



ADDITIONAL MATERIALS AVAILABLE ON THE HEI WEBSITE

Research Report 192

Multicenter Ozone Study in oldEr Subjects (MOSES): Part 1. Effects of Exposure to Low Concentrations of Ozone on Respiratory and Cardiovascular Outcomes

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Additional Materials 7. Deviations from Protocol and SOPs

These Additional Materials were not formatted or edited by HEI. These documents were part of the HEI MOSES Review Panel's review process.

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ADDITIONAL MATERIALS 7

TABLE 1. List of deviations from the protocol and SOPs

Obs	Subject_ID	Criteria	Procedure	Other	Description
1	11012	No	Yes	No	Deviation of the relative humidity (too low for entire 3 hours, 33.9 +/- 1.8%) was due to a broken steam generator at the facility level. It has since been rectified.
2	11023	No	Yes	No	Blood pressure was only measured once at screening visit. Because BP was 99/56, coordinator should have repeated BP measurements because BP was below minimum required. Per Dr Frampton, coordinator repeated screening BP measurements at training visit. The 3rd BP measurement at Training Visit was above minimum threshold, so subject was considered eligible based on BP criteria.
3	11023	No	Yes	No	Vital Sign SOP deviation. Average of the second and third BP measurements was 89/48. Because this was less than 90/50 , on-call physician should have been paged. Subject was thoroughly checked 2 hours later by Dr Frampton during physical exam before subject was sent home.
4	11136	No	Yes	No	Coordinator did not measure blood pressure during rest period 4 (9:56am) so measured blood pressure at rest period 5 (10:27). Coordinator error.
5	11169	No	Yes	No	Blood samples sent for analysis on day of screening visit were delayed by Hurricane Sandy. CBC results were not determined because sample was expired by the time it arrived at LabCorp in New Jersey. 1 tube of blood (blue citrate ~2.5mL) was drawn at Training Visit and sent to URM labs for screening CBC results.
6	11249	No	Yes	No	Spirometry stopped with only 2 successful trials because subject complained of headach, rating pain 3 out of 10.
7	11272	No	Yes	No	The blood pressure measurement that was supposed to be done 1hr 55min into the exposure (rest period 4) was done 2hr 26min into exposure (rest period 5) because of coordinator error.
8	11272	No	Yes	No	First minute ventilation was not measured during first exercise period of exposure 3 (minute 8-10). Technician error.
9	11294	Yes	No	No	Subject was enrolled despite reporting smoking 1 joint per day for 2 years on Home and Health Questionnaire.
10	11307	No	Yes	No	Subject took a multivitamin and vitamin C on 9Sept2013, 10Sep2013, and 11Sept2013. Subject took Benedryl 10Sep2013 and 11Sep2013. Subject should have avoided these medications starting 9Sep2013. Dr Frampton approved going ahead with PRE1 visit on 16SEP2013, as scheduled.
11	11307	No	Yes	No	Subject completed the before exposure Symptom Questionnaire AFTER lying down for before exposure HRV measurement instead of BEFORE it.

Obs	Subject_ID	Criteria	Procedure	Other	Description
12	11318	No	Yes	No	FedEx had mechanical problems with a plane, so the screening blood sample (drawn 3may2013) arrived at LabCorp 6may2013, which was outside the stability window for the hematology panel. Subject was asked to return 17may2013 to redraw blood for screening hematology panel. Analysis was done by URM labs.
13	11318	No	Yes	No	Subject did not wear nose clips during spirometry measurements post-exposure.
14	11329	No	Yes	No	Completed exposure 3 before receiving Holter report for exposure 2. I put the Holter data card for the POS2 visit in intercampus mail on 2OCT2013, but the Holter core did not receive it until 4NOV2013. Holter cards will be hand delivered to the Holter Core from now on.
15	11329	Yes	No	No	Subject was enrolled despite reporting smoking 1 joint per day for 2 years on Home and Health Questionnaire.
16	11341	No	Yes	No	Normal order of PRE1 events is: Subject arrival, monitor collection, lunch, vital signs, physician exam, phlebotomy, BAU. On 4NOV2013, ultrasound technicians were unavailable after 12:30, so events were performed in the following order: Subject arrival, monitor collection, BAU, lunch, vital signs, physician exam, phlebotomy. BAU was performed ~2.5hrs before target time on checklist and lunch was eaten ~50 minutes later than checklist target time. All other events took place at or close to target times. This revised order of events will be repeated at PRE2 and PRE3 for consistency per Dr Frampton.
17	11341	Yes	No	No	Subject was enrolled despite reporting smoking 1 joint per day for 3 years on Home and Health Questionnaire.
18	11567	No	No	Yes	Coordinator did not write down measured post RH blood pressure and heart rate on BAU Case Report form. Coordinator data recording mistake.
19	21036	No	Yes	No	systolic blood pressure was measured at 96mmhg. Per protocol it should have been repeated and it was not at this time. She was admitted to the protocol despite not having a systolic pressure of at least 100mmhg at this reading. subsequent systolic values on this day were measured at over 100mmhg.
20	21127	No	No	Yes	The BAU technician misread the schedule and was not available to make the measurement.
21	21150	No	Yes	No	I neglected to initiate the "record" button on the holter monitor when it was placed. I noted it about 3:30pm and started the recording at that time.
22	21207	No	No	Yes	This subject was rescheduled multiple times due to inclement weather. On the day she was scheduled for her post visit sputum induction, we did not have staff to process the sample, therefore it was not collected.
23	21376	No	Yes	No	I neglected to enter the complete training data into the electronic database prior to the pre 1 visit.

Obs	Subject_ID	Criteria	Procedure	Other	Description
24	21387	No	Yes	No	The 3rd exposure for this subject falls outside of the 6 month window as outlined in the MoO. This subject has occupational requirements which forced us to reschedule several times; however we are now about 1 month beyond the acceptable time. After discussion with the sponsor, we are continuing with his 3rd session. He has arrived at the research lab and undergone vital signs measurement and physical exam, there are no findings which should keep us from continuing.
25	21547	No	Yes	No	I neglected to have the study subject complete the symptom questionnaire at the end of the exposure day.
26	31141	No	No	Yes	UCSF has decided to reschedule 31141's exposure visit 1 set. Two important outcome measurements were not obtained at today's PRE1 attempt. 1) The cytoflow analysis was not done due to the tech not being available to process the sample due to being involved in a car accident while in transit. 2) The FMD BAU was attempted for 1 and half hours and an adequate image of the brachial artery was not obtained. In addition an adequate brachial artery image was not obtained after release of the cuff due to movement of the vessel. The plan if agreed, (HEI and Peter Ganz approved.) is to image both arms at the next PRE1 visit before the blood draw to identify the better arm for the FMD BAU procedure. The arm with the better brachial artery for imaging will be dedicated for all FMD BAU procedures and blood samples drawn from the contra arm. Should an adequate imaging not be available again we will note this and continue forward.
27	31141	No	Yes	No	PRE3 & EXP3 FMD BAU not done due to no reliable PRE1, EXP1, PRE2, and EXP2 FMD BAU measurements. HEI and Peter Ganz consulted and approved.
28	31141	No	Yes	No	PRE3 & EXP3 FMD BAU not done due to no reliable PRE1, EXP1, PRE2, and EXP2 FMD BAU measurements.
29	31141	No	Yes	No	EXP3 post exposure symptom questionnaire completed earlier than timeline listed due to FMD BAU not done.
30	31141	No	Yes	No	EXP3 post exposure vital signs completed earlier than timeline listed due to FMD BAU not done.
31	31152	No	No	Yes	Vital signs: BP measure and confirmed at 102/48. Subject is very fit and low BP is usual. Covering physician ok to proceed with visit.
32	31163	No	Yes	No	Due to a technical problem, our LabView program (use to measure VE) required a reboot and re calibration. As such an extra minute of exercise was performed at EX1.
33	31174	Yes	No	No	Subject enrolled and completed study with MJ hx > 1 jt/yr.
34	31209	No	Yes	No	In line pneumotach heated, and therefore the reported VE need not be BTPS corrected.
35	31209	No	Yes	No	Subject reported AE on 06Jan2014 not reported within 5 working days in eCOS.
36	31221	No	Yes	No	Due to time constraint, only the reported second and third BP, HR and SpO2 measurements done at end of EXP2.

Obs	Subject_ID	Criteria	Procedure	Other	Description
37	31254	No	Yes	No	Two ozone filters were found stuck together in PES #66. Both ozone filters were loaded into the cassette for analysis and noted in the PES Return and Process comments for Analyzing Lab/Unusual Circumstances. Maria (HEI) consulted and agrees with reporting in both places and sending both ozone filters together for analysis.
38	31334	No	Yes	No	Whereas blood for cytoflow, TF, and vWF were drawn at the scheduled time, blood for CBC, platelets, cell diff, soluble markers, and plasma archive was successfully drawn an hour later, after the FMD procedure. This was done so that the FMD would be done on schedule and give the subject a phlebotomy break.
39	31378	No	No	Yes	Pre exposure visit set #1 PES monitoring is being repeated due to not being able to proceed with EXP1: due to malfunctioning chamber equipment.
40	31378	No	Yes	No	Subject 31378 stopped taking her multivitamin on 5 August 2014 instead of 4 August, 2014.
41	31378	No	Yes	No	Blood drawn from right arm as no vein identified for blood draw found in left arm. FMD BAU performed on right arm as well. Tomorrow;s EXP1 blood will also be drawn from the right arm so that like circumstances occur in the EXP #3 visit set. John Balmes consulted and agrees.
42	31390	No	Yes	No	For induced sputum supernatant volume of about 1.6 mL, 3 aliquots of 0.5 mL instead of 2 aliquots of 0.9 mL were stored at -80C.
43	31403	No	Yes	No	Abnormal baseline EKG missed and V2 Training visit done.