CHILDREN'S HOSPITAL
& RESEARCH CENTER OAKLAND
Department of Hematology Oncology
747 Fifty Second Street
Oakland, CA 94609
www.childrenshospitaloakland.org

FACSIMILE TRANSMITTAL SHEET

To:	**CHRIS HEMPEL**	From:	Caroline Hastings, M.D. Director, Fellowship Program
Attn:		Dept:	Hematology/Oncology Associate Hematologist/ Oncologist
Faxed to:	**775-201-0589**	Faxed from:	(510) 601-3916
Phone:		Phone:	510-428-3631
Date:	**5/18/09**	# Pages Sent:	**23 includes cover sheet**
Subject:	**FDA submission from 5/15/09 - complete copy attached for Addi and Cassi.**		

☐ **Urgent** X For Review ☐ Per Discussion ☐ Please Reply

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0014.
Expiration Date: May 31, 2009
See OMB Statement on Reverse.

INVESTIGATIONAL NEW DRUG APPLICATION (IND)
(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)

NOTE: No drug may be shipped or clinical investigation begun until an IND for that investigation is in effect (21 CFR 312.40).

1. NAME OF SPONSOR
CAROLINE HASTINGS, M.D.

2. DATE OF SUBMISSION
05/15/2009

3. ADDRESS *(Number, Street, City, State and Zip Code)*
CHILDRENS' HOSPITAL & RESEARCH CENTER OAKLAND
747 52nd STREET
OAKLAND, CA 94609

4. TELEPHONE NUMBER *(Include Area Code)*
510-428-3631

5. NAME(S) OF DRUG *(Include all available names: Trade, Generic, Chemical, Code)*
Trappsol Brand of Endotoxin controlled Hydroxyl-Propyl-Beta-Cyclodoxtrin (HPBCD)

6. IND NUMBER *(If previously assigned)*
104114

7. INDICATION(S) *(Covered by this submission)*

8. PHASE(S) OF CLINICAL INVESTIGATION TO BE CONDUCTED:
☐ PHASE 1 ☐ PHASE 2 ☐ PHASE 3 ☑ OTHER compassionate use *(Specify)*

9. LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS (21 CFR Part 312), NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, DRUG MASTER FILES *(21 CFR Part 314.420)*, AND PRODUCT LICENSE APPLICATIONS (21 CFR Part 601) REFERRED TO IN THIS APPLICATION.

10. ***IND submission should be consecutively numbered. The initial IND should be numbered "Serial number: 0000." The next submission (e.g., amendment, report, or correspondence) should be numbered "Serial Number: 0001." Subsequent submissions should be numbered consecutively in the order in which they are submitted.***

SERIAL NUMBER

11. THIS SUBMISSION CONTAINS THE FOLLOWING: *(Check all that apply)*

☐ INITIAL INVESTIGATIONAL NEW DRUG APPLICATION (IND)
☐ RESPONSE TO CLINICAL HOLD

PROTOCOL AMENDMENT(S):	INFORMATION AMENDMENT(S):	IND SAFETY REPORT(S):
☐ NEW PROTOCOL	☐ CHEMISTRY/MICROBIOLOGY	☑ INITIAL WRITTEN REPORT
☐ CHANGE IN PROTOCOL	☐ PHARMACOLOGY/TOXICOLOGY	☐ FOLLOW-UP TO A WRITTEN REPORT
☐ NEW INVESTIGATOR	☐ CLINICAL	

☐ RESPONSE TO FDA REQUEST FOR INFORMATION
☐ ANNUAL REPORT
☐ GENERAL CORRESPONDENCE
☐ REQUEST FOR REINSTATEMENT OF IND THAT IS WITHDRAWN, INACTIVATED, TERMINATED OR DISCONTINUED
☐ OTHER *(Specify)*

CHECK ONLY IF APPLICABLE

JUSTIFICATION STATEMENT MUST BE SUBMITTED WITH APPLICATION FOR ANY CHECKED BELOW. REFER TO THE CITED CFR SECTION FOR FURTHER INFORMATION.

☐ **TREATMENT IND 21 CFR 312.35(b)** ☐ **TREATMENT PROTOCOL 21 CFR 312.35(a)** ☐ **CHARGE REQUEST/NOTIFICATION 21 CFR312.7(d)**

FOR FDA USE ONLY

CDR/DBIND/DGD RECEIPT STAMP	DDR RECEIPT STAMP	DIVISION ASSIGNMENT:
		IND NUMBER ASSIGNED:

12. **CONTENTS OF APPLICATION**

This application contains the following items: *(Check all that apply)*

- [x] 1. Form FDA 1571 *[21 CFR 312.23(a)(1)]*
- [ ] 2. Table of Contents *[21 CFR 312.23(a)(2)]*
- [ ] 3. Introductory statement *[21 CFR 312.23(a)(3)]*
- [ ] 4. General Investigational plan *[21 CFR 312.23(a)(3)]*
- [ ] 5. Investigator's brochure *[21 CFR 312.23(a)(5)]*
- [ ] 6. Protocol(s) *[21 CFR 312.23(a)(6)]*
  - [ ] a. Study protocol(s) *[21 CFR 312.23(a)(6)]*
  - [ ] b. Investigator data *[21 CFR 312.23(a)(6)(iii)(b)]* or completed Form(s) FDA 1572
  - [ ] c. Facilities data *[21 CFR 312.23(a)(6)(iii)(b)]* or completed Form(s) FDA 1572
  - [ ] d. Institutional Review Board data *[21 CFR 312.23(a)(6)(iii)(b)]* or completed Form(s) FDA 1572
- [ ] 7. Chemistry, manufacturing, and control data *[21 CFR 312.23(a)(7)]*
  - [ ] Environmental assessment or claim for exclusion *[21 CFR 312.23(a)(7)(iv)(e)]*
- [ ] 8. Pharmacology and toxicology data *[21 CFR 312.23(a)(8)]*
- [ ] 9. Previous human experience *[21 CFR 312.23(a)(9)]*
- [x] 10. Additional information *[21 CFR 312.23(a)(10)]*

13. IS ANY PART OF THE CLINICAL STUDY TO BE CONDUCTED BY A CONTRACT RESEARCH ORGANIZATION? [ ] YES [x] NO

IF YES, WILL ANY SPONSOR OBLIGATIONS BE TRANSFERRED TO THE CONTRACT RESEARCH ORGANIZATION? [ ] YES [ ] NO

IF YES, ATTACH A STATEMENT CONTAINING THE NAME AND ADDRESS OF THE CONTRACT RESEARCH ORGANIZATION, IDENTIFICATION OF THE CLINICAL STUDY, AND A LISTING OF THE OBLIGATIONS TRANSFERRED.

14. NAME AND TITLE OF THE PERSON RESPONSIBLE FOR MONITORING THE CONDUCT AND PROGRESS OF THE CLINICAL INVESTIGATIONS

CAROLINE HASTINGS, M.D.

15. NAME(S) AND TITLE(S) OF THE PERSON(S) RESPONSIBLE FOR REVIEW AND EVALUATION OF INFORMATION RELEVANT TO THE SAFETY OF THE DRUG

CAROLINE HASTINGS, M.D.

I agree not to begin clinical investigations until 30 days after FDA's receipt of the IND unless I receive earlier notification by FDA that the studies may begin. I also agree not to begin or continue clinical investigations covered by the IND if those studies are placed on clinical hold. I agree that an Institutional Review Board (IRB) that complies with the requirements set fourth in 21 CFR Part 56 will be responsible for initial and continuing review and approval of each of the studies in the proposed clinical investigation. I agree to conduct the investigation in accordance with all other applicable regulatory requirements.

16. NAME OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE

CAROLINE HASTINGS, M.D.

17. SIGNATURE OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE

Caroline Hastings

18. ADDRESS *(Number, Street, City, State and Zip Code)*

Children's Hospital & Research Center Oakland
747 52nd Street
Oakland, CA 94609

19. TELEPHONE NUMBER *(Include Area Code)*

510-428-3631

20. DATE

05/15/2009

(**WARNING**: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)

Public reporting burden for this collection of information is estimated to average 100 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (HFM-99)
1401 Rockville Pike
Rockville, MD 20852-1448

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

Please DO NOT RETURN this application to this address.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

INVESTIGATIONAL NEW DRUG APPLICATION (IND)
(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)

Form Approved: OMB No. 0910-0014.
Expiration Date: May 31, 2009
See OMB Statement on Reverse.

NOTE: No drug may be shipped or clinical investigation begun until an IND for that investigation is in effect (21 CFR 312.40).

1. NAME OF SPONSOR
CAROLINE HASTINGS, M.D.

2. DATE OF SUBMISSION
05/15/2009

3. ADDRESS *(Number, Street, City, State and Zip Code)*
CHILDRENS' HOSPITAL & RESEARCH CENTER OAKLAND
747 52nd STREET
OAKLAND, CA 94609

4. TELEPHONE NUMBER *(Include Area Code)*
510-428-3631

5. NAME(S) OF DRUG *(Include all available names: Trade, Generic, Chemical, Code)*
Trappsol Brand of Endotoxin controlled Hydroxyl-Propyl-Beta-Cyclodextrin (HPBCD)

6. IND NUMBER *(If previously assigned)*
104116

7. INDICATION(S) *(Covered by this submission)*

8. PHASE(S) OF CLINICAL INVESTIGATION TO BE CONDUCTED:
☐ PHASE 1 ☐ PHASE 2 ☐ PHASE 3 ☑ OTHER compassionate use *(Specify)*

9. LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS (21 CFR Part 312), NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, DRUG MASTER FILES *(21 CFR Part 314.420)*, AND PRODUCT LICENSE APPLICATIONS (21 CFR Part 601) REFERRED TO IN THIS APPLICATION.

10. ***IND submission should be consecutively numbered. The initial IND should be numbered "Serial number: 0000." The next submission (e.g., amendment, report, or correspondence) should be numbered "Serial Number: 0001." Subsequent submissions should be numbered consecutively in the order in which they are submitted.***

SERIAL NUMBER

11. THIS SUBMISSION CONTAINS THE FOLLOWING: *(Check all that apply)*

☐ INITIAL INVESTIGATIONAL NEW DRUG APPLICATION (IND)
☐ RESPONSE TO CLINICAL HOLD

PROTOCOL AMENDMENT(S):
☐ NEW PROTOCOL
☐ CHANGE IN PROTOCOL
☐ NEW INVESTIGATOR

INFORMATION AMENDMENT(S):
☐ CHEMISTRY/MICROBIOLOGY
☐ PHARMACOLOGY/TOXICOLOGY
☐ CLINICAL

IND SAFETY REPORT(S):
☑ INITIAL WRITTEN REPORT
☐ FOLLOW-UP TO A WRITTEN REPORT

☐ RESPONSE TO FDA REQUEST FOR INFORMATION
☐ REQUEST FOR REINSTATEMENT OF IND THAT IS WITHDRAWN, INACTIVATED, TERMINATED OR DISCONTINUED
☐ ANNUAL REPORT
☐ GENERAL CORRESPONDENCE
☐ OTHER *(Specify)*

CHECK ONLY IF APPLICABLE

JUSTIFICATION STATEMENT MUST BE SUBMITTED WITH APPLICATION FOR ANY CHECKED BELOW. REFER TO THE CITED CFR SECTION FOR FURTHER INFORMATION.

☐ TREATMENT IND 21 CFR 312.35(b) ☐ TREATMENT PROTOCOL 21 CFR 312.35(a) ☐ CHARGE REQUEST/NOTIFICATION 21 CFR312.7(d)

FOR FDA USE ONLY

CDR/DBIND/DOD RECEIPT STAMP	DDR RECEIPT STAMP	DIVISION ASSIGNMENT:
		IND NUMBER ASSIGNED:

12. **CONTENTS OF APPLICATION**

This application contains the following items: *(Check all that apply)*

- [x] 1. Form FDA 1571 *[21 CFR 312.23(a)(1)]*
- [ ] 2. Table of Contents *[21 CFR 312.23(a)(2)]*
- [ ] 3. Introductory statement *[21 CFR 312.23(a)(3)]*
- [ ] 4. General investigational plan *[21 CFR 312.23(a)(3)]*
- [ ] 5. Investigator's brochure *[21 CFR 312.23(a)(5)]*
- [ ] 6. Protocol(s) *[21 CFR 312.23(a)(6)]*
  - [ ] a. Study protocol(s) *[21 CFR 312.23(a)(6)]*
  - [ ] b. Investigator data *[21 CFR 312.23(a)(6)(iii)(b)]* or completed Form(s) FDA 1572
  - [ ] c. Facilities data *[21 CFR 312.23(a)(6)(iii)(b)]* or completed Form(s) FDA 1572
  - [ ] d. Institutional Review Board data *[21 CFR 312.23(a)(6)(iii)(b)]* or completed Form(s) FDA 1572
- [ ] 7. Chemistry, manufacturing, and control data *[21 CFR 312.23(a)(7)]*
  - [ ] Environmental assessment or claim for exclusion *[21 CFR 312.23(a)(7)(iv)(e)]*
- [ ] 8. Pharmacology and toxicology data *[21 CFR 312.23(a)(8)]*
- [ ] 9. Previous human experience *[21 CFR 312.23(a)(9)]*
- [x] 10. Additional information *[21 CFR 312.23(a)(10)]*

13. IS ANY PART OF THE CLINICAL STUDY TO BE CONDUCTED BY A CONTRACT RESEARCH ORGANIZATION? [ ] YES [x] NO

IF YES, WILL ANY SPONSOR OBLIGATIONS BE TRANSFERRED TO THE CONTRACT RESEARCH ORGANIZATION? [ ] YES [ ] NO

IF YES, ATTACH A STATEMENT CONTAINING THE NAME AND ADDRESS OF THE CONTRACT RESEARCH ORGANIZATION, IDENTIFICATION OF THE CLINICAL STUDY, AND A LISTING OF THE OBLIGATIONS TRANSFERRED.

14. NAME AND TITLE OF THE PERSON RESPONSIBLE FOR MONITORING THE CONDUCT AND PROGRESS OF THE CLINICAL INVESTIGATIONS

CAROLINE HASTINGS, M.D.

15. NAME(S) AND TITLE(S) OF THE PERSON(S) RESPONSIBLE FOR REVIEW AND EVALUATION OF INFORMATION RELEVANT TO THE SAFETY OF THE DRUG

CAROLINE HASTINGS, M.D.

I agree not to begin clinical investigations until 30 days after FDA's receipt of the IND unless I receive earlier notification by FDA that the studies may begin. I also agree not to begin or continue clinical investigations covered by the IND if those studies are placed on clinical hold. I agree that an Institutional Review Board (IRB) that complies with the requirements set fourth in 21 CFR Part 56 will be responsible for initial and continuing review and approval of each of the studies in the proposed clinical investigation. I agree to conduct the investigation in accordance with all other applicable regulatory requirements.

16. NAME OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE

CAROLINE HASTINGS, M.D.

17. SIGNATURE OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE

Caroline Hastings

18. ADDRESS *(Number, Street, City, State and Zip Code)*

Children's Hospital & Research Center Oakland
747 52nd Street
Oakland, CA 94609

19. TELEPHONE NUMBER *(Include Area Code)*

510-428-3631

20. DATE

05/15/2009

(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)

Public reporting burden for this collection of information is estimated to average 100 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (HFM-99)
1401 Rockville Pike
Rockville, MD 20852-1448

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

Please DO NOT RETURN this application to this address.

CHILDREN'S HOSPITAL
& RESEARCH CENTER OAKLAND

Department of Hematology/Oncology

Elliott Vichinsky, M.D.
Director/Division Chief
James Feusner, M.D.
Director, Oncology
Caroline Hastings, M.D.
Director, Fellowship Program
Mark Walters, M.D.
Director, BMT Program
Barbara Beach, M.D.
Jacob Garcia, M.D.
Carla Golden, M.D.
Carolyn Hoppe, M.D.
Ashutosh Lal, M.D.
Alison Matsunaga, M.D.
Lynne Neumayr, M.D.
Keith Quirolo, M.D.
Robert Raphael, M.D.
Sylvia Singer, M.D.
Lori Styles, M.D.
Joseph Torkildson, M.D., M.B.A.

Adult Hematology
Ward Hagar, M.D.
Eugene McMillan, M.D.

May 15, 2009

Ruyi He, M.D.
Acting Deputy Director
Food & Drug Administration
Center for Drug Evaluation and Research
Division of Gastroenterology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

RE: IND 104,114 Addison Hempel
IND 104,116 Cassidy Hempel

Dear Dr. He:

I have enclosed a summary report of the toxicity profiles and efficacy endpoints regarding the above INDs for Cassidy and Addison Hempel. The girls initiated therapy with HPBCD on April 13, 2009. They each received treatment as specified in the protocol, beginning with a 4 day continuous intravenous infusion for a total of 80 mg/kg. Then, beginning on April 23rd, and each week for 4 consecutive weeks, the girls received HPBCD at a dose of 160 mg/kg IV over 8 hours. Per protocol, the vitals were monitored carefully and frequently through all the infusions and there were no deviations from normal. They tolerated the infusions very well, no interruptions were needed nor did they receive any emergent medications.

Additionally, as specified per protocol, we monitored chemistry panels, urinalyses, and complete blood counts. Again, they remained stable. An interesting observation is that the eosinophil percentage increased after the 4 day infusion and steadily declined over the next month. In other words, whatever may have stimulated this increase in both girls during the continuous infusion was not able to be sustained with weekly infusions. This may be an inflammatory response and may be able to serve as a marker for us as we proceed with alterations in dosage and/or frequency of infusion. They both have had borderline low white blood cell counts (WBC), which I have attributed to in the past to splenomegaly. During the last infusion I did note a much lower WBC in both girls, however, they both appear to have an intercurrent viral illness. I have seen this in the past with both girls and will monitor it carefully.

I have attached a spreadsheet for each girl with all the raw data for the laboratory results. Please note no new toxicity, in particular, no renal or hepatic toxicity. Both girls had mildly elevated ASTs at baseline (and in fact for several years).

The physical examinations remained stable. They are developmentally delayed and ataxic. Interestingly, we noted early on (after the 4 day infusion) an increase in speech with both a few new words and increased repetition of prior known words. This is truly amazing as the girls had both completely stopped speaking in the 2-3 months prior to the beginning o the infusions. This effect seemed to lessen with fewer words, less

activity and alertness, and again more ataxia, as the week progressed. Again, after each infusion they appeared brighter, more cognizant of their environment, more responsive to repetition and engagement in conversation, and more stability on their feet.

I have also attached the work sheets documenting all their vitals. Should you need further details of each physical examination, please do let me know.

At this time, we are ready to proceed with the dose escalation to 320 mg/kg IV over 8 hours, beginning on May 21. We would also be very interested to hear your thoughts of increasing dosing frequency, especially due to the interesting findings on evaluation, most notably the increased speech. It appears they have tolerated the current dosage very well, without toxicity, and could likely tolerate this dose twice weekly. We are interested in obtaining data on both dose escalation and increased frequency and would like to consider after this dose escalation (assuming a safe toxicity profile) an increase of frequency of infusions.

I look forward to your rapid response as we move forward in this exciting and promising new protocol. I appreciate you assistance and guidance.

Sincerely,

Caroline Hastings, M.D.

Cc: Cristi L. Stark, M.S.
Regulatory Project Manager
U.S. Food & Drug Administration
CDER/OND/ODEIII/HFD-180
White Oak, Bldg. 22, Room 5137
10903 New Hamshire Ave.
Silver
Spring, M.D. 20993

Stacy Barley, R.N., M.S., M.H.A.
LCDR, U.S. Public Health Service Commissioned Corps
Division of Gastroenterology Products
Office of Drug Evaluation III
CDER/FDA
White Oak, Bldg 22, Room 5110
10903 New Hampshire Ave.
Silver Spring, MD 20993

Sample order Set

To: Renown Pharmacy
Attn: Adam Porath, PharmD
Fax: 775-982-4038

From: Caroline Hastings MD
Phone: 510-428-3631

Patient: Cassidy Hempel
DOB: 1/23/04

Diagnosis: Niemann Pick Type C Weight: 21kg

Pre infusion labs:

1. CBC with diff, platelets, CMP, fractionated bili, GGT, Amylase, Uric Acid, LDH, Lipid panel, APTT, PT, ESR
2. Spot urine for protein/creatinine, Urinalysis

HPBCD (cyclodextrin) 160mg/kg = 3360mg. Mix in 0.45NS to total volume of 160ml. Infuse at 20ml/hour x 8 hours

Have cardiac monitor and O2 available at bedside

Vital signs: T, P, R, BP q 15 mins x 4; q 30 mins x 2, q 4 hrs until infusion completed

Emergency meds to be readily available:
Albuterol nebulizer 2.5mg in 3cc NS q 20 minutes x 3 then q hour as needed
Benadryl 1mg/kg = 21mg IV
Methylprednisolone 2mg/kg = 42mg IV
Epinephrine 1:10,000; 0.1cc/kg = 2.1cc SC or IV

For hypotension with SBP < 60 or DBP < 40, call MD
Place child in Trendelenberg position, head at 30-degree angle below feet
IV fluid bolus: NS 20ml/kg = 500ml IV over 60 minutes. Repeat as needed

Stop infusion for Respiratory or Hypotensive reaction

Flush port with 20ml NS and 5ml Heparin (100u/cc) prior to deaccess

HPBCD infusion to be given weekly x 4 weeks: 4/23/09, 4/30/09, 5/7/09, and 5/14/09

MD signature: _____ Date: _____

DATE	TIME	Temp	Pulse	Resp	BP		
Admit 4/13/09	0930	98.8	100	24	97/51		SS
Infusion Start	1245	98.0	118	20	117/67	100%	SS
	1305	97.0	99	24	119/73	98%	SS
	1325	98.3	117	28	119/74	100%	SS
	1340	99.0	133	32	123/74	98%	SS
	1355	99.2	132	28	118/69	99%	YB
	1425	98.8	115	24	103/58	97% sleeping	YB
	1500	99.0	133	28	112/68	98%	SS
	1600	98.4	114	28	134/60	100% crying	SS
4.13	2000	98.4	123	24	113/66	97% RA	SK
4.14	2400	98.2	104	24	Dad refused	95% RA	SK
4.14	0400	98.3	102	24		95% RA	SK
	0800	99	116	20	112/84	100% RA	YB
	1200	98.4	105	28	107/71	97% RA	YB
	1600	98.3	126	24	118/72	98% RA	YB
4.14	2000	98.3	115	24	103/54	97% RA	SK
4.15	2400	97.9	103	22	—	94% RA	SK
4.15	0400	97.3	97	22	—	95% RA	SK
4.15	08	98.7	97	20	121/74	99% RA	DG
4.15	12	99.9	117	24	121/81	99% RA	DG

Renown HEALTH

Regional Medical Center
775-982-4100

South Meadows Medical Center
775-982-7000

Rehabilitation Hospital
775-982-3500

Patient Information

F - HEMPEL, ADDISON
1101965679 MR 3081623 FC:P
DOB: 01/23/2004 ADM: 04/13/2009
HASTINGS CAROLINE A

Progress Notes

Stores #766 200/722.153 (9/06)

4/23/09 Week 2

Addison Hempel	Wt : 25kg Date:	Week (2) 3 4 5	Dose: 160mg/kg = 4000mg
Pre infusion labs Date:_____ Time: _____	CBC, diff, platelets, Sed Rate, CMP, LDH T.Bili, Uric Acid, Amylase	Spot urine for protein/creatinine Urinalysis	Biomarkers: 2ml in BHT tube 5ml in green top 5ml in purple top
Vital Signs Temp, HR, RR, BP 1015 1030 1045 1100	Q 15 mins x 4 99.2 116/68, 119 24 98.3, 122/84, 115 28 99.3 127/80 109 28 99.5, 109/66 109, 28	Q 30 mins x 2 1130 99.1 128/84, 108 24 1200 98.7, 123/78, 121, 28	Q 4 hours 1500 98.2 117/67 106 28 1800 98.8 114/57, 105, 28
Toxicity Criteria Per NCI guidelines	**Hematology** WBC 5.0 ANC 22-80 Hgb 12.0 Platelets 196 Eos 12	Grade	Comments
	Renal BUN < 5 Creat 0.4 Urine protein (=) BP	Grade	Comments
	Hepatic SGOT 29 SGPT 17 T Bili 0.9 D Bili 0.1 I Bili 0.4	Grade	Comments

Infusion started 1020 A.M.

F - HEMPEL, ADDISON
8103177369 MR 3081623 FC: H
DOB: 01/23/2004 ADM: 04/10/2009
HASTINGS CAROLINE A

Date: 4/23/09 Time Started: 1030

Day Shift

Week 2 CASSidy Hempel

Time	Type	Oral Amt. In cc's
11:45	Juice	8oz,
12:30	Juice	8oz
2:00	Juice	8oz
3:50	Water Juice	6oz
4:40	Water Juice	8oz
5:00	Water Juice	8oz
Total		

Time	Urine*	Urine / Stool	Stool	Emesis	Other
11:45	120				
12:30	124				
2:30	120				
4:40	250				
Total					

IV Solutions Type	Total
Total	

Night Shift

Time	Type	Oral Amt. In cc's
Total		

Time	Urine	Urine / Stool	Stool	Emesis	Other
Total					

IV Solution Type	Total
Total	

Renown HEALTH

Regional Medical Center 775-982-4100
South Meadows Medical Center 775-982-7000
Rehabilitation Hospital 775-982-3500

PEDIATRICS

24 HOUR INTAKE AND OUTPUT RECORD

F - HEMPEL, CASSIDY H
8103177377 MR 3002231 FC: H
DOB: 01/23/2004 ADM: 04/10/2009
HASTINGS CAROLINE A

90032 Rev. 9/07

week 3 , 4/30/09

wt. 23.5 kg Ht. 116.7

Addison Hempel	Wt : 25kg Date:	Week 2 (3) 4 5	Dose: 160mg/kg = 4000mg
Pre infusion labs Date: 4/30/09 Time: ~~0920~~	CBC, diff, platelets, Sed Rate, CMP, LDH T.Bili, Uric Acid, Amylase	Spot urine for protein/creatinine Urinalysis	Biomarkers: 2ml in BHT tube 5ml in green top 5ml in purple top
Vital Signs Temp, HR, RR, BP ~~0945~~ 1000 1015 1020	Q 15 mins x 4 ~~98.7, 121, 22, 122/83~~ ~~98.6 119 24 91/66~~ ~~98.8 106 24 105/75~~ ~~98.9 104 24 108/68~~	Q 30 mins x 2 ~~1145~~ ~~98.4, 109, 24, 109/69~~ ~~1200~~ ~~98.3, 101, 24, 111/78~~	Q 4 hours ~~1500~~ 98.3, 104, 24, 106/61 ~~1730~~ ~~98.4, 101, 24, 112/57~~
Toxicity Criteria Per NCI guidelines	**Hematology** WBC 4.7 ANC 2411.1 Hgb 11.7 Platelets 182 Eos 5.2	Grade	Comments
	Renal BUN 8 Creat 0.5 Urine protein (-) BP 122/83	Grade	Comments
	Hepatic SGOT 75 SGPT 13 T Bili 0.4 D Bili 0.1	Grade	Comments

Date: April 30th, 09 Time Started: 0930

Week #3

Day Shift

Time	Type	Oral Amt. In cc's
0900	Juice	240
1100	Juice	240
1600	Juice	240
Total		720

Time	Urine	Urine / Stool	Stool	Emesis	Other
1100		120			
1300	160				
1530	450				
1700		440			
Total	610	560			

IV Solutions Type	Total
Cyclodextrin	160
Total	160

Night Shift

Time	Type	Oral Amt. In cc's
Total		

Time	Urine	Urine / Stool	Stool	Emesis	Other
Total					

IV Solution Type	Total
Total	

Renown HEALTH

Regional Medical Center 775-982-4100
South Meadows Medical Center 775-982-7000
Rehabilitation Hospital 775-982-3500

PEDIATRICS

24 HOUR INTAKE AND OUTPUT RECORD

Patient Information

F - HEMPEL, ADDISON
8103177369 MR3081623 FC:H
DOB: 01/23/2004 ADM: 04/10/2009
HASTINGS CAROLINE A

90032 Rev. 9/07

Date: May 7th, 09 Time Started: 1015

Day Shift

Juice week #4

Time	Type	Oral Amt. In cc's
12:30	Water	90
12:45	"	80
2:45	"	80
3:30	"	80
4:00	Juice	80
Total		1110

Time	Urine	Urine / Stool	Stool	Emesis	Other
1200		320			
1:40-1:32					
1:55	261				
2:30	175				
2:45		100			
3:30	210				
4:15	300				
4:50	135				
6:10	150				
Total	1263	420			

IV Solutions Type	Total
Cyclodextrin	
Total	160

Night Shift

Time	Type	Oral Amt. In cc's
Total		

Time	Urine	Urine / Stool	Stool	Emesis	Other
Total					

IV Solution Type	Total
Total	

Renown HEALTH

Regional Medical Center 775-982-4100
South Meadows Medical Center 775-982-7000
Rehabilitation Hospital 775-982-3500

PEDIATRICS

24 HOUR INTAKE AND OUTPUT RECORD

Patient Information

F - HEMPEL, ADDISON
8103195767 MR 3081623 FC: H
DOB: 01/23/2004 ADM: 05/01/2009
HASTINGS CAROLINE A

90032 Rev. 9/07

May 7, 09 Week #4

[redacted] Hempel Addison	Wt: [redacted]g Date: 23.5kg	Week 2 3 (4) 5	Dose: 160mg/kg = 3360mg
Pre infusion labs Date: 5/7/09 Time: 0945 wt. 23.5kg 115.0 cm	CBC, diff, platelets, ESR Sed Rate, CMP, LDH T.Bili, Uric Acid, GGT, Amylase, PT Lipid panel	Spot urine for protein/creatinine Urinalysis	Biomarkers: 2ml in BHT tube 5ml in green top 5ml in purple top
Vital Signs Temp, HR, RR, BP 1015 99.0, 114, 24, 129/76 1030 98.4, 112, 24, 118/93 1045 98.7, 94, 24, 124/56 1100 98.2, 104, 24, 91/52	Q 15 mins x 4	Q 30 mins x 2 1130 98.6, 115, 28, 114/81 1200 99.0, 110, 28, 107/78	Q 4 hours 1500 98.6, 111, 28, 124/69 1600 98.8, 104, 28, 122/83
Toxicity Criteria Per NCI guidelines	**Hematology** WBC 3.8 ANC 1789.8 Hgb 11.4 Platelets 116 Eos 0.6	Grade	Comments
	Renal BUN 8 Creat 0.3 Urine protein <6.0 BP 129/76	Grade	Comments
	Hepatic SGOT 93 SGPT 19 T Bili 0.5 D Bili 0.1	Grade	Comments

5/14/09

Wt: 23.7kg / 115.2cm Week #5

Addison Hempel	Wt : 25kg Date: 5/14/09	Week 2 3 (5)	Dose: 160mg/kg = 4000mg
Pre infusion labs Date: 5/14/09 Time: _____	CBC, diff, platelets, Sed Rate, CMP, LDH T.Bili, Uric Acid, Amylase	Spot urine for protein/creatinine Urinalysis	Biomarkers: 2ml in BHT tube 5ml in green top 5ml in purple top
Vital Signs Temp, HR, RR, BP	Q 15 mins x 4 1015 99.7, 133, 121/74, 28 1015 ~~99.7, 123, 110/64, 28~~ 1030 ~~99.2, 132, 94/75, 28~~ 1045 ~~99.2, 119, 125/77, 24~~	Q 30 mins x 2 1115 ~~99.1, 124, 125/69, 28~~ 1130 ~~99.1, 133, 118/68, 28~~	Q 4 hours 1215 ~~99.2, 124, 128/64, 28~~ 1615 ~~95.1, 128, 124/69, 32~~
Toxicity Criteria Per NCI guidelines	**Hematology** WBC 1.7 ANC ~~4~~ 2.1 Hgb 9.5 Platelets 108 Eos 2.8	Grade _____ _____ _____ _____ _____	Comments
	Renal BUN 5 Creat 0.3 Urine protein 14 BP ~~124/74~~ ~~118/68~~	Grade _____ _____ _____ _____	Comments
	Hepatic SGOT 83 SGPT 17 T Bili 0.7 D Bili 0.1	Grade _____ _____ _____ _____	Comments

Cough - Tussinex guidelines

Date: 5/14/09 Time Started: 1000

Day Shift Week # 8

Time	Type	Oral Amt. In cc's
1100	juice	240
1500	juice	240
2100	juice	240
Total		720

Time	Urine	Urine / Stool	Stool	Emesis	Other
1015	92				
1155	82				
1:40	65				
3:20	120				
4:00		Stool			
4:45	240				
5:30	140				
6:45	234				
Total	973				

IV Solutions Type	Total
Explolitas	1600
Total	1600

Night Shift

Time	Type	Oral Amt. In cc's
Total		

Time	Urine	Urine / Stool	Stool	Emesis	Other
Total					

IV Solution Type	Total
Total	

Renown HEALTH

Regional Medical Center 775-982-4100
South Meadows Medical Center 775-982-7000
Rehabilitation Hospital 775-982-3500

PEDIATRICS
24 HOUR INTAKE AND OUTPUT RECORD

Patient Information
F - HEMPEL, ADDISON
8103195767 MR3081623 FC: H
DOB: 01/23/2004 ADM: 05/01/2009
HASTINGS CAROLINE A

90032 Rev. 9/07

ADDISON HEMPEL						TOXICITY
			BASELINE STUDIES			GRADE
DATE:	4/7/2009	4/8/2009				
HEMATOLOGY						
WBC	4.5					
HGB	12.1					
HCT	34.8					
RBC	4.14					
MCV	84.1					
MCH	29.2					
MCHC	34.7					
RDW	12.9					
PLTS	137					
MPV	9.3					
NEUTS/POLYS	49.3					
LYMPH/ATYP	34.7					
MONO	9.5					
EOS	6.3					
BASO	0.2					
HYPOCHROMIA	1+					
ESR						
APTT						
CHEMISTRIES						
SODIUM	138					
POTASSIUM	3.9					
CHLORIDE	109					
CO2	21					
BUN	8					
CREATININE	0.4					
GLUCOSE	89					
CALCIUM	9.6					
ALK PHOSPHATE	179					
SGOT/ALT	74					
SGPT/AST	13					
GAMMA GT						
BILIRUBIN, TOTAL	0.4					
BILIRUBIN, DIRECT						
TOTAL PROTEIN						
ALBUMIN	4.6					
GLOBULIN	2.4					
A/G RATIO	1.9					
AMYLASE						
URIC ACID						
LDH						

ADDISON HEMPEL						TOXICITY
			BASELINE STUDIES			GRADE
DATE:	4/7/2009	4/8/2009				
LIPID PANEL						
CHOLESTEROL						
TRIGLYCERIDES	7					
LDL						
VLDL						
HDL						
TOTAL CHOLE/HDL						
CHOLEST RATIO						
URINALYSIS:						
COLOR	yellow					
CLARITY	hazy					
SPECIFIC GRAVITY	1.008					
pH URINE	8					
GLUCOSE	negative					
KETONES	negative					
PROTEIN	negative					
BILIRUBIN	negative					
NITRATE	negative					
LEUK ESTERASE	negative					
OCCULT BLOOD	negative					
WBC						
RBC						
EPITHEL CELL						
BACTERIA						
CRYSTALS						
CASTS						
MUCOUS						
AM SPOT URINE						
CREATININE URINE	21	16.6				
PROTEIN URINE	<6.0					
CREATININE CLEARANCE		102				
COLLECTION PERIOD		24				
WEIGHT/HEIGHT		25/115				
CREATININE, EXCRETED		299				
CREATININE, PLASMA		0.4				
TOTAL VOLUME		1800				

ADDISON HEMPEL						TOXICITY
WEEK 1	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	GRADE
DATE:	4/13/2009	4/14/2009	4/15/2009	4/16/2009	4/17/2009	
HEMATOLOGY						
WBC			5.4	5.7	3.8	
HGB			11.4	12.8	106	
HCT			32.2	36.1	29.5	
RBC			3.82	4.29	3.51	
MCV			84.1	84.1	84	
MCH			29.7	29.8	30.1	
MCHC			35.3	35.4	35.9	
RDW			13.6	13.6	13.8	
PLTS			140	146	CLUMPED	
MPV			9.2	9.3	9.6	
NEUTS/POLYS			36.2	79.2	57	
LYMPH/ATYP			42.1	6.7	32	
MONO			8.1	6.9	2	
EOS			12.9	7	9	
BASO			0.7	0.2	0	
HYPOCHROMIA			1+	1+		
ESR						
APTT						
CHEMISTRIES						
SODIUM			136	141	138	
POTASSIUM			3.9	3.7	3.4	
CHLORIDE			105	108	106	
CO2			23	24	25	
BUN			6	<5	5	
CREATININE			0.4	0.4	0.3	
GLUCOSE			86	91	92	
CALCIUM			9.3	8.9	8.9	
ALK PHOSPHATE			160	109	126	
SGOT/ALT			72	76	66	
SGPT/AST			13	13	14	
GAMMA GT	14					
BILIRUBIN, TOTAL	0.5		0.4	0.5	0.7	
BILIRUBIN, DIRECT	0.1					
TOTAL PROTEIN			6.5	5.6	5.7	
ALBUMIN			3.9	3.5	3.6	
GLOBULIN			2.6	2.1	2.1	
A/G RATIO			1.5	1.7	1.7	
AMYLASE	27					
URIC ACID	4					
LDH						

ADDISON HEMPEL						TOXICITY
WEEK 1	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	GRADE
DATE:						
LIPID PANEL						
CHOLESTEROL	154				103	
TRIGLYCERIDES	119				72	
LDL	99				67	
VLDL	23.8				14.4	
HDL	31				22	
TOTAL CHOLE/HDL	5				4.68	
CHOLEST RATIO						
URINALYSIS:						
COLOR					yellow	
CLARITY					hazy	
SPECIFIC GRAVITY					1.008	
pH URINE					8	
GLUCOSE					negative	
KETONES					negative	
PROTEIN					negative	
BILIRUBIN					negative	
NITRATE					negative	
LEUK ESTERASE					negative	
OCCULT BLOOD					negative	
WBC					0-2	
RBC						
EPITHEL CELL					few	
BACTERIA					few	
CRYSTALS					mod amorph	
CASTS						
MUCOUS					few	
AM SPOT URINE						
CREATININE URINE	<10					
PROTEIN URINE	<6					
CREATININE CLEARANCE						
COLLECTION PERIOD						
WEIGHT/HEIGHT						
CREATININE, EXCRETED						
CREATININE, PLASMA						
TOTAL VOLUME						

ADDISON HEMPEL					TOXICITY
	WEEK 2	WEEK 3	WEEK 4	WEEK 5	GRADE
DATE:	4/23/2009	4/30/2009	5/7/2009	5/14/2009	
HEMATOLOGY					
WBC	5	4.7	3.8	1.7	
HGB	12	11.7	11.4	9.5	
HCT	34.2	33.2	31.9	26.5	
RBC	4.04	3.95	3.8	3.15	
MCV	84.6	84.1	84	84	
MCH	29.8	29.7	29.9	30	
MCHC	35.2	35.3	35.6	35.8	
RDW	13.7	13.6	13.8	14	
PLTS	196	182	166	108	
MPV	8.9	8.9	8.6	8.6	
NEUTS/POLYS	45.6	51.3	47.1	60.1	
LYMPH/ATYP	29.7	33.9	39.9	29.5	
MONO	7.1	8.1	8.3	7.1	
EOS	17.2	5.2	4.1	2.8	
BASO	0.4	1.5	0.6	0.5	
HYPOCHROMIA	1	1	1		
ESR	11	16	8	22	
APTT	28.9	29.5	29.8	33	
CHEMISTRIES					
SODIUM	138	135	135	136	
POTASSIUM	3.7	3.8	4.2	3.9	
CHLORIDE	105	99	101	107	
CO2	22	25	24	21	
BUN	0.4	8	8	5	
CREATININE	0.4	0.5	0.3	0.3	
GLUCOSE	117	102	97	103	
CALCIUM	9.8	9.4	9.6	8.9	
ALK PHOSPHATE	130	137	110	109	
SGOT/ALT	79	75	93	83	
SGPT/AST	17	13	19	17	
GAMMA GT	12	13	15		
BILIRUBIN, TOTAL	0.7	0.4	0.5	0.7	
BILIRUBIN, DIRECT	0.1	0.1	0.1	0.1	
TOTAL PROTEIN	6.8	7	6.8	6.4	
ALBUMIN	4.3	4.2	4.3	4.1	
GLOBULIN	2.5	2.8	2.5	2.3	
A/G RATIO	1.7	1.5	1.7	1.8	
AMYLASE	21	28	46	16	
URIC ACID	3.7	3.1	3.2	2.8	
LDH	321	301	300	323	

ADDISON HEMPEL					TOXICITY
	WEEK 2	WEEK 3	WEEK 4	WEEK 5	GRADE
DATE:	4/23/2009	4/30/2009	5/7/2009	5/14/2009	
LIPID PANEL					
CHOLESTEROL	133	130	131	106	
TRIGLYCERIDES	274	192	178	80	
LDL	55	74	76	66	
VLDL	55	38.4	35.6	16	
HDL	23	18	19	24	
TOTAL CHOLE/HDL	5.8	7.2	6.9	4.4	
CHOLEST RATIO					
URINALYSIS:					
COLOR	yellow	yellow	yellow	yellow	
CLARITY	turbid	turbid	cloudy	clear	
SPECIFIC GRAVITY	1.001	1.014	1.006	1.013	
pH URINE	8.5	8.5	8.5	8.5	
GLUCOSE	neg	neg	neg	neg	
KETONES	neg	neg	neg	neg	
PROTEIN	neg	neg	neg	neg	
BILIRUBIN	neg	neg	neg	neg	
NITRATE	neg	neg	neg	neg	
LEUK ESTERASE	small	neg	neg	neg	
OCCULT BLOOD	neg	neg	neg	neg	
WBC	0-2				
RBC	0-2				
EPITHEL CELL	few	few			
BACTERIA	mod	few			
CRYSTALS	few	mod	mod		
CASTS					
MUCOUS					
AM SPOT URINE					
CREATININE URINE	11	44	10	29	
PROTEIN URINE	<6.0		<6	14	
CREATININE CLEARANCE					
COLLECTION PERIOD					
WEIGHT/HEIGHT					
CREATININE, EXCRETED					
CREATININE, PLASMA					
TOTAL VOLUME					