	3. Study team should be re-trained on proper documentation practices.		
Action Taken/Response:			
Person Provided Response:		**Date:**	DD-MMM-YYYY

FINDING #8	**CATEGORY: SDV**	**RATING: Major**

FINDING:

Discrepancies were identified for 5 of 5 subjects reviewed between source and EDC (REDCap). Examples include:

Subject 2155149 (#22)

	Source	REDCap
8/4/17: Lesion 1	2.7 cm	2.5 cm
Total measurements	13 cm	12.8 cm
8/4/17	Progression is not noted for both osseous metastases and pulmonary nodules	Indicates progression = no
8/16/17	Clinical notes from EPIC indicates subject instructed to take 2 pills today. Research medication diary (hand written lists date of clinic 8/17/18 and 2 pills taken at 9:30 am	Not available
Study start date	Epic notes on 3/28/18 incorrectly state study start date of 8/14/17 but subject did not sign consent until 8/16/17	

Subject 2258901(#71)

	Source	REDCap
Informed consent	Subject agreed to the optional procedures	These spaces are blank.
Tumor measurements	Done on 4/26/18 and 7/17/18	Missing from REDCAP

Subject 2251291 (#69)

	Source	REDCap
Tumor measurements	Done on 2/27/18 and 5/9/18.	Missing from REDCAP

2246025 (#65)

	Source	REDCap
Concomitant Medications	11 are listed in EPIC	8 listed in REDCap
Tumor measurements	Target Mass is a "Right Breast Mass" and not one of the lungs.	Value is not listed in Red Cap.

#24 (MRN 2155369)

		Source	REDCap
	Concomitant Medications	Several listed in EPIC	None are listed in REDCap
	Tumor Measurements		have not been entered in REDCap for the scans run on 11/15/2017
REFERENCE(S):	21 CFR 312.57 ICH E6 R2 4.9		
Recommendation:	100% SDV of manual data entry into REDCap should occur.		
Action Taken/Response:			
Person Provided Response:		**Date:**	DD-MMM-YYYY

Finding #9	**CATEGORY: Investigational Product Accountability**	**RATING: Major**

FINDING:	Inadequate documentation of IP and CAPA recommendation for Pharmacy finding:
	• 2155369 (#24)
	  ○ Research Medication Diary
	  ▪ Entries on Days 29-31 are illegible. Clarification comments should be made by staff in these instances.
	  ▪ Patient signed the form on Day 1. Study staff should have had her re-sign when she returned with the document.
	• 2246025 (#65)
	  ○ Research Medication Diary
	  ▪ Document is incomplete with no explanation.
	  ▪ IP accountability is on a Post-It note but not documented in Progress Notes.
	  ○ Progress Note 2/22/18 – states that no study drug was dispensed; however, the Research Medication Diary document has 15 dose dates recorded.
	• 2251291 (#69)
	  ○ Research Medical Diary (March/April)
	  ▪ Not signed by subject
	  ▪ Has 56 tablets dispensed as per EPIC. Diary records 27 days of dosing (note: 3/26/2018 did not have a dose recorded) from 3/12/18 through and including 4/9/18. Progress notes in EPIC for 4/9/2018 state that [0] drug was returned. There are two 8mg pill unaccounted for.
	  ▪ There is no documentation that the empty bottle from the second round of treatment were ever returned by the subject. Progress notes indicate that he forgot to bring them to the 5/7/2018 visit and that he would mail them back.	

	• 2155149 (#22)
	  ○ Research Medication Diary for Aug/Sept ends with day 26 being 9/11/17 and subject took 2 pills at 6:15 am; the next diary starts as Sept diary and indicates day 1 as 9/11/17 and indicates that 2 pills were taken in the clinical at 9:30 am. Same dates were included on 2 different diaries with 2 different dose times noted.
	  ○ No pills taken on 10/10/17 per patient diary, EDC states all pills taken
	  ○ Research Medication Diary notes 11/6/18 on 2 different diary sheets for months Oct/Nov: and Nov/Dec and the different diaries notes 2 pills taken at 5:10 am and 7:00 am
	  ○ No pills taken on 12/5/17 per patient diary
	  ○ 3/1/18 on is noted on 2 different diary pages and indicates pills taken at different times; 2 pills taken at 6:40 am and 6:30 am
	  ○ 3/28/18 is noted on 2 different diary pages and indicates that pills were taken at 2 different times; 2 pills taken at 6:45 am and 8:30 am
	  ○ 4/24/18 is noted on 2 different diary pages and indicates that pills were taken at 2 different times; 2 pills taken at 6:20 am and 6:30 am respectively.
	  ○ No diary charts after 5/20/18; per EPIC last dose is 5/20/18; per REDCap subject d/c from study on 6/12 due to disease progression.
	  ○ REDCap 9/11-10/11/17 indicates 56 tabs dispensed, 0 tabs returned, 56 tabs taken; Source Research medication diary indicates between 9/11-10/9 "2 pills" take each day (total of 60 pills); additionally, source indicates not pills taken on 10/10/17.
	  ○ Source Research medication diary indicates between 10/11-11/6 "2 pills" take each day (total of 54 pills); REDCap 10/11-11/6/17 indicates 56 tabs dispensed, 0 tabs returned, 56 tabs taken.
	  ○ Source Research medication diary indicates between 11/6/17-12/4/17 "2 pills" take each day (total of 58 pills); there is no source record for dosage on 12/5/17; REDCap 11/6/17-12/6/17 indicates 56 tabs dispensed, 0 tabs returned, 56 tabs taken.
	  ○ Source Research medication diary indicates between 12/6/17-1/3/18 "2 pills" take each day (total of 58 pills); REDCap 12/6/17-1/3/18 indicates 56 tabs dispensed, 0 tabs returned, 56 tabs taken.
	• 2258901 (#71)
	  ○ Medication diary card started dose on 5/17/18; REDCap has start date of 5/2/18
	  ○ Medication diary card shows 1 pill per day taken from 5/17-5/27 (11 dosages); REDCap indicates 56 tabs dispensed, 30 returned. 26 actually taken.
	  ○ Medication diary card shows dosages not taken on 6/13-14; 7/5-8; 7/11, 7/14 and 7/17/18- medication diary card shows 26 pills taken in above time period; REDCap drug compliance screen for 6/13-7/17/18 indicates dosage missed on 6/13-14; 7/5-8 only;

	REDCap indicates 70 tablets dispensed, 18 returned therefore 52 actually taken for the above time period. ○ 15 pills of 12 mg taken from 7/19-8/5 per research medication diary; Drug accountability not completed in REDCap for 7/18-8/5 period. • Drug Dispensing Error (2016-0783/2013-0090): The preventive action implemented is not sufficient in that may not prevent incorrect labeling and dispensing of IP in the future.		
REFERENCE(S):	21 CFR Part 312.57; ICH E6 R2 4.6,		
Recommendation:	1. IIS team should document IP accountability methodology for REDCap. 2. 100% QC of IP accountability should be done 3. IIS team should follow up on recommendation for improving the CAPA plan for pharmacy finding to ensure a more complete action such as: Labels should be placed on the bag with the drug prior to verification. If the drug does not match the label, then the process starts over again. Additionally, when filling a prescription, only the label needed for that prescription should be printed at that time. A "line clearance" should happen to ensure that only the study drug being dispensed and its associated labels are the only items in the area when dispensing and packaging. All bulk bottles and any protocol related documentation should be removed from the area prior to dispensing and packing the next protocol drug.		
Action Taken/Response:			
Person Provided Response:		**Date:**	DD-MMM-YYYY

Finding #10	**CATEGORY: Study Monitoring**	**RATING: Major**	
FINDING:	Lack of demonstration of adequate monitoring of the IIS as demonstrated by: • The overall findings identified during the audit on a limited number of subjects reviewed. • Lack of clarity on the differences with the two monitoring plans. • Inability to see documentation of exactly what was monitoring during the monitoring visits (based on the monitoring practices of only documenting what needed to be addressed based on the monitoring visit). • Incomplete monitoring log.		
REFERENCE(S):	21 CFR Part 312.50, .53, .56; ICH E6 R2 5.18		
Recommendation:	Spectrum should work with Dr. Heymach and the IIS team to establish understanding of current monitoring practices and determine if additional documentation and/or monitoring activities are needed.		
Action Taken/Response:			
Person Provided Response:		**Date:**	DD-MMM-YYYY

Recommendation	**CATEGORY: See Below**	**RATING: NA**

FINDING:	Since the following audit categories could not be fully assessed given time constraints, a monitoring/assessment plan should be established to evaluate the qualifications/documentation to assure adherence to GCP: • Training and Qualification documentation of all study team members • Pharmacy Storage and IP accountability • Facilities and maintenance/calibration documentation for equipment used during the course of the trial • Biostatistics Processes; there was no Statistical Analysis Plan for this study, only the statistical considerations outlined in the protocol.		
REFERENCE(S):	21 CFR Part 312.50, .53, .59; ICH E6 R2 4.6, 5.13, 5.18		
Recommendation:	1. Spectrum should work with Dr. Heymach and the IIS team to establish expectations and documentation of a complete review of: • Study team member qualification and training documentation, including GCP training records • Assessment of IP storage and accountability • Assessment of maintenance and calibration documentation for equipment used during the course of the trial • Determine if a SAP should be created prior to study closure/data cleaning and if there is any impact from the preliminary results reported at recent conferences.		
Action Taken/Response:			
Person Provided Response:		**Date:**	DD-MMM-YYYY