Clinical Trials Monitoring Branch Final Report

Attachment D04

Audit Date: 01/19/2017 **Credited Group:** ECOG-ACRIN **Auditing Group:** ECOG-ACRIN **Audit Category:** Treatment **Audit Type:** Routine audit

Institution CTEP Code: PA412 **Name:** Susquehanna Cancer Center, Williamsport, Pennsylvania - 17701, USA **Membership Study Type:** Treatment

Audit Location: Susquehanna Cancer Center, 1100 Grampian Boulevard, Williamsport, Pennsylvania-17701, USA

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Date of Prior Audit: **Number of Cases Audited:** 6 **Average Annual Accrual:** 10 **Principal Investigator:** Warren Lewis Robinson, Jr, MD

Institution Details

Institution CTEP Code	Institution Name	Role
PA042	**Penn State Milton S Hershey Medical Center**	**Main Member**
PA412	Susquehanna Cancer Center	Affiliate

Audit Outcome Summary

Component	Assessment	Follow up Required (Y/N)	Follow up Due Date	Reaudit Required (Y/N)	Reaudit Time (in months)
IRB and Informed Consent Content Review	Acceptable	No		No	
Accountability of Investigational Agents	Acceptable needs follow-up	Yes		No	
Patient Case Review	Acceptable	No		No	

Institution Staff	Title	Affiliation
Robinson, Warren Lewis Jr (MD)	Senior Investigator	Susquehanna Cancer Center
Yohn, Marianne (MMGT, CCRP)	Clinical Trials Data Specialist	Susquehanna Cancer Center
Miller, Susan (RN, OCN)	Clinical Trial Research Nurse	Susquehanna Cancer Center
Gaida, Michelle	Executive Director, Cancer Services	Susquehanna Cancer Center
Stank, Elaine (RN)	Clinical Trial Research Nurse	Susquehanna Cancer Center
LeCrone, Joseph (PharmD)	Pharmacist	Susquehanna Cancer Center
Narret, Cindy (PSCHI)	Clinical Trials Director	Susquehanna Cancer Center

Audit Team	Title	Affiliation
Lawson, David (MD)	Physician Auditor	Emory University
Pitts, Susan (B.Sc., SRN)	ECOG-ACRIN Lead Auditor	ECOG-ACRIN Cancer Research Group
Harwood, Suzanne (RN, BSN, OCN, CCRP)	ECOG-ACRIN Lead Auditor	ECOG-ACRIN Cancer Research Group

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IRB Review

Protocol#	# of Patients	IND or NCI Supplied Agents	Diseases	CTMB Guidelines Deficiency Major / Lesser	Overall IRB Deficiency	Description of Deficiency and Comments
A071102* (PA412)	1	ABT-888 (Veliparib) (IND ,NCI/PMB)	Glioblastoma multiforme	0/0	OK	
CALGB-80702* (PA412)	1	Celecoxib (Celebrex) (IND ,NCI/PMB)	Adenocarcinoma of the colon	0/0	OK	
E1609 (PA412)	1	Ipilimumab (BMS-734016; MDX-010 Transfectoma-derived) (IND ,NCI/PMB)	Melanoma	0/0	OK	
E1912* (PA412)	1	Ibrutinib (PCI-32765) (IND ,NCI/PMB)	Chronic lymphocytic leukemia, NOS	0/0	OK	
EAY131 (PA412)	1	Dasatinib (BMS-354825, Sprycel) (IND ,NCI/PMB), Sunitinib malate (SU011248 L-malate) (IND ,NCI/PMB), GDC-0449 (Vismodegib) (IND ,NCI/PMB), BMS-936558 (Nivolumab, MDX-1106) (IND ,NCI/PMB), Crizotinib (PF-02341066) (IND ,NCI/PMB), Trametinib (GSK1120212B) (IND ,NCI/PMB), Dabrafenib (GSK2118436B) (IND ,NCI/PMB), Afatinib (IND ,NCI/PMB), AZD4547 (IND	Lymphoma, NOS, Myeloma, NOS, Solid tumor, NOS	0/0	OK	

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IRB Review

Protocol#	# of Patients	IND or NCI Supplied Agents	Diseases	CTMB Guidelines Deficiency Major / Lesser	Overall IRB Deficiency	Description of Deficiency and Comments
		,NCI/PMB), Palbociclib (PD-0332991) (IND ,NCI/PMB), GDC-0032 (taselisib) (IND ,NCI/PMB), ado-trastuzumab emtansine (IND ,NCI/PMB), AZD9291 (osimertinib) (IND ,NCI/PMB), GSK2636771B (IND ,NCI/PMB), VS-6063 (defactinib hydrochloride) (IND ,NCI/PMB), AZD5363 (IND ,NCI/PMB), Binimetinib (IND ,NCI/PMB)				

Total# of Patients: 5 **Total Protocols Reviewed:** 5 **Total Major/Protocol(s):** 0/5 **Total Lesser/Protocol(s):** 0/5

*** after Protocol# indicates that Informed Consent Content was reviewed for that protocol**

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Informed Consent Content (ICC) Review

Protocol#	Number of Missing/Incomplete Elements from ICC	Overall ICC Deficiency	Description of Missing/Incomplete Elements and Comments
A071102 (PA412)	0	OK	
CALGB-80702 (PA412)	0	OK	
E1912 (PA412)	0	OK	

Total# of Patients: 3 **Total Protocols Reviewed:** 3 **Total Major/Protocol(s):** 0/3 **Total Lesser/Protocol(s):** 0/3

IRB and Informed Consent Content Assessment

IRB and Informed Consent Content assessment: Acceptable

Follow-up required for IRB deficiency: No

Follow-up required for Informed Consent Content deficiency: No

Re-audit required for IRB and Informed Consent Content section: No

Overall Comments:

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Pharmacy Review

Were INDs or NCI supplied agents used at this site during the period covered by this audit: Yes

Drug accountability checked during this audit: Yes

Protocol#	Number of NCI DARFs compared to shelf inventory	Number of patients cross checked with NCI
A071102 (PA412)	1	1
CALGB-80702 (PA412)	1	1
E1912 (PA412)	1	1

Compliant	Non-Compliant	Not Reviewed	
[ ]	[X]	[ ]	NCI DARFs Completely and Correctly Filled Out

Protocol A071102 (PA412) Compliant

Protocol CALGB-80702 (PA412) Non-Compliant
COMMENTS: DATA MASKED

Deficiency: - Oral NCI DARF not maintained or not completely and accurately filled out

Protocol E1912 (PA412) Non-Compliant
COMMENTS: DATA MASKED

Deficiency: - Oral NCI DARF not maintained or not completely and accurately filled out

[ ]	[X]	[ ]	NCI DARFs Protocol and Agent specific

Protocol A071102 (PA412) Compliant

Protocol CALGB-80702 (PA412) Non-Compliant
COMMENTS: DATA MASKED

Deficiency: - Single DARF used for multiple patients/study participants on study when patient-specific DARF should be maintained

Protocol E1912 (PA412) Compliant

[ ]	[ ]	[X]	Satellite Records of Dispensing Area

Protocol A071102 (PA412) Not Reviewed
COMMENTS: DATA MASKED

Protocol CALGB-80702 (PA412) Not Reviewed
COMMENTS: DATA MASKED

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Compliant	Non-Compliant	Not Reviewed	
			Protocol E1912 (PA412) Not Reviewed COMMENTS: DATA MASKED
[X]	[ ]	[ ]	NCI DARFs Kept as Primary Transaction Record
			Protocol A071102 (PA412) Compliant
			Protocol CALGB-80702 (PA412) Compliant
			Protocol E1912 (PA412) Compliant
[X]	[ ]	[ ]	Return of Study Agent
			Protocol A071102 (PA412) Compliant
			Protocol CALGB-80702 (PA412) Compliant
			Protocol E1912 (PA412) Compliant
[X]	[ ]	[ ]	Study Agent Storage
			Protocol A071102 (PA412) Compliant
			Protocol CALGB-80702 (PA412) Compliant
			Protocol E1912 (PA412) Compliant
[X]	[ ]	[ ]	Adequate Security
			Protocol A071102 (PA412) Compliant
			Protocol CALGB-80702 (PA412) Compliant
			Protocol E1912 (PA412) Compliant
[X]	[ ]	[ ]	Authorized Prescription(s)
			Protocol A071102 (PA412) Compliant
			Protocol CALGB-80702 (PA412) Compliant
			Protocol E1912 (PA412) Compliant

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Pharmacy Assessment

Pharmacy Assessment: Acceptable needs follow-up

Follow-up Required: Yes **COMMENTS:** Please provide a corrective and preventative action plan to ensure DARFs are completed accurately.

Re-audit Required: No

Pharmacy Narrative: Ms. Harwood performed an on-site review of the control pharmacy located at Susquehanna Cancer Center with Joseph LeCrone, Pharm.D. The INDs are being stored appropriately in the control pharmacy, and the control pharmacy has adequate security measures in place. There are ten members of the control pharmacy staff who have access to the INDs. Ms. Pitts and Ms. Harwood reviewed the drug accountability record forms (DARFs) along with the transaction forms (orders, receipts, returns, and/or transfers) for the control pharmacy for three of the INDs associated with the review of the patient case records. There are no satellite pharmacies associated with this control pharmacy.

During the review of the control DARFs and transaction forms, all of the transactions recorded on the control DARFs coincided with the transaction forms and the medical records.
However, the following noncompliance was noted:
C80702: The shelf inventory balance carried forward was not recorded on pages 2 or 3 of the DARF.
C80702: A single DARF for celecoxib/placebo capsules was maintained for two patients. The site discovered this non-compliance during preparation for the audit and a CAPA dated 01/12/2017 was developed and has been appended to this report.
E1912: The shelf inventory balance carried forward was not recorded on pages 3 and 4 of the DARF.

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Patient Case Review

Protocol#	Patient#	Category	Result	Description of Deficiency and Comments
A071102 (PA412)	9103695	Informed Consent	OK	
		Eligibility	OK	
		Treatment	OK	
		Disease Outcome/Response	OK	
		Adverse Event	Lesser	**Deficiency:** - Recurrent under- or over-reporting of adverse events COMMENTS: DATA MASKED
		General Data Management Quality	OK	
CALGB-80702 (PA412)	137686	Informed Consent	OK	
		Eligibility	OK	
		Treatment	OK	
		Disease Outcome/Response	OK	
		Adverse Event	Lesser	**Deficiency:** - Recurrent under- or over-reporting of adverse events COMMENTS: DATA MASKED
		General Data Management Quality	Lesser	**Deficiency:** - Recurrent missing documentation in the patient/study participant records COMMENTS: DATA MASKED
E1609 (PA412)	17643	Informed Consent	OK	
		Eligibility	OK	
		Treatment	OK	
		Disease Outcome/Response	OK	
		Adverse Event	Lesser	**Deficiency:** - Recurrent under- or over-reporting of adverse events COMMENTS: DATA MASKED

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Patient Case Review

Protocol#	Patient#	Category	Result	Description of Deficiency and Comments
E1609 (PA412)	17643	General Data Management Quality	Lesser	**Deficiency:** - Errors in submitted data COMMENTS: DATA MASKED
E1912 (PA412)	19221	Informed Consent	OK	
		Eligibility	OK	
		Treatment	OK	
		Disease Outcome/Response	OK	
		Adverse Event	Lesser	**Deficiency:** - Recurrent under- or over-reporting of adverse events COMMENTS: DATA MASKED
		General Data Management Quality	OK	
EAY131 (PA412)	11311	Informed Consent	OK	
		Eligibility	OK	
		Treatment	Not Reviewed	
		Disease Outcome/Response	Not Reviewed	
		Adverse Event	OK	
		General Data Management Quality	OK	
S1207 (PA412)	261646 *Unannounced Case	Informed Consent	OK	OVERALL COMMENTS: DATA MASKED
		Eligibility	OK	OVERALL COMMENTS: DATA MASKED
		Treatment	Not Reviewed	OVERALL COMMENTS: DATA MASKED
		Disease Outcome/Response	Not Reviewed	OVERALL COMMENTS: DATA MASKED
		Adverse Event	Not Reviewed	OVERALL COMMENTS: DATA MASKED
		General Data Management Quality	Not Reviewed	OVERALL COMMENTS: DATA MASKED

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Patient Case Review

Protocol#	Patient#	Informed Consent	Eligibility	Treatment	Disease Outcome / Response	Adverse Event	General Data Management Quality
A071102 (PA412)	9103695	OK	OK	OK	OK	Lesser	OK
CALGB-80702 (PA412)	137686	OK	OK	OK	OK	Lesser	Lesser
E1609 (PA412)	17643	OK	OK	OK	OK	Lesser	Lesser
E1912 (PA412)	19221	OK	OK	OK	OK	Lesser	OK
EAY131 (PA412)	11311	OK	OK	Not Reviewed	Not Reviewed	OK	OK
S1207 (PA412)	261646 *Unannounced Case	OK	OK	Not Reviewed	Not Reviewed	Not Reviewed	Not Reviewed

Total # of Patient cases: 6 **Total # of Major deficiencies:** 0 **Total # of Lesser deficiencies:** 6 **Total # of items Not Reviewed:** 6

Patient Case Review Assessment

Patient Case Review Assessment: Acceptable
Follow-up required for Informed Consent: No
Follow-up required for Eligibility: No
Follow-up required for Treatment: No
Follow-up required for Disease Outcome/Response: No
Follow-up required for Adverse Event: No
Follow-up required for General Data Management Quality: No
Reaudit required: No

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Audit Procedures: The ECOG-ACRIN Operation Center records were compared with the hospital records. The audit was conducted in accordance with CTMB Guidelines.

General Comments: The auditors were very impressed with the quality of the documentation reviewed and the processes put in place at the site to ensure protocol adherence.

Exit Interview Comments: Dr. Lawson, Ms. Pitts and Ms. Harwood conducted the exit interview with Dr. Robinson, and the staff noted on the first page of this audit report; Ms. Narret attended by telephone. On behalf of the audit team, Ms. Pitts thanked Dr. Robinson and the staff for their hospitality, audit preparation, assistance during the audit, and participation in ECOG-ACRIN.

Ms. Pitts indicated that the audit team will be recommending an Acceptable outcome for the regulatory review to the ECOG-ACRIN Audit Committee as no deficiencies were noted in the review of the selected protocols and consent forms.

In the review of the pharmacy component, Ms. Pitts provided a summary of the noncompliance that was identified during the review of the DARFs and pharmacy. Ms. Pitts indicated that the audit team will be recommending an Acceptable Needs Follow-up outcome for the pharmacy component to the ECOG-ACRIN Audit Committee.

Dr. Lawson along with the other auditors reviewed the chart component and indicated that only lesser deficiencies were identified. An unannounced case (S1207 Subject # 261646) was included in this audit and included a review of the informed consent and eligibility audit categories. The auditors indicated that they found the source documentation to be very detailed. The charts were extremely well prepared and the CRAs were present to assist the auditors with navigating the charts. In general, the site did an excellent job in obtaining the protocol-related parameters and ensuring that the patients were treated according to the protocols. Ms. Pitts indicated that the audit team would be recommending an Acceptable outcome to the ECOG-ACRIN Audit Committee.

In preparation for the audit, the site identified the pharmacy non-compliance regarding the use of a DARF for the C80702 study; transactions for two patients were reported on a single DARF when a separate DARF should have been used for each patient. Ms. Pitts acknowledged that the site provided a copy of a corrective and preventative action (CAPA) plan in regard to this issue; that document is appended to this report. As an additional pharmacy non-compliance was noted, when the audit report is finalized, ECOG-ACRIN will provide a copy of the report and request an amended or additional CAPA plan. The CAPA plan must be submitted to ECOG-ACRIN within two weeks of receiving the final version of the audit report. The CAPA will need to be reviewed and approved by the ECOG-ACRIN Audit Committee as well as the Clinical Trials Monitoring Branch.

Debra Springfield	02/02/2017		
Prepared By	**Date**	**Approved By**	**Date**