



**DATE:** December 3, 2010  
**FROM:** Pamela Harris, M.D., Investigational Drug Branch, CTEP, DCTD, NCI  
**SUBJECT:** Sunitinib Malate (SU-011248) Investigator Notification: **Pulmonary Hypertension**  
Mfr Report #: 2010130150  
**TO:** Investigators Using Sunitinib Malate (NSC 736511)

The U.S. Food and Drug Administration (FDA) regulations require sponsors of clinical studies conducted under a U.S. IND to notify the FDA and all participating investigators of any serious and unexpected adverse experiences that are possibly related to the investigational agent. A MedWatch Report, which describes pulmonary hypertension in a patient participating in a Pfizer-sponsored clinical study utilizing the investigational agent sunitinib malate, was recently distributed to investigators.

The following must be completed by all investigators using sunitinib malate under IND 74019:

- Send a copy of this letter to your Institutional Review Board (IRB) according to your local IRB's policies and procedures.
- File a copy of this letter in your protocol file.

If your study is not covered under IND 74019, it is strongly recommended that you follow the instructions above.

Please note that for Cooperative Group studies, the Cooperative Group Operations Office will provide instructions for IRB submissions, any patient notifications, etc.

Based on CTEP's assessment of the current information in light of previous experience with sunitinib malate, there does not appear to be a change in the risk-benefit ratio for sunitinib malate studies; therefore, CTEP is not requiring a protocol amendment at this time.

Please continue to report events according to the adverse event reporting guidelines in your protocol(s).

The MedWatch Report that describes the following adverse event is attached.

A 73-year-old female with colorectal cancer experienced pulmonary hypertension and subsequently died while participating in a randomized, phase 2 study utilizing the investigational agent sunitinib malate in combination with oxaliplatin, 5-fluorouracil and leucovorin.

There have been no cases of pulmonary hypertension reported to the NCI through ADEERS under the sunitinib malate NSC and/or IND. A total of 2779 patients have been enrolled in NCI-sponsored clinical trials under the sunitinib malate IND and/or NSC.

Attachments: Dear Investigator Letter  
MedWatch Report

Pfizer Inc  
Drug Safety Surveillance  
Safety & Risk Management  
235 East 42<sup>nd</sup> Street 150/3/18  
New York, NY 10017



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## **Pfizer Global Pharmaceuticals**

### **Subject: Suspected Unexpected Serious Adverse Reaction Report (SUSAR)**

Dear Investigator:

In accordance with applicable guidelines and regulations governing the conduct of clinical trials<sup>1</sup>, you are being notified of a serious adverse event involving a product that you are investigating.

The attached letter is being provided for your information and we suggest that you file a copy of this document in the labeling section of your study documents. A copy of the document should be provided to your Institutional Review Board (IRB) and confirmation of receipt by your IRB filed in your study file. In addition, please notify your sub-investigators and other appropriate personnel in your clinical trial.

If you have any questions regarding this report, please contact your designated Pfizer medical contact.

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<sup>1</sup> Code of Federal Regulations (CFR) 312.32 IND Safety Reports; International Conference on Harmonization (ICH): Good Clinical Practice (CPMP/ICH/135/95)

For use by user-facilities,  
importers, distributors and manufacturers  
for MANDATORY reporting

**MEDWATCH**  
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A. PATIENT INFORMATION			
1. Patient Identifier PRIVACY  In confidence	2. Age at Time of Event: 73 Years or Date of Birth: 03/01/1937	3. Sex <input checked="" type="checkbox"/> Female <input type="checkbox"/> Male	4. Weight ____ lbs or ____ kgs

B. ADVERSE EVENT OR PRODUCT PROBLEM	
1. <input checked="" type="checkbox"/> Adverse Event and/or <input type="checkbox"/> Product Problem (e.g., defects/malfunctions)	
2. Outcomes Attributed to Adverse Event (Check all that apply)	
<input checked="" type="checkbox"/> Death: 10/29/2010 (mm/dd/yyyy)	<input type="checkbox"/> Disability or Permanent Damage
<input type="checkbox"/> Life-threatening	<input type="checkbox"/> Congenital Anomaly/Birth Defect
<input checked="" type="checkbox"/> Hospitalization - initial or prolonged	<input type="checkbox"/> Other Serious (Important Medical Events)
<input type="checkbox"/> Required Intervention to Prevent Permanent Impairment/Damage (Devices)	
3. Date of Event (mm/dd/yyyy) 10/12/2010	4. Date of This Report (mm/dd/yyyy) 11/29/2010

5. Describe Event or Problem  
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)  
Pulmonary hypertension [Pulmonary hypertension]

Case Description:  
A RANDOMIZED, PHASE 2B STUDY OF SUNITINIB PLUS OXALIPLATIN, 5-FLUOROURACIL AND LEUCOVORIN (FOLFOX) VERSUS BEVACIZUMAB PLUS FOLFOX AS FIRST-LINE TREATMENT IN PATIENTS WITH METASTATIC COLORECTAL CANCER

This is a report from Pfizer Sponsored Interventional Study source, for Protocol ID A6181104, CenterID/Subject ID 11151005.  
A 73-year-old female subject started to receive sunitinib malate, oxaliplatin, fluorouracil and levofolinate calcium (FOLFOX therapy) on 23Jul2009 for colorectal cancer. The continued in additional info section...

6. Relevant Tests/Laboratory Data, Including Dates
Blood urea nitrogen (12Oct2010): 6, units not provided
Blood urea nitrogen (14Oct2010): 7, units not provided
Creatinine (12Oct2010): 0.58, units not provided
Creatinine (14Oct2010): 0.64, units not provided
Blood pH (12Oct2010): 7.487
Blood pH (13Oct2010): 7.442
continued in additional info section...

7. Other Relevant History, Including Preexisting Medical Conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)
#1 Relevant Med History, Dizziness
#2 Relevant Med History, Constipation
#3 Relevant Med History, Insomnia
#4 Relevant Med History, Gastric ulcer

C. SUSPECT PRODUCT(S)	
1. Name (Give labeled strength & mfr/labeler)	
#1. Sunitinib Malate (SUNITINIB MALATE) Unknown	
#2. *FLUOROURACIL (FLUOROURACIL) Unknown	
2. Dose, Frequency & Route Used	3. Therapy Dates (if unknown, give duration from/to (or best estimate))
#1. 12.5 mg, 1x/day, Oral	#1. 07/23/2009 to 09/29/2010
#2. every 2 weeks, IV bolus	#2. 07/23/2009 to 08/25/2009
4. Diagnosis for Use (Indication)	5. Event Abated After Use Stopped or Dose Reduced?
#1. Colorectal cancer (Continued)	#1. <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply
#2. Colorectal cancer (Continued)	#2. <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply
6. Lot #	7. Exp. Date
#1.	#1.
#2.	#2.
9. NDC# or Unique ID	
10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)	
#1. OXYCODONE HYDROCHLORIDE HYDRATE (OXYCODONE HYDROCHLORIDE) 10/07/2010 to ongoing continued in additional info section...	

G. ALL MANUFACTURERS	
1. Contact Office - Name/Address (and Manufacturing Site for Devices) Pfizer Inc. 150 East 42nd Street New York, NY 10017 UNITED STATES	2. Phone Number
	3. Report Source (Check all that apply)
	<input checked="" type="checkbox"/> Foreign JPN
	<input checked="" type="checkbox"/> Study
	<input type="checkbox"/> Literature
	<input type="checkbox"/> Consumer
	<input checked="" type="checkbox"/> Health Professional
	<input type="checkbox"/> User Facility
	<input type="checkbox"/> Company Representative
	<input type="checkbox"/> Distributor
	<input type="checkbox"/> Other:
4. Date Received by Manufacturer (mm/dd/yyyy) 11/17/2010	5. (A)NDA # IND # 62,382 STN # PMA/510(k) # Combination Product <input type="checkbox"/> Yes Pre-1938 <input type="checkbox"/> Yes OTC Product <input type="checkbox"/> Yes
6. If IND, Give Protocol # A6181104	
7. Type of Report (Check all that apply)	
<input type="checkbox"/> 5-day <input type="checkbox"/> 30-day	
<input type="checkbox"/> 7-day <input type="checkbox"/> Periodic	
<input type="checkbox"/> 10-day <input type="checkbox"/> Initial	
<input type="checkbox"/> 15-day <input checked="" type="checkbox"/> Follow-up #1	
9. Manufacturer Report Number 2010130150	8. Adverse Event Term(s) Pulmonary hypertension

E. INITIAL REPORTER			
1. Name and Address JAPAN Name and address withheld.		Phone # Withheld	
2. Health Professional? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	3. Occupation Physician	4. Initial Reporter Also Sent Report to FDA <input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Unk	

Submission of a report does not constitute an admission that medical personnel, user, facility, distributor, manufacturer or product caused or contributed to an event.

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C. SUSPECT PRODUCT(S)	
1. Name (Give labeled strength & mfr/labeler) <b>(Regimens Continued)</b>	
#3. *FOLINIC ACID (FOLINIC ACID) Unknown	
#4. *OXALIPLATIN (OXALIPLATIN) Unknown	
2. Dose, Frequency & Route Used	3. Therapy Dates (if unknown, give duration from/to (or best estimate)
#3. 279 mg, every 2 (Continued)	#3. 07/23/2009 to 09/30/2010
#4. UNK, Intravenous	#4. 07/23/2009 to 01/07/2010
4. Diagnosis for Use (Indication)	5. Event Abated After Use Stopped or Dose Reduced?
#3. Colorectal cancer (Continued)	#3. <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply
#4. Colorectal cancer (Continued)	#4. <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply
6. Lot #	7. Exp. Date
#3.	#3.
#4.	#4.
9. NDC# or Unique ID	8. Event Reappeared After Reintroduction?
NA	#3. <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply
	#4. <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply
10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)	

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**ADDITIONAL INFORMATION****B5. EVENT DESCRIPTION (Continued)**

subject had a history of hospital admission on 13Mar2009 because of ileus due to cancer of transverse colon. On 01Apr2009, since tumour invasion into the head of pancreas and duodenal wall was observed, partial colectomy transverse, partial pancreatectomy and partial duodenectomy were conducted. Computed tomography on 06Jul2009 showed recurrent cancer in the head of pancreas. Computed tomography with contrast on 14Jul2009 showed peritoneal dissemination, local recurrence of the colon and metastases to lung. The subject had also a history of gastric ulcer, insomnia, constipation and dizziness from unknown date but no medical history of lung disease.

The subject received sunitinib 12.5 mg daily (per protocol 4 weeks on, 2 weeks off), fluorouracil 2750 mg (46hr continuous infusion, every 2 weeks) and levofofinate calcium 279 mg daily (every 2 weeks) as most recent dose. The latest dose of sunitinib prior to the onset of the event was taken on 29Sep2010. Prior to the onset of the event, the subject received 26 cycles of FOLFOX and 10 cycle of Sutent therapy. The administration of fluorouracil (bolus and infusion) and oxaliplatin was stopped from cycle 3 and cycle 10, respectively; it was reported that the stop date of fluorouracil (bolus) and oxaliplatin were 25Aug2009 and 07Jan2010, respectively. After discontinuation of fluorouracil bolus, fluorouracil continuous infusion and calcium folinate continued.

The findings of echocardiography on 21Jul2009, when the subject was enrolled into the study were as follows: left ventricular end-diastolic dimension (LVDd): 40, left ventricular internal dimension in systole (LVDs): 22, %, FS (fractional shortening): 45%, left ventricular ejection fraction (LVEF): 77% (Teichholz method). Mild sclerosis was observed at leaflet of aortic valve. Aortic stenosis (AS) and aortic regurgitation (AR) were not observed. There were no significant organic change for other valves. Left ventricular internal diameter was within normal limits. There was no left ventricular hypertrophy. Wall motion was within normal limits. Significant asynergy was not observed.

Relevant concomitant medications included oxycodone taken from 07Oct2010, prochlorperazine (NOVAMIN) from 07Oct2010 to 09Oct2010, rabeprazole sodium (PARIET), herbal preparation, senna (PURSENNID), all since Mar2009, loxoprofen sodium (LOXONIN) from 15Sep2009, mecobalamin (METHYCOBAL), difenidol hydrochloride (CEPHADOL), magnesium oxide, all from 25Mar2010, clonazepam (RIZE) from 16Sep2010, zolpidem tartrate (MYSLEE) from 09Oct2009, paracetamol (PYRINAZIN) from 23Jun2010, triamcinolone acetonide (KENALOG) from 04Aug2009, heparinoid (HIRUDOID) from 17Aug2009, sodium bicarbonate and sodium guelenate (HACHIAZULE), lidocaine hydrochloride and benzethonium chloride, all from 23Jun2010.

On 12Oct2010, the subject visited the site due to dyspnoea, and had a consultation in the cardiovascular medicine department. According to the subject, she had been experiencing chest pain, dyspnoea and feeling of palpitations for about one month. Objective findings were as follows: blood pressure: 128/80, pulse: 80 and regular, no finding of pulmonary thromboembolism, lung: clear and no rale, heart: no murmur, electrocardiogram: heart rate was 78 bps, sinus rhythm, poor in lead II, III, aVF and V1-5, axis was -80 degree and left anterior fascicular block was firstly found, chest X-ray: cardiothoracic ratio (CTR): 50%, no congestion, right pulmonary artery dilatation was observed, echocardiograph: LVDd: 35, LVDs: 23, Rdd: 28, interventricular septum (IVS): 9, left ventricular posterior wall (LVPW): 9, inferior vena cava (IVC): 10, %FS: 34%, pulmonary arterial systolic pressure (PASP): 67 mmHg (moderate pulmonary hypertension), pulmonary arterial diastolic pressure (PADP): 14 mmHg, mild mitral regurgitation, mild tricuspid regurgitation, left ventricular wall motion was normal, but interventricular septum was displaced by right ventricle and became thin, right ventricular internal diameter was mild enlarged and hypokinesis was observed in the lower portion from middle, small amount of pericardial effusion. Based on the above data, the subject was assessed with pulmonary hypertension although left ventricular wall motion was normal. The value of D dimer was high, therefore the investigation for pulmonary embolism was recommended.

Contrast enhanced computed tomography was conducted and it showed no thrombosis in pulmonary artery, inferior vena cava or lower extremities. There was no significant change from the findings on Aug2010. Final diagnosis was not made at that point and pulmonary hypertension was suspected as a provisional diagnosis.

The subject went home on 12Oct2010 according to her wishes, and then she was admitted to the hospital on 13Oct2010.

On 13Oct2010 the subject had shortness of breath, but no palpitations, chest pain and syncope. NYHA class was III. No heart sounds abnormal, llp sounds were louder (accentuated), no cardiac murmur, no breath sounds abnormal. Based on the findings that shortness of breath was increased for one month, brain natriuretic peptide (BNP) increased, pulmonary hypertension was suspected as the cause of hypoxemia. Ventilation/perfusion scintigraphy, respiratory function tests, tests of coagulation and autoimmune disorders and repeated echocardiography were planned. Final diagnosis would be made based on the results of cardiac catheter test of right ventricle.

On 14Oct2010, respiratory function tests were conducted. On 15Oct2010, ventilation/perfusion scintigraphy was conducted. Multiple perfusion defect areas were observed in peripheral, but ventilation of the same area was good. Based on the findings, microscopic chronic pulmonary thromboembolism was suspected. Ventilation defect area was observed in the "middle lobe" of left lung. There was no abnormal accumulation outside lung.

The subject developed the reported SAE (pulmonary hypertension) during off-treatment period of sunitinib; therefore, no action was taken with this drug due to the event. The start of the next cycle of study treatment was planned from 14Oct2010, but it was delayed until the symptoms associated with the event were resolving. Fluorouracil and levofofinate calcium were temporarily withdrawn as a result of the event, while for oxaliplatin the action taken was reported as not applicable. The date of last administration of sunitinib malate before the onset of the event was 29Sep2010 while for calcium folinate the last administration before the event was 30Sep2010 and for fluorouracil continuous infusion was 02Oct2010.

On 17Oct2010, SpO2 at moving was low (the latter half of 70%), but it gradually improved by rest. On 18Oct2010, SpO2 at speaking

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was low (the first half of 80%), but it improved to a level of 90% by deep breathing. On 19Oct2010, cardiac catheter test was conducted under 2 liters of oxygen supplementation and the findings were as follows; Pulse: 76, blood pressure: 128/71, pulmonary capillary wedge pressure (PCWP): 8, pulmonary artery pressure systolic/diastolic/mean (PA; s/d/m): 63/13/38, right ventricle (RV): 63/ -5, right atrium (RA): 3, cardiac output (CO)/cardiac index (CI): 2.89/2.10, RVR: 830, mixed venous oxygen saturation (SvO2): 62%, arterial blood gas (ASG): pH 7.46, PCO2: 38.0, PO2: 53.0, HCO3- 27.0, SpO2 89.0.

Based on the above findings, the subject was assessed as having moderate pulmonary hypertension, and cardiac output decreased was observed. The investigation of blood gas in room air showed that PCO2 was low (53.0 mmHg) at prone position under 2 liters of oxygen supplementation. Increase of oxygen supplementation to 4 liters was recommended.

On 20Oct2010, SpO2 at speaking decreased to a level of 80%, but it was stable at rest. Therefore, 4 liters of oxygen supplementation was sustained. On the same day, computed tomography was conducted and the findings were as follows; irregular shape nodules of 7mm and about 6mm in the size were observed at the apex and S4/S5 of right lung. Comparing the findings on 12Oct2010 and 31Aug2010, the size of nodules increased. Multiple small nodular opacities were observed around trachea and bronchial wall thickening was also observed, these findings were similar to that on 12Oct2010. Obstructive bronchitis was suspected. The minor axis 14mm of right hilar lymphadenopathy was newly confirmed and the inside contrast-enhanced effects were uneven. Metastasis was suspected. There was no significant change for other metastases and new lesion. On 21Oct2010, pH 7.42, pCO2 42.6, pO2 66.1, HCO3- 27.1 and BE 2.8. On the same day, magnetic resonance imaging (MRI) was conducted. Left ventricular function was normal. Left ventricular dimension was reduced, cardiac septal fluttering and paradoxical motion were observed. Right ventricular pressure increased was suspected. Right ventricular dimension was mildly increased, and right ventricular wall thickness was observed. These findings suggested right ventricular overload. Right ventricular wall motion was totally decreased and right ventricular ejection fraction decreased was observed. Delayed-enhancement imaging showed enhanced effects from right ventricular inferior wall to left ventricular junction. These findings were specific to pulmonary hypertension. On 22Oct2010, the subject's SpO2 was kept by 4 liters of oxygen supplementation. On 23Oct2010, the subject had dyspnoea at exertion, but she did not have dyspnoea at rest. On 25Oct2010, the subject complained of dyspnoea after moving. Shortness of breath, SpO2 decreased and heart rate increased (a level of 100 bpm) were observed, but dyspnoea improved for minutes. The subject's performance status was 1, body temperature: 36.9 degree centigrade, pulse: 88 bpm, blood pressure: 91/63 mmHg, SpO2: 96% under 4 liters of oxygen supplementation, body weight: 42.4 kg. On 26Oct2010, the subject had no dyspnoea at rest and SpO2 was good, but she had dyspnoea after moving. On 27Oct2010 the performance status was 2, body temperature: 36.5 degree centigrade, blood pressure: 109/62 mmHg, SpO2: 94% under 4 liters of oxygen supplementation, body weight: 42.6 kg. Best supportive care was considered as next therapy. On 28Oct2010, pH: 7.473, pCO2: 34.6, pO2: 51.0, HCO3-: 25.1, anion gap: 12.4. SpO2 dropped to 80% by waking up from the bed. The subject had difficulty breathing and pallor facial. Oxygen supplementation was conducted 4mL/min. SpO2 could not be kept in a level of 90% by oxygen supplementation from nose, therefore, it was changed to oxygen supplementation through mask. SpO2 was around 92% by oxygen supplementation through mask. SpO2 increased to 98% by deep breathing, but it returned to 92% by normal breathing. Pulmonary hypertension aggravated was suspected. The subject started anticoagulant therapy on the same day. The possibility that the subject's condition would be worsen suddenly for 1 or 2 weeks was considered. The following drugs were reported as of 29Oct2010: oxycodone hydrochloride hydrate (OXINORM), morphine hydrochloride hydrate (OPSO), morphine hydrochloride hydrate (PACIF), sodium rabeprazole (PARIET), hotyuekkitou (herbal medicine), sennoside A/B (PURSENNID), mecobalamin (METHYCOBAL), difenidol hydrochloride (CEPHADOL), magnesium oxide (MAGLAX), clotiazepam (RIZE), acetaminophen (PYRINAZIN), triamcinolone acetonide (KENALOG), heparinoid (HIRUDOID) and fondaparinux sodium (ARIXTRA).

At 10 PM on 29Oct2010, the subject's condition aggravated suddenly without any trigger, and she had dyspnoea exacerbated. The volume of oxygen supplementation was increased, but breathing condition did not become better. Condition aggravated progressed rapidly, the subject had cyanosis, and had cardio-respiratory arrest soon. Cardiopulmonary resuscitation was conducted, but heartbeats did not restart. At 10:57 PM, the subject's death was confirmed. Autopsy was not performed due to the family's hope.

The investigator considered that there was a reasonable possibility that the pulmonary hypertension was related to sunitinib, fluorouracil and levofolinate calcium, but not to oxaliplatin. The investigator also considered that there was not a reasonable possibility that the event was related to clinical trial procedure and concomitant drugs. In the Investigator's opinion pulmonary embolism related to cancer was suspected. Embolism of great vessels in lung might be considered, but it was a speculation and not confirmed.

Follow-up (01Nov2010): this follow-up contains medically significant information. Additional reported information included updated outcome of the event (from not recovered to fatal), action taken with sunitinib, and additional information on the disease under study.

Follow-up (17Nov2010): New information reported included updated stop date of fluorouracil infusion (from 30Sep2010 to 02Oct2010), clarification on number of cycles with sunitinib prior to the onset of the event and date of echography done when the subject was enrolled, additional details on clinical course till patient's death date, lab data and an Investigator's comment concerning suspicion on pulmonary embolism.

This is a follow-up to a previously submitted fatal event for 15-day reporting to regulators and investigators/ethics committees as

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required.

**Case Comment:**

The reported fatal pulmonary hypertension is unlisted in the Investigator's Brochure for sunitinib malate and in the UK-SPC for fluorouracil and levofolinate calcium.

The company cannot exclude the possibility of a causal association between the fatal pulmonary hypertension and the study drugs sunitinib malate, fluorouracil, and levofolinate calcium, while the event is not causally related to the co-suspect study drug oxaliplatin, or to any clinical procedure.

The impacts of this report on the benefit/risk profile of the products and on the conduct of the study are evaluated as part of Pfizer procedures for safety evaluation, including the review and analysis of aggregate data for adverse events. Any safety concern identified as part of this review, as well as any appropriate action in response, will be promptly notified to Regulatory Authorities, Ethics Committees and Investigators as appropriate.

**B6. RELEVANT TESTS (Continued)**

PCO<sub>2</sub> (12Oct2010): 32.4  
 PCO<sub>2</sub> (13Oct2010): 36.8  
 PaO<sub>2</sub> (12Oct2010): 38.3  
 PaO<sub>2</sub> (13Oct2010): 54.5  
 SaO<sub>2</sub> (12Oct2010): 70.4  
 SaO<sub>2</sub> (13Oct2010): 85.9  
 HCO<sub>3</sub><sup>-</sup> (13Oct2010): 24.7  
 Base excess (12Oct2010): 1.7  
 Base excess (13Oct2010): 1.2  
 PCO<sub>2</sub> (19Oct2010): 38  
 PO<sub>2</sub> (19Oct2010): 53  
 HCO<sub>3</sub><sup>-</sup> (19Oct2010): 27  
 SpO<sub>2</sub> (19Oct2010): 89  
 PCO<sub>2</sub> (21Oct2010): 42.6  
 PO<sub>2</sub> (21Oct2010): 66.1  
 HCO<sub>3</sub><sup>-</sup> (21Oct2010): 27.1  
 SpO<sub>2</sub> (25Oct2010): 96%  
 PCO<sub>2</sub> (28Oct2010): 34.6  
 PO<sub>2</sub> (28Oct2010): 51  
 HCO<sub>3</sub><sup>-</sup> (28Oct2010): 25.1  
 Anion gap (28Oct2010): 12.4  
 SpO<sub>2</sub> (28Oct2010): 80%

**C2. DOSE, FREQUENCY & ROUTE USED (Continued)**

Suspect Medication #3: 279 mg, every 2 weeks, Intravenous

**C4. DIAGNOSIS FOR USE (Continued)**

#1:Colorectal cancer (Colorectal cancer)  
 #2:Colorectal cancer (Colorectal cancer)  
 #3:Colorectal cancer (Colorectal cancer)  
 #4:Colorectal cancer (Colorectal cancer)

**C10. CONCOMITANT MEDICAL PRODUCTS (Continued)**

#2. NOVAMIN (PROCHLORPERAZINE) 10/07/2010 to 10/09/2010  
 #3. PARIET (RABEPRAZOLE SODIUM) 03/--/2009 to ongoing  
 #4. HERBAL PREPARATION (HERBAL NOS) 03/--/2009 to ongoing  
 #5. PURSENNID (SENNA LEAF) 03/--/2009 to ongoing

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- #6. LOXONIN (LOXOPROFEN SODIUM) 09/15/2009 to ongoing
- #7. METHYCOBAL (MECOBALAMIN) 03/25/2010 to ongoing
- #8. CEPHADOL (DIFENIDOL HYDROCHLORIDE) 03/25/2010 to ongoing
- #9. MAGNESIUM OXIDE (MAGNESIUM OXIDE) 03/25/2010 to ongoing
- #10. RIZE (CLOTIAZEPAM) 09/16/2010 to ongoing
- #11. MYSLEE (ZOLPIDEM TARTRATE) 10/09/2009 to ongoing
- #12. PYRINAZIN (PARACETAMOL) 06/23/2010 to ongoing
- #13. KENALOG (TRIAMCINOLONE ACETONIDE) 08/04/2009 to ongoing
- #14. HIRUDOID (HEPARINOID) 08/17/2009 to ongoing
- #15. HACHIAZULE (SODIUM BICARBONATE, SODIUM GUALENATE) Gargle 06/23/2010 to ongoing
- #16. LIDOCAINE HYDROCHLORIDE (LIDOCAINE HYDROCHLORIDE) Gargle 06/23/2010 to ongoing
- #17. BENZETHONIUM CHLORIDE (BENZETHONIUM CHLORIDE) Gargle 06/23/2010 to ongoing

## Block C - Additional Dosage Regimens

Suspect Product	2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration)	6. Lot #	7. Exp. date
#2 *FLUOROURACIL Regimen # 2	2750 mg, 46 hr continuous infusion, every 2 weeks, Intravenous	07/23/2009 to 10/02/2010		

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