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What is Quality Management?

- Quality Management (QM) is an overall system for oversight of the
- conduct of clinical research.QM ensures the rights and safety of participants in clinical research are protected and that data collected are accurate and complete.
- QM activities:
 - facilitate planning for protocol implementation
 assure compliance with regulations and requirements

 - identify areas in need of corrective action
 verify the accuracy of data
 - assure readiness for external monitoring and auditing

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- QM encompasses both Quality Control (QC) and Quality Assurance (QA) activities and provides staff with a system to identify and resolve problems with protocol implementation and regulatory compliance.

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	QC C	hart Audit Wo	rksheet		
CCHM Clinica Cincin	IC Gamble Program For al Studies nati Children's Hospital	Quality Cont	ol Notes		
Protoco	ol #: PID #:	Reviewer	Name:	Date Review	ed:
Docum	ents requiring action (check all tha	t apply):			
Inc/ Visi Lab Preş Oth	Exc criteria Informed consent it 1 Visit 2 Visit 3 Vis tests Concomitant Medication mory Aid/Diary Card 1 Memo gnancy Test log er	form ☐ HIV it 4 ☐ Visit 5 is ☐ Adverse ry Aid/Diary C	consent form (i Visit 6 Events Se ard 2	f indicated) Visit 7 5 fious Adverse	Supplemental vi Event
			Correction	Correction	Verified
Page	Corrective Actions Rec	uired	d initials:		completed initials:
-					
	AND THE OTHER DESIGNATION OF THE OTHER DESIGNATION.				



INDUSTR CCHM0 Cincinn Reviewer Subject N Date:	VY STUDES DA CHART AUET TOOL Camble Program for Clinical Studies, Division of Infections Diseases at Children's Hospital Medical Center Review Date: 	eriod: Fro	m Dale:		Through
	Informed Consent / Assent Form(s) and Process (See Code of Federal Regulations: 45 CFR 46, Section	ons <u>46.116</u>	and 46.1	17)	Action Required*
1.	Enrolment: Was the IRB approved version used to consent/assent the subject, valid at the time of signature? Vi #bate: Note: Rokew the regulatory IRE for IRB subsequent revisionsamendments to the consent forms.	No	Date Resolved		
2.	Was the informed Consent/Assent Form signed and dated in ink by the subject, parentlyuardian and/or legally au preprior to the prior to implementation of screening interfaced-specific netroduces?	shorized	Yes	No	
3.	Amendments to consent: If applicable, are amended versions of the ICF signed and dated in ink by the subject, parent/suardian and/or legally authorized representative on file? Version # Date:	No			
4.	Are all applicable Informed Consent/Assent Forms present in their entirety?	No			
5.	If applicable, are informed Consent deviations documented?	Yes	No		
6a.	Was the DMID Protocol Deviation Form completed, submitted to DMID and the IRB per reporting guidelines, and filed in the resultator (Ik-2	NA	Yes	No	
	Eligibility Criteria – Inclusion/Exclusion Criteria				Action Required?
1.	Is documentation of eligibility criteria (inclusion/exclusion) in the source documents?		Yes	No	Disc IN JURY
2.	Are the Concernitant Medications documented accurately? Note: Check spelling, coding, and consistency between medical history and adverse events.		Yes	No	
3.	Was the eligibility documentation signed, credentialed, and dated by the clinician responsible for enrolling the sub	bjed?	Yes	No	
3a.	Is this individual listed on the Study Personnel Signature/Responsibility List?		Yes	No	
4.	If applicable, were enrolment deviation documented?	NA	Yes	No	
4a.	Was the DMID Protocol Deviation Form completed, submitted to DMID and the IRB per reporting guidelines, and filed in the regulatory file?		Yes	No	
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Study Product – Administration and Documentation Note: unblinded personnel must not perform chart reviews	Action Required/ Date Resolved			
Was the study product dispensed upon written order of the investigator (or designee) as listed on the FDA Form 1572?				
s this study product administrator listed on the Study Personnel Signature/Responsibility List?	Ö			
s documentation present describing the study product administration (according to the current version of the protocol a MOV/2 Noviem 8	and			
New J. Visional P. Montham J. Market and A. Market and	D NA	Yes	No No	
Are deviations documented in the source documents and the DMID Protocol Deviation Form completed and interesting to DMID and the IDB nor constitution acidations?	D NA	U Yes		
s the final verification box on the physician order form signed by a second pharmaciti or un-blinded vaccinater who ob that the following lines were double-becked: final product was labeled with the correct subject and randomization nur dose and product were prepared correctly, and the product appearance was according to protocel specification? "Performed by autoficial personant". Unifielded personant Signature 2.	nbors; the	Pes	DN0	
Adverse Event (AE) and Serious Adverse Event (SAE) Identification and Reporting				Action Required/ Date Resolved
Are all adverse events and/or laboratory abnormalities found in the subject chart identified?	□ N/A	Yes	No	
tre all adverse events assessed for clinical significance and/or seventy, and relationship to the study product and locumented in the source documents?	🗆 N/A	Yes	No	
Were all adverse events identified in the protocol as critical to safety evaluations reported according to the protocol archive MOP within the searcific time periods?	D NA	Yes		
Vere all solicited adverse events (i.e. reactogenicity) recorded at protocol-specified timeframes with appropriate draws of 2	□ N/A	U Yes		
Nere all adverse events meeting the serious adverse event criteria (see DMID SAE Recording and Reporting Criterines) constant within the DMID snar-flast timetimes of site assurances or as snar-flast by the meterol/2	□ N/A	Yes		
Was the Serious Adverse Event(s) Report completed accurately? Max- See DMID SAE Docenting and Reporting California	□ N/A			
Vere all serious adverse events been reported to the local IRB, as required?	□ NA	0		
Deviations from Protocol – Missed Tests/procedures and Missed Visits				Action Required/
Vere all protocol-specific tests and/or procedures completed?		U.Ver		
no, was the DMID Protocol Deviation Form completed and submitted appropriately?	I NA			
Nas the deviation(s) documented in the source documents?	□ NA	0		
Nere all missed visits and/or out of window visits identified?				
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	Sample QA Tool I	Pa	ge	3	- Anton
28.	If yes or no, was the DMID Protocol Deviation Form completed and submitted appropriately?	N/A	Yes	No	
2b.	Was the deviation documented in the source documents?	N/A	Yes	No	
	Endpoints				Action Required/ Date Resolved
1.	Were applicable study-defined clinical and/or laboratory assessments/endpoints documented in the subject's source d and/or an endpoint-specific CRF/eCRF as required by the protocol?	ocuments	Yes	No	
	Intervention/Study Discontinuation			-	Action Required/ Date Resolved
1.	If the subject discontinued study intervention; were protocol-required steps followed?		Yea	No	
2	If the subject discontinued from the study: were protocol-required steps followed?				
	Documentation Standards				Action Required/
1.	Were source documents complete and accurate?				
2.	Does the CRF/eCRF data and source documentation data match?				
1.	Addenda: Are all addenda signed or initialed and dated in present time by the person making the entry i.e. 7				
2	Note: Lio hit allor pare-based addenda, chart notes, progress notes, etc. Chart Note(s): Are all handaritien notes legible and signed and dated by the responsible credentialed clinician?				
2	Case Report Forms (CRF/eCRF): Prior to commencement of the study, were CRFs/eCRFs used as source				
34	Are the CPEsic CPEs used as yource documents signed and dated?		Ü		
4.	Error Correction(s): Are all error corrections clear with a single line drawn through the incorrect information, initialed, o a reason for change (if necessary)?	fated, and	Ves		
5	Note: Never obserate entries or destroy origina documents that require correction. Never use writeout or percas Datent Identification Numbers: Are all source documents labeled with annormale national identification numbers (DIT)	7			
۵.	Dealth: If a subject dealth was identified, has the incident been documented in the source documents by one of the footware, 3. Oktavry 2. Aktory Report	I NIA	Ven		
7.	Least Communication Contract Report More Communication Contract Report Sen DMD Ack Report Report Sen DMD Ack Report Report Contract Copies and Verification. Are all documents recruised in cubic data (and and account on the other (and a indicated by signalized and data, and exact copy having all the same attributes and contract copy having at Report Report of the same attributes and	N/A			
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I.	Flow-sheets used as Source Documents: Are all entries onto flow-sheets initialed and dated by the responsible clinician?	Yes	No		
2.	Chronology of Source Documents: Are source documents maintained chronologically?	Yes	No		then Demonstrati
_	Case Report Form and electronic Case Report Form Submission			~	ate Resolved
-	Are all scheduled CRF's present?	Yes	No		
-	Were the CRF's submitted within the required timeframe?	Yes	No		
L	within the required irreframe?	Yes	No		tion Demonstrad
	Laboratory Review - Specimen Collection and Results INOT APPLICABLE		i —	~	ate Resolved
	Were all splichners concerted and documented in the solucie incomments. Note that the splichners concerted and documents of the protocol occurs of the protocol occurs of the protocol occurs	Yes	No		
1	Were specimens prepared, labeled, and transported properly per the international Air Transport Association (IATA) regulations?	Yes	No		
L	Are temperature logs for stored specimens current and accurate?	Yes.	No		
un	imany of Findings: < Provide a summary of any accumulated issues from above and provide the optimeter of the control we accumulated issues from above and provide the optimeters of information and accumulated issues of the optimeters of information accumulated issues from above and provide the optimeters of information accumulated issues from above and provide the optimeters of information accumulated issues from above and provide the optimeters of information accumulated issues from above and provide the optimeters of information accumulated issues from above and provide the optimeters of information accumulated issues from above and provide the optimeters of information accumulated issues from above and provide the optimeters of information accumulated issues from above accumulated issues from accumulated issu	CONCELLA	actors	and appreated	roeow-up >
	over Skynolater (<u>nat Article)</u> Date:	compare a	d too dastado	or for agreement.	Be save to include lab :
đ	should be find in the QM binder at the size. "Alt of unblinded to instanticle will be assigned to QA-QC reviews of instanticle strange, handling, as binded in the twin attack will not be assigned to these tasks.		ty and ada	delaterities. To es	ure integrity of the cludy

Review of Regulatory Files (Binder)

- Performed by Quality Manager (or designee) at study start-up, annually, and as needed
 - Complete regulatory review tool
 - Return to Quality Manager for review

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- Review Tool returned to coordinator for corrections
 Follow-up review with Quality Manager after corrections
- Quality Manager meets with staff to discuss trends, issues, and resolutions

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 Quality manager reports findings & actions in monthly report to Director and Clinic Manager



Protocols : 0047, 005 Recruitme	and consents v I, 0060, 0073 Int and study or ober 2009 wit	vere created an pordinators resp	d IRB applications	were submitte nately 10,500 o	ed in record ti calls generati	ime for DMID p ed by media co N1	rotocols: 0032, 004 verage and genera	3, 0053, 0039, I interest from			
DMID Study #		Target Enrollmen	Approximat e # telephone Screens	Total # Screened	Number Enrolled	Visits Complete d	Vaccines Randomized & Administered	Specimens Processed and Shipped			
DMID		200	400	260	220	1600	1041	10854 / 4658			
0039	Adult				102						
	Fiderly				118						
DMID 0047		100	250	113	108	966	322	3078 / 1539			
	6-36 mo			44	41	365	1				
	3-9 yrs			35	33	297 304 169	297	_	-		
DMID 0058	10-17 yrs	60	95	79	60		115	115 2340 / 0			
	Adult			49	40		1				
	Elderly			30	20						
DMID 0073	Adults	20	10	3	3	3	3	3/0			
	10.0100.001	119.1									

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- Performed by designated lab and investigational pharmacist and/or un-blinded study personnel
- QC:
- Complete QC checks using appropriate tools
- QA: Review first 10 records and a minimum of
- 10% of subject charts for each study and record on QA forms
- Submit monthly reports to Quality Manager
- Monthly meetings with Quality Manager to review processes and trends

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QM Oversight of Multi-Center Studies

- Quality Manager provides oversight of subcontractor's quality management activities
 - Reviews and approves sites QMP prior to submission to sponsor
 - Reviews sites monthly QM reports
 - Participates in monitor de-briefing and QM reviews
 - Resource for site quality management activities







Corrective Actions

- Majority of corrective actions were related to data collection and entry

 Modified QC systems to identify errors prior to and during data entry
- Identified potential for study product administration error
- Modified Physician Order form to include additional QC check at point of vaccine administration
- Identified issue with process for emergency rescue of study product
 Modified SOP to clarify procedures for maintaining cold chain
- Based on initial QC results, identified visit window error
 Modified online visit scheduler and contacted subject to reschedule able
 to prevent protocol deviation
- Identified issue with sponsor's electronic data entry reports
 Communicated this information to Data Center, who corrected the reports

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					QA Trei	nds/Issu	les					
Study Number	r											
Review Month Total Number of Charts Reviewed		0										
Date	# of Charts Reviewed	Consent Process	Eligibility Criteria	AE/SAE Issues	Missing Data - SD	Incorrect Data	Improper Error Correction	Signature Missing	Product Admin	Visit Schedule	Specimen Collection	Other (Specify
Totals	0			0	0	0	0	0	0	0	0	











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