AsthmaNet APRIL and OCELOT STUDY FORMS AND DATASETS

Referencing the APRIL/OCELOT Study Forms and Datasets

Annotated APRIL/OCELOT case report forms (CRFs) are included on the enclosed CD in pdf format (APRIL_OCELOT_forms.pdf). Each CRF has an abbreviated name that is located in a shaded box in the lower right-hand corner of the form. Some of these abbreviated names begin with a 'P2_' prefix, and some do not. As a general rule, data corresponding to each CRF are stored in a data file of the same name. If the CRF abbreviation begins with a 'P2_' prefix, the name of the corresponding data file will have the 'P2_' prefix removed. All data file names must be 8 or less characters in length to be included in the transport file. If the CRF abbreviation has more than 8 characters, the name of the corresponding data file will be adjusted to only have 8 characters. This is specified in Table 1. Variable names for a particular CRF begin with the prefix that is assigned to that form followed by an underscore and the number of the field. Fields within each CRF are usually numbered sequentially and are located (in most cases) in parentheses on the left hand side of the responses to each question. For example, data regarding adverse events experienced by the APRIL/OCELOT subjects are collected on the Clinical Adverse Events form (form name AECLIN). Corresponding data are stored in file aeclin.sas7bdat. The variable name corresponding to the ICD9 code for a particular adverse event (field #1010) on the Clinical Adverse Events form is aec_1010.

Table 1 below outlines the relationship between each form name, dataset, and variable prefix. Where no form name is given, no CRF existed for collection of the relevant information during study implementation. Where no dataset name is given, the corresponding "form" was simply a reference card that was used to explain some element of data collection.

Table 2 below shows the CRFs that were completed at each study visit, either routinely or only on an as-needed basis.

Standard Data Edits

Each APRIL/OCELOT CRF includes a set of key variables in the upper right-hand corner. These variables may include: Participant ID (part_id), participant initials, visit number (vnum), visit/current date (vdate), and interviewer/technician/supervisor/coordinator ID. For the purpose of de-identifying the dataset, the following standard changes were applied to all public use datasets:

- Participant initials were omitted.
- All visit dates were converted to intervals representing the number of days from the participant's Visit 1 (initial screen visit).
- All interviewer/technician/supervisor/coordinator IDs were omitted.

All dates collected within a given CRF were converted to days from Visit 1. Unless otherwise noted, converted dates were stored in the original variable names given on the CRFs.

Data collected in source documentation boxes or fields (for example, heq_1000D, heq_1160D, heq_1250D from the Home Environment Questionnaire (HEQ form)) were omitted from the public datasets. Variables in the source documentation boxes remain annotated on the forms but they were not included in the datasets.

Comment fields and text descriptions related to a given question were deleted. These fields contain free text which may include dates or other participant-related details that risk possible identification.
Any additional changes made to a given dataset are summarized in Table 1 below.

Background

This protocol was originally comprised of two separate but linked clinical trials: APRIL and OCELOT.

Participants initially entered APRIL, a study to examine the efficacy of a macrolide antibiotic (azithromycin 12mg/kg once daily for 5 days, maximum dose 500mg/day) versus placebo administered at the early signs of respiratory tract illnesses (RTI) and continued for 5 days in attenuating the progression of an upper RTI into development of clinically significant lower respiratory tract (LRT) symptoms. The primary outcome measure for APRIL was the number of RTI that do not progress to treatment failure. If APRIL treatment failure is achieved, the participant will immediately proceed to OCELOT.

The APRIL protocol was originally designed as a 52-week study allowing participants to experience up to 3 respiratory tract illnesses instead of 4. The protocol was extended to 78 weeks in June 2012 because the North American 2011/2012 viral season was unusually mild and it was apparent that the power of both the APRIL and OCELOT studies had been compromised

due to the unexpectedly low rate of respiratory tract illnesses in the study population. At that time, approximately one-half of the study population had been enrolled. Of those, 60% were still in the original 52-week APRIL follow-up and 40% had completed the 52-week APRIL follow-up. All participants enrolled after the protocol change entered the 78-week follow-up period. Participants enrolled before the protocol change and still in the 52-week follow-up at the time of the protocol change were invited to join the 78-week follow-up and reconsented if they agreed. Participants who declined to join the 78-week follow-up were permitted to complete the 52-week follow-up under their original consent.

OCELOT was a study designed to evaluate the efficacy of oral corticosteroids (prednisolone 1mg/kg twice daily for 5 days, maximum dose 60mg/day) versus placebo when an upper respiratory tract illness has already progressed to significant LRT symptoms. The primary outcome measure of OCELOT was the Pediatric Respiratory Assessment Measure (PRAM) score 15 minutes post-bronchodilator, measured in the AsthmaNet clinic 36-72 hours after the initiation of OCELOT therapy. Study participation is terminated after one course of OCELOT therapy. OCELOT visits are visits 20 and 21.

In March 2013, an interim analysis was conducted and it was determined that the OCELOT study was not feasible and should be halted due to the low number of participants entering the OCELOT study. Therefore, two versions of the study protocol are included here, one pertaining to the original design with both APRIL and OCELOT components, and one pertaining to the remaining APRIL component following the discontinuation of OCELOT.

780 participants were enrolled into APRIL/OCELOT at Visit 1. They were 12-71 months of age with histories of recurrent, severe lower respiratory tract illnesses. 607 participants were randomized at Visit 2.

Table 1. APRIL/OCELOT Forms and Datasets

Form Name Abbreviation	Dataset Name	Variable Prefix	Form Name or Description	Field Changes/ Comments
AECLIN	aeclin.sas7bdat	aec	Clinical Adverse Events	• aec_1020, aec_1030 (dates) were altered as described above • aec_1000 is a sequential number assigned to each adverse event within a participant (starting from 01 up to 99) • Variables added to this dataset include: - icd9_cat: ICD-9 category - icd9long: Full description of ICD-9 code - icd9shrt: abbreviated description of ICD-9 code • The dataset used to code adverse events and link to descriptions was downloaded from www.cms.gov. ICD-9-CM Diagnosis and Procedure Codes: Abbreviated and Full Code Titles effective October 1, 2009 were used.
ASTHMA_HX_PED	asthmahx.sas7bdat	aha	Pediatric Asthma and Allergy History	• aha_1400D, aha_1410D, aha_1420D, aha_1460D, aha_1560D were omitted (description fields) • Comment field in aha_6000 was deleted

CMED	cmed.sas7bdat	cme	Concomitant Medications for Asthma/Allergy and Adverse Events	• cme_1060, cme_1070 (dates) have been altered as described above • cme_1000 is a sequential number assigned to each medication within a participant (starting from 01 up to 99) • Variables added to this dataset include: - class: drug class text - class_id: class ID number - gen_name: generic drug name • Units (cme_1040), frequency (cme_1050) and route (cme_1055) contain formatted values • Drug codes and classes were obtained from the American Society of Health-System Pharmacists, Inc. drug coding system (AsthmaNet purchased a license to use and update the data annually)
HEQ	heq.sas7bdat	heq	Home Environment Questionnaire	• heq_1710, heq_1720 were omitted (source doc fields) • heq_1000D, heq_1160D, heq_1250D, heq_1340D, heq_1410D, heq_1420D, heq_1460D, heq_1620D were omitted (description fields) • Comment field in heq_6000 was deleted
HOUSEHOLD__SEI	sei.sas7bdat	sei	Household Socio-Economic Information	• sei_1000D was omitted (description field) • Comment field in sei_6000 was deleted • Due to sparseness, sei_1030 was recoded such that all responses coded ≥6 were set to 6.
IMMUNOCAP	immune.sas7bdat		ImmunoCap Data	• Includes IgE, cat, dog, cockroach, mite, egg white, rat, ragweed, milk mouse, peanut, weed, tree, mold and grass.

PARENT_QOL	qol.sas7bdat	qol	Effects of a Child's Asthma Flare-up on the Parents	• AsthmaNet received permission to use the questionnaire for the APRIL/OCELOT study from the author Francine M. Ducharme. • The form is a validated 21-item questionnaire, completed by caregivers, to assess the impact of an asthma flare-up in their child on their quality of life. • pqol_1250D was omitted (description field)
PRAM	pram.sas7bdat	prm	Pediatric Respiratory Assessment Measure	AsthmaNet received permission to use the PRAM score for the APRIL/OCELOT study from the author Francine M. Ducharme. • The PRAM score is a validated measure for assessing asthma severity and response to treatment.
PRIOR_COND_ALL	cond_all.sas7bdat	pal	Prior Conditions for All Participants	• pal_1000D, pal_1010D, pal_1060D, pal_1110D, pal_1130D, pal_1150D, pal_1170D, pal_1180D were omitted (description fields) • Comment field in pal_6000 was deleted

PRIOR_TRT	priortrt.sas7bdat	ptr	Prior Asthma/Allergy Treatment	• ptr_1000D, ptr_1470D, ptr_1500D, ptr_1600D, ptr_1830D, ptr_1870D, ptr_1910D were omitted (description fields) • Comment field in ptr_6000 was deleted • Date intervals for the medication dates in Questions 2-22 were stored in variables date_q02-date_q22. If day was missing, but month and year were present, we calculated the date using the 1st of the month. If only the year was present, no date interval was computed (i.e., missing data).
	regimen.sas7bdat		Randomized treatment assignments	File contains the following variables: • part_id • apr_reg (either “Placebo” or “Azithromycin”) • oce_reg (either “Placebo” or “Prednisolone”)

REGISTRY	registry.sas7bdat	reg	AsthmaNet Registry information, including demographics	• reg_1020, reg_1040, reg_1060 (dates) were altered as described above • reg_1070 (birth date) was omitted; the participant's age at visit 0 was calculated and is stored in variable 'age' (as a whole number) • ethnicity and individual race variables have been omitted due to sparseness (reg_1090, reg_1100, reg_1110, reg_1120, reg_1130, reg_1140) • reg_1150 (primary racial identification) has been re-coded such that those who were in categories 1, 2 and 6 were included in the 'other' category (code 6) • reg_1160 (description for the 'other' race category was omitted
SERIOUS	serious.sas7bdat	ser	Serious Adverse Event Reporting Form	• ser_1000, ser_1080, ser_1090 (dates) were altered as described above • ser_1010D, ser_1180D, ser_1210D, ser_1220D were omitted (description fields) • Comment field in ser_6000 was deleted
LEXAM	lexam.sas7bdat	lx	Pediatric Long Physical Exam	• lx_1120D was omitted (description field) • Comment field in lx_6000 was deleted
SEXAM	sexam.sas7bdat	sx	Pediatric Short Physical Exam	• sx_1120D was omitted (description field) • Comment field in sx_6000 was deleted
P2_APRIL_COMPLY	a_comply.sas7bdat	cmp	APRIL Compliance Checklist	• cmp_1010 was altered (date) as described above • Comment field in cmp_6000 was deleted

P2_APRIL_TERM	a_term.sas7bdat	atr	Termination of APRIL	• atrm_1040, atrm_1050, atrm_1060 and atrm_1070 were omitted (source doc fields) • atrm_1010D was omitted (description field) • Comment field in atrm_6000 was deleted
P2__APRIL_TRTQX	a_trtqx.sas7bdat	att	APRIL Study Treatment Questionnaire	• atrt_1040D was omitted (description field) • Comment field in atrt_6000 was deleted
P2_DIARY_RUNIN	diary.sas7bdat	dry	APRIL Run-In Diary (only completed during Run-In period)	• dry_1010 (date) was altered as described above
P2_ELIG1	elig1.sas7bdat	e1	APRIL Eligibility Checklist 1	• e1_1010 (date) was altered as described above • e1_1850Dwas omitted (description field) • Comment field in e1_6000 was deleted
P2_ELIG2	elig2.sas7bdat	e2	APRIL Eligibility Checklist 2	• e2_1100D was omitted (description field) • Comment field in e2_6000 was deleted
P2_FONE_MED	fonemed.sas7bdat	fn	FONEMED	• fone_1000 (date) was altered as described above • Comment field in fone_6000 was deleted
P2_ILLNESS	illness.sas7bdat	ill	APRIL Respiratory Illness Follow-up Contact	• ill_1010, ill_1080, ill_1130, and ill_1160 (dates) were altered as described above • ill_1000D was omitted (description field) • Comment field in ill_6000 was deleted
P2_IMMUNOCAP	immune.sas7bdat	imm	APRIL Immunocap Results	• No changes
P2_LAB	lab.sas7bdat	lab	APRIL Laboratory Results	• Comment field in lab_6000 was deleted
P2_OCELOT_COMPLY	o_comply.sas7bdat	ocp	OCELOT Compliance Checklist	• ocmp_1010 (date) was altered as described above • Comment field in ocmp_6000 was deleted

P2_OCELOT_SCHED	o_sched.sas7bdat	oce	OCELOT Scheduling Form	• oce_1010, oce_1130, ice_1140 (dates) were altered as described above • oce_1000D and oce_1110D were omitted (description fields) • Comment field in oce_6000 was deleted
P2_OCELOT_TERM	o_term.sas7bdat	otr	Termination of OCELOT	• otrm_1020, otrm_1030, otrm_1040 and otrm_1050 were omitted (source doc fields) • otrm_1010D was omitted (description field) • Comment field in otrm_6000 was deleted
P2_OCELOT_TRTQX	o_trtqx.sas7bdat	ott	OCELOT Study Treatment Questionnaire	• otrt_1030D was omitted (description field) • Comment field in otrt_6000 was deleted
P2_PAD	pad.sas7bdat	pad	Pre-School Asthma Symptom Diary	• AsthmaNet received permission to use the Diary for the APRIL/OCELOT study from the author Francine M. Ducharme. • The diary is a validated 17-item questionnaire, completed by caregivers from onset of an upper respiratory tract infection until asthma symptom resolution. • ddate (date) was altered as described above • pad_1210D was omitted (description field)
P2_PERS_SYMP	perssymp.sas7bdat	ps	APRIL Persistent Symptoms	• Comment field in pers_6000 was deleted
P2_PHONE_CONTACT	phone.sas7bdat	phn	APRIL Phone/Visit Symptom Assessment	• Comment field in phn_6000 was deleted
P2_PRED	pred.sas7bdat	pr	APRIL Prednisolone Medication Form	• pred_1000 (date) was altered as described above • Comment field in pred_6000 was deleted

P2_STUDY_FAIL	study_fl.sas7bdat	fl	Study Failure	• fail_1130 (date) was altered as described above • fail_1140, fail_1150 and fail_1160 were omitted (source doc fields) • fail_1110D was omitted (description field) • Comment field in fail_6000 was deleted
P2_SURVEY	survey.sas7bdat	srv	APRIL Symptoms of Respiratory Illness Survey	• srv_1130 (date) was altered as described above • srv_1140, srv_1150 and srv_1160 were omitted (source doc fields) • Comment field in srv_6000 was deleted
P2_SYMP_CC	sympcc.sas7bdat	sym	APRIL Symptoms of Respiratory Illness	• Comment field in sym_6000 was deleted
P2_TERMR	termr.sas7bdat	trr	APRIL Run-In Termination	• trmr_1020, trmr_1030, trmr_1040 and trmr_1050 were omitted (source doc fields) • trmr_1010D was omitted (description field) • Comment field in trmr_6000 was deleted
P2_TRTFAIL	trtfail.sas7bdat	txf	APRIL Treatment Failure	• txf_1060 (date) was altered as described above • txf_1070, txf_1080 and txf_1090 were omitted (source doc fields) • txf_1040D was omitted (description field) • Comment field in txf_6000 was deleted

Table 2. Forms/Procedures Completed at each Study Visit (Visits 1-9, 20, 21)
(•=regular visit procedure; ❍=completed only as needed)

Form Abbreviation or Procedure Description	Visit Number											
	1	2	3	4	5	6	7	8	9	20	21	PC
AECLIN	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍
ASTHMA_HX_PED	•											
CMED	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍
HEQ	•											
HOUSEHOLD_SEI	•											
IMMUNOCAP		•										
PARENT_QOL											•	
PRAM										•		
PRIOR_COND_ALL	•											
PRIOR_TRT	•											
Randomization		•										
REGISTRY	•											
SERIOUS	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	
LEXAM_PED	•									•		
SEXAM_PED		•	•	•	•	•	•	•	•		•	
P2_APRIL_COMPLY			•	•	•	•	•	•	•	•	•	
P2_APRIL_TERM		❍	❍	❍	❍	❍	❍	❍	•			
P2_APRIL_TRTQX		❍	❍	❍	❍	❍	❍	❍	•			
P2_DIARY_RUNIN	•	•										
P2_ELIG1	•											

Form Abbreviation or Procedure Description	Visit Number											
	1	2	3	4	5	6	7	8	9	20	21	PC
P2_ELIG2		•										
P2_FONEMED	❍	❍	❍	❍	❍	❍	❍	❍	❍			
P2_ILLNESS		❍	❍	❍	❍	❍	❍	❍	❍			
P2_IMMUNOCAP		•										
P2_LAB		•	❍	❍	❍	❍	❍	❍	•		•	
P2_OCELOT_COMPLY											•	
P2_OCELOT_SCHED		❍	❍	❍	❍	❍	❍	❍				
P2_OCELOT_TERM											•	
P2_OCELOT_TRTQX											•	
P2_PAD			❍	❍	❍	❍	❍	❍	❍	❍	❍	
P2_PERS_SYMP			❍	❍	❍	❍	❍	❍	❍			
P2_PHONE_CONTACT			•	•	•	•	•	•				•
P2_PRED			❍	❍	❍	❍	❍	❍	❍			❍
P2_STUDY_FAIL		❍	❍	❍	❍	❍	❍	❍	❍	❍		
P2_SURVEY	•	•										
P2_SYMP_CC		❍	❍	❍	❍	❍	❍	❍	❍			❍
P2_TERMR	•	•										
P2_TRTFAIL		❍	❍	❍	❍	❍	❍	❍	❍			❍