header) = [just = center];
```

Table 1.1
Frequency of Adverse Events by Dose, per Visit
Population: All Subjects Treated

SYSTEM ORGAN CLASS Preferred Term	A- no BF/CF		A + BF/CF		B- no BF/CF		B + BF/CF		No SP	
	n (%)	nAE (%)	n (%)	nAE (%)	n (%)	nAE (%)	n (%)	nAE (%)	n (%)	nAE (%)

Table II: Effect of COLUMN and DEFINE COL_1 statement

c) Bold font for all SOC terms and their counts is done at data set level. To add empty line after each SOC and its PTs could be done by COMPUTE BLOCK or adding empty row in data set. Another way here shown in Data Set VIII is using space before '\sbN' RTF keyword where N is number in twips. Advantage of using '\sbN' is it could be adjusted to appropriate space which can save some pages in big RTF output compared to adding empty line.

6	\sb200\b EYE DISORDERS	\sb200\b 2 (3.3)	\sb200\b 2 (7.4)	\sb200\b 2 (3.8)	\sb200\b 2 (6.9)
7	\li300 Conjunctivitis	1 (1.6)	1 (3.7)	1 (1.9)	1 (3.4)
8	\li300 Dacryostenosis Congenital	1 (1.6)	1 (3.7)	0	0
9	\li300 Eye Discharge	0	0	1 (1.9)	1 (3.4)

Data Set VIII: RTF codes in to data set for bold font and empty space

<div align="center">

Table
Frequency of Adverse Events by Dose, per Visit
Population: All Subjects Treated

</div>

SYSTEM ORGAN CLASS	A- no BF/CF		A + BF/CF		B- no BF/CF		B + BF/CF		No SP	
Preferred Term	n (%)	nAE (%)	n (%)	nAE (%)	n (%)	nAE (%)	n (%)	nAE (%)	n (%)	nAE (%)
Visit 1										
N	27		61		29		53		189	
Subjects with >= one AE	19 (70.4)		41 (67.2)		18 (62.1)		35 (66.0)		48 (25.4)	
Subjects with no AE	8 (29.6)		20 (32.8)		11 (37.9)		18 (34.0)		141 (74.6)	
nAE		47		120		64		128		113
EYE DISORDERS	2 (7.4)	4 (8.5)	2 (3.3)	2 (1.7)	2 (6.9)	6 (9.4)	2 (3.8)	3 (2.3)	5 (2.6)	12 (10.6)
Conjunctivitis	1 (3.7)	2 (4.3)	1 (1.6)	1 (0.8)	1 (3.4)	2 (3.1)	1 (1.9)	1 (0.8)	3 (1.6)	6 (5.3)
Dacryostenosis Congenital	1 (3.7)	2 (4.3)	1 (1.6)	1 (0.8)	0	0	0	0	1 (0.5)	2 (1.8)
Eye Discharge	0	0	0	0	1 (3.4)	2 (3.1)	1 (1.9)	1 (0.8)	1 (0.5)	2 (1.8)
Lacrimation Increased	0	0	0	0	1 (3.4)	2 (3.1)	1 (1.9)	1 (0.8)	1 (0.5)	2 (1.8)
GASTROINTESTINAL DISORDERS	6 (22.2)	10 (21.3)	17 (27.9)	27 (22.5)	7 (24.1)	19 (29.7)	9 (17.0)	20 (15.6)	14 (7.4)	22 (19.5)
Abdominal Distension	0	0	0	0	0	0	0	0	1 (0.5)	1 (0.9)
Abdominal Pain	0	0	3 (4.9)	3 (2.5)	5 (17.2)	8 (12.5)	5 (9.4)	7 (5.5)	4 (2.1)	5 (4.4)

Table III: RTF output showing effect from Data Set VIII

d) Printing page number Page x of y in header or footer is simple in RTF using tag set "Page ^{pageof}". Due to overflowing data, sometimes, a page gets split when information flows onto a new page, as it cannot be accommodated on the same page.

	A- no BF/CF		A + BF/CF		B- no BF/CF		B + BF/CF		No SP	
INFECTIONS AND INFESTATIONS	5 (18.5)	6 (12.8)	21 (34.4)	29 (24.2)	9 (31.0)	17 (26.6)	19 (35.8)	38 (29.7)	11 (5.8)	13 (11.5)
Bronchiolitis	0	0	0	0	1 (3.4)	1 (1.6)	2 (3.8)	5 (3.9)	1 (0.5)	1 (0.9)
Bronchitis	0	0	0	0	0	0	0	0	1 (0.5)	1 (0.9)
Exanthema Subitum	0	0	1 (1.6)	1 (0.8)	0	0	0	0	0	0

n (%) = Number (percent) of subjects, nAE = Number of adverse events, BF=Breast-feeding, CF=Complementary foods, SP = Study product
AEs are allocated to the state where the subject was at time of AE occurrence.
Program Source: H:\PharmaSUG\Raw\T_1_1.sas   Run Date: 02FEB2015   10:18
Data Source: H:\PharmaSUG\Raw

<div align="center">

Table
Frequency of Adverse Events by Dose, per Visit
Population: All Subjects Treated

</div>

SYSTEM ORGAN CLASS	A- no BF/CF		A + BF/CF		B- no BF/CF		B + BF/CF		No SP	
Preferred Term	n (%)	nAE (%)	n (%)	nAE (%)	n (%)	nAE (%)	n (%)	nAE (%)	n (%)	nAE (%)
Eye Infection	0	0	1 (1.6)	2 (1.7)	0	0	1 (1.9)	1 (0.8)	0	0
Gastritis Viral	0	0	1 (1.6)	1 (0.8)	0	0	0	0	0	0
Gastroenteritis	0	0	1 (1.6)	1 (0.8)	2 (6.9)	2 (3.1)	5 (9.4)	5 (3.9)	2 (1.1)	2 (1.8)

Table IV: RTF output with page split

 When such a file is opened in Notepad, one needs to be aware that, this split page, would not lead to an increase in the number of times the RTF tag set occurs. To work around this, a simple step is to check last value of page variable (PgBy – mentioned above) or print it in log output and compare against y value of page x of y after you open the RTF file. In case there is an issue with the split, we just need to adjust macro variable NOB value

CONCLUSION

This paper illustrated a unique alternative of summarizing AEs, on the basis of study product consumption patterns, for infant nutrition trials. The classification of AEs into different states, depending on SP, BF or CF, provides a more informative way of analysing AEs for such trials. The SAS programming snippets discussed towards the end can easily be adopted for other situations in reporting.

REFERENCES

[1] Long-term effects of breastfeeding A SYSTEMATIC REVIEW WHO
[2] CDISC Analysis Data Model (ADaM) Data Structure for Adverse Event Analysis Version 1.0

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