



NF Clinic Network (NFCN) Application Form*

Clinic Name:

Indiana University Neurofibromatosis Clinic

Affiliated Hospital:

Riley Hospital for Children

Affiliated University or Institution:

Indiana University School of Medicine

Clinic Address:

Riley Hospital for Children
702 Barnhill Drive
Indianapolis, IN 46202

Clinic Director:

Cynthia M. Hingtgen, MD, Ph.D.

Clinic Coordinator Name:

TBA

**Note: Some non-public information has been removed from this application form.*



The Neurofibromatosis Clinic Network (NFCN)

FORM PART A: Affiliate Clinic Application

1. ABOUT YOUR NF CLINIC

a. Is your NF Clinic:

- Freestanding
- Hospital based
- In an academic center
- Other (please describe)

b. Describe overall your NF Clinic, when it meets and how it functions.

The Indiana University Neurofibromatosis Clinic is based at Riley Hospital. This clinic provides diagnosis, genetic counseling, and management for patients of all ages with neurofibromatosis (NF). Patients with NF Type 1, NF Type 2 and schwannomatosis are cared for through this clinic. We provide the only comprehensive NF clinic in the state of Indiana. The clinic currently sees patients the 1st and 3rd Tuesday of each month between 1PM and 5PM. Starting September 1, 2007, we will see patients every Tuesday from 1 to 5PM. We encourage seeing all members of a family with NF at the

same visit. Our clinic is staffed by an adult and a child neurologist and a genetic counselor. The clinic also provides referrals to other specialists, including dermatologists, neurosurgeons, oncologists, ophthalmologists, orthopedic surgeons, and otolaryngologists who work closely with the NF clinic. Services in the Indiana University Neurofibromatosis Program are tailored to the patient's specific needs, as NF is a highly variable condition. Besides patient care, collaboration with researchers to further the understanding of NF is a main goal of this program. There is a great deal of federally funded basic NF research at Indiana University School of Medicine. The research is focused on understanding tumor formation, changes from benign to malignant tumors, abnormalities in bone formation, vascular changes and abnormal pain sensation. Patients are updated on ongoing research in NF at their appointments and, as available, are informed about studies and trials in which they may be enrolled.

2. CLINIC DIRECTOR and STAFF EXPERTISE

a. CLINIC DIRECTOR: Please describe:

i. Your experience to date with NF care

I have been the co-director of the IU NF clinic since July, 2002 and am now the director. I have been involved in expanding the care that our clinic provides to those with NF since 2002.

ii. Your past and current association with NF clinical trials

We have two active studies related to NF1. The first involves characterizing pain associated with NF1 and using quantitative electrodiagnostic testing to evaluate sensory responses. The second is a limited phase II study of imatinib for treatment of plexiform neurofibromas in adults and children with NF1.

iii. Your past and current association with other clinical trials e.g. oncology trials

See above. We have a close relationship with the Hematology/Oncology Division and the IU Cancer center to assist us in current and future trials.

b. CLINIC DIRECTOR: Please provide information on:

i. Present and past funding you have received for NF research. Include funding source, date received, amount and project description.

Current Research Support

- a) R01 NS051668 (NIH-NINDS). Actions of GTPase-Activating Proteins on Sensory Neurons. \$2,500,854; 1/10/06 – 12/31/2010, Role: **Principal Investigator**. This study examined the effects of altering the expression of GTPase activating proteins, including neurofibromin, on the sensitivity of primary sensory neurons involved in pain signaling and neurogenic inflammation.
- b) New Investigator Award, Neurofibromatosis Research Program (Department of Defense, US Army Medical Research and Materiel Command's Office of the Congressionally Directed Medical Research Programs (CDMRP)). Function of Neurofibromin in Endothelial Cells. \$677,250; 01/01/05-12/30/07, Role: **Co-**

Principal Investigator (PI, D. Ingram). This study examined the actions of neurofibromin in the development and function of endothelial cells.

Completed Research Support

- a) Biomedical Research Grant (Indiana Univ., School of Medicine). The Actions of Vascular Endothelial Growth Factor on Schwann Cells with the Neurofibromatosis Type I Mutation. \$35,000, 04/01/02 – 03/31/03, Role: **Principal Investigator**. This study examined effects of dysregulation of the Ras pathway in Schwann cells from mice with the *Nf1* mutation. Biochemical and functional consequences were examined.
- b) Young Investigator Award (National Neurofibromatosis Foundation). Growth Factor Effects on Stimulus-Evoked Release of Neuropeptides from Sensory Neurons with the *Nf1* Mutation. \$70,000, 07/01/02 – 06/30/04, Role: **Principal Investigator**. This study initiated the examination of the effects of nerve growth factor and vascular endothelial growth factor on the release of substance P and calcitonin gene-related peptide from *Nf1* mutated mouse embryonic sensory neurons grown in culture.
- c) APRC Supplement to 5R01CA074177-07 (National Cancer Institute). *Nf1*^{+/-} Mast Cells Promote Inflammation and Angiogenesis. \$79,982 for section; 07/01/03 - 06/30/05, Role: **Section Principal Investigator** (Overall Principal Investigator, D. W. Clapp). This study was a collaboration of investigators studying the actions of *Nf1* haploinsufficient mast cells on other cell types. The aims of Dr. Hingtgen's section were to investigate the effects of *Nf1* haploinsufficient mast cells on sensory neuron excitability.
- d) New Investigator Award, Neurofibromatosis Research Program (Department of Defense, US Army Medical Research and Materiel Command's Office of the Congressionally Directed Medical Research Programs (CDMRP)). Growth Factor Actions on *Nf1* Haploinsufficient Sensory Neurons. \$672,419; 04/15/03 – 4/14/06, Role: **Principal Investigator**. This study examines the actions of nerve growth factor, stem cell factor and vascular endothelial growth factor to cause hyperalgesic behavior and enhanced sensory neuron transmitter release in a mouse model of neurofibromatosis type 1.

ii. Your NF-related clinical and scientific publications.
Include Journal, Citation and Title.

- 1) Smith LH, Christensen CK, Walsh LE, **Hingtgen CM**. Pain in patients with neurofibromatosis type 1. Submitted to *Pain*.
- 2) **Hingtgen CM**, Fehrenbacher JC, Roy SL. Stem cell factor causes increased sensitivity of Wildtype and *Nf1*^{+/-} mouse sensory neurons. Submitted to *Neuroscience Letters*.
- 3) Nebesio TD, Ming W, Chen S, Clegg T, Yuan J, Estwick SA, Morgan TL, Li XH, **Hingtgen CM**, Yang F-C. (2007) Neurofibromin-deficient Schwann cells have increased lysophosphatidic acid dependent survival and migration - implications for increased neurofibroma formation during pregnancy. *Glia* 55:527-36.

- 4) **Hingtgen CM**, Roy SL, Clapp DW (2006) Stimulus-evoked release of neuropeptides is enhanced in sensory neurons from mice with a heterozygous mutation of the *Nf1* gene. *Neuroscience* 137:637-645.
- 5) Wang Y, Nicol GD, Clapp DW, **Hingtgen CM** (2005) Sensory neurons from *Nf1* haploinsufficient mice exhibit increased excitability. *J. Neurophysiol.* 94:3670-3676.
- 6) Yang F-C, Ingram, DA, Chen S, **Hingtgen CM**, Ratner N, Monk KR, Clegg T, White H, Mead L, Wenning MJ, Williams DA, Kapur R, Atkinson SJ, Clapp DW (2003) Neurofibromin deficient Schwann cells secrete a potent migratory stimulus for *Nf1* +/- mast cells. *J. Clin. Invest.* 112:1851-1861.

c. Who are the key staff in your NF clinic facility?

Provide Name; Title; Degree/Qualifications; Role in Clinic.

- 1) Cynthia M. Hingtgen, MD, PhD; Associate Professor Department of Neurology, Indiana University School of Medicine; Board Certified neurologist practicing since July, 2000; Director of Indiana University Neurofibromatosis Clinic.
- 2) Laurence E. Walsh, MD; Assistant Professor Clinical Medical and Molecular Genetics and Clinical Neurology, Indiana University School of Medicine; Board Certified in Neurology with Special Qualification in Child Neurology since 1993 and with special qualifications in Neurodevelopmental Disabilities since 2004, Board Certified in Clinical Genetics since 1999; Has provided care for children in the Indiana University Neurofibromatosis Clinic since 2001 and served as co-director of the clinic from 2001-2006.
- 3) Celanie K. Christensen, MS, CGC; Genetic Counselor, Departments of Neurology and Pediatrics (Metabolism and Genetics Division); certified genetic counselor serving the NF Clinic since 2002 and also serving as the clinic coordinator.

Medical assistant and nursing services are provided through Clarian Health Partners, the hospital corporation with which Riley Hospital for Children is affiliated. These personnel are affiliated with neurology services but are not specific to the NF clinic.

d. Who within this core staff currently coordinates NF patient services?

Describe this individual's NF clinic related duties.

Our clinic coordinator, Celanie Christensen coordinates the NF patient services. Since all of our scheduling for the NF clinic is completed through our central scheduling team for the Department of Neurology, Ms. Christensen assures that patients have access to information on NF, have appropriate follow-up and referrals and reviews consent forms for any ongoing studies. In addition, she provides genetic counseling service to the patients.

e. Describe any areas of NF care in which your clinic has particular

expertise (e.g. optic glioma, vestibular schwannoma, bone manifestations, learning disabilities etc.) and the clinic staff that provide this care.

We provide comprehensive care to adults and children with NF, but do not have any particular area of clinical expertise in terms of treatment.

3. PATIENT SCHEDULING and REFERRALS

- a. Provide the details of the 'typical' timeframe in which patients receive a response to a request for scheduling, are actually scheduled for an appointment, how patients are prioritized, etc.

New patients referred from primary care physicians, other specialists or "self-referrals" contact the scheduling team for the Department of Neurology. They are scheduled into the next available new patient appointment with either Dr. Walsh (for those under the age of 3 years) or Dr. Hingtgen. If a patient has an urgent issue (growing tumor, intractable pain, etc.), Dr. Walsh and/or Dr. Hingtgen are notified and make arrangements to see the patient as soon as possible. This occurs within 2 business days of the original contact but more typically within 24 hours as the scheduling number is answered by an actual person during office hours. Return visits are scheduled at the end of each appointment, but can be moved up if acute issues arise after contacting Dr. Walsh or Dr. Hingtgen through our clinic nurses.

- b. Provide details of those specialists to whom (either within or outside our own clinic facility) your clinic refers NF patients for the following specialty care. **These should individuals familiar and experienced with consensus guidelines for care of individuals with NF** (Please provide information for PEDIATRIC CARE referrals in the first table and ADULT CARE in the second table).

PEDIATRIC CARE

SPECIALTY	DOCTOR	CLINIC ADDRESS	PHONE	EMAIL (if available)
Genetics	Laurence E. Walsh, MD	Riley Hospital for Children	317-278-5450	lewalsh@iupui.edu
Neurology	Laurence Walsh, MD Cynthia M. Hingtgen, MD, PhD (over age 3 years)	Riley Hospital for Children	317-278-5450	lewalsh@iupui.edu chingtge@iupui.edu
Orthopedics	Richard Lindseth, MD Randall Loder, MD John Lubicky, MD	Riley Hospital for Children	317-274-2500	
Developmental pediatrics/learning disabilities	Stephen Pongonis, Psy.D.	Riley Hospital for Children	317-278-5450	
Ophthalmology	David Plager, MD	Riley Hospital	317-274-8103	

		for Children		
Neurosurgery	Joel C. Boaz, MD	Riley Hospital for Children	317-274-8852	
Plastic surgery	Robert Havlik, MD	Riley Hospital for Children	317-274-2430	
Neurooncology	Kent Robertson M. D.	Riley Hospital for Children	317-274-7810	krobert@iupui.edu
Medical Oncology/Radiation Oncology	Kent Robertson M. D.	Riley Hospital for Children	317-274-7810	krobert@iupui.edu
Endocrinology	Todd Nebesio, MD	Riley Hospital for Children	317-274-3889	
Audiology/ENT	Richard T. Miyamoto, MD	Riley Hospital for Children	317-274-3556	
Radiology/Neuroradiology	Mary Edwards-Brown, MD	Riley Hospital for Children	317-274-3394	
General Surgery/Surgical Oncology	Scott Engum, MD	Riley Hospital for Children	317-274-5437	
Dermatology	Patricia Treadwell, MD	Riley Hospital for Children	317-274-7744	
Cardiovascular Disease	Mark Hoyer, MD	Riley Hospital for Children	317-274-8906	
Oral and Maxillofacial Surgery	Robert Havlik, MD	Riley Hospital for Children	317-274-2430	
Behavioral Issues	Kelda Walsh, MD	Riley Hospital for Children	317-274-8162	

ADULT CARE

SPECIALTY	DOCTOR	CLINIC ADDRESS	PHONE	EMAIL (if available)
Genetics	Laurence E. Walsh, MD	Riley Hospital for Children	317-278-5450	lewash@iupui.edu
Neurology	Cynthia M. Hingtgen, MD, PhD	Riley Hospital for Children	317-278-5450	chingtge@iupui.edu
Orthopedics	L. Daniel Wurtz, MD	Indiana University Hospital	317-274-8318	
Developmental pediatrics/learning disabilities	N/A			

Ophthalmology	Robert D. Yee, MD	Indiana University Hospital	317-274-7101	
Neurosurgery	Mitesh V. Shah, MD	Indiana University Hospital	317-274-8422	
Plastic surgery	Robert Havlik, MD	Riley Hospital for Children	317-274-2430	
Neurooncology	Edward J. Dropcho, MD	Indiana University Hospital	317-278-5450	
Medical Oncology/Radiation Oncology	Daniel A. Rushing, MD	Indiana University Hospital	317-274-3515	drushing@iupui.edu
Endocrinology	Division of Endocrinology	Indiana University Hospital	317-274-7577	
Audiology/ENT	Richard T. Miyamoto, MD	Riley Hospital for Children	317-274-3556	
Radiology/Neuroradiology	Radiology Services	Indiana University Hospital	317-274-1866	
General Surgery/Surgical Oncology	Department of Surgery	Indiana University Hospital	317-274-4966	
Dermatology	Jeffrey B. Travers, MD, PhD	Indiana University Hospital	317-274-7744	
Cardiovascular Disease	Division of Cardiology	Clarian Health Partners - Methodist Hospital	317-962-0500	
Oral and Maxillofacial Surgery	Robert Havlik, MD	Riley Hospital for Children	317-274-2430	
Behavioral Issues	Psychiatry Services	Clarian Health Partners - Methodist Hospital	317- 274-4012	

4. NUMBER OF NF PATIENTS YOUR CLINIC SEES

- a. How many NF PATIENTS did you see in the past 12 months? 208
- b. How many of these were **NEW** patients to your clinic? 80

Insert numbers below

	NF1	NF2	SCHWANNOMATOSIS	OTHER
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NUMBER OF PATIENTS SEEN IN PAST 12 MONTHS (return patients)	123	5	0	0
NUMBER OF <u>NEW</u> PATIENTS SEEN IN PAST 12 MONTHS	78	0	2	11
TOTAL	201	5	2	11

c. Overall what proportion of patients seen in the past year were (give finite numbers if these are available, or estimate percentage):

Under 18_ 153__ 18+ __ 66__ (give numbers - if data available)

OR estimate

Under 18 (%)__ 18+ (%)__

5. TRANSITIONING PEDIATRIC TO ADULT NF CARE

How does your clinic facilitate continuity of care for patients transiting from pediatric to adult care?

Since our clinic provides care to adults and children at the same time, the transition is smooth. The only difference for the patient may be in switching from Dr. Walsh to Dr. Hingtgen at some point during adolescence. Many of the pediatric subspecialists that have cared for an NF patient will continue to see the patient in adulthood. When this is not possible we coordinate their care with one of our adult subspecialists.

Explain how continuity of care is accomplished. Describe those partnering clinics with which you coordinate services, and explain any limitations:

This transition is very smooth from a scheduling standpoint since we are one clinic that cares for all ages. Unfortunately, we lose many patients after they turn 18 because they no longer have insurance and are no longer covered by state funds for pediatric care and yet are not impaired enough to qualify for disability. We do a great deal to try to educate the late teens about adult NF issues (heralds of malignant transformation of tumors, hypertension and pregnancy issues, etc.). Although we try to anticipate this "financial" transition and help find resources and file disability

paperwork, when appropriate, we often are unable to care for these adults with limited resources.

6. INTERNAL CONFERENCES

Provide details on internal conferences in your institution which are related to NF patient care in your clinic (e.g. NF Clinic case management conference, etc.)

Currently, we have informal internal conferences as needed for research trials and difficult case management. The key members of the NF Clinic (Drs. Walsh, Hingtgen and Ms. Christensen) are in the clinic together and often discuss clinic related issues and difficult cases management issues during and after the clinic period. With our transition on September 1, 2007 to weekly NF Clinic, we will have a weekly conference at 4:30 PM on the 1st Tuesday of each month. These will be a mixture of discussion of relevant NF research topics, guideline education, clinic management issues and difficult case presentations. Many of the subspecialists to whom we refer our patients and the basic scientist conducting NF-related research on campus will attend, depending on the topic.

7. CLINICAL TRIALS

Our clinic is willing and able to provide our NF patients with information on, and to facilitate their participation in, clinical trials for which NF patients are eligible (check box)

Yes No

If 'no', briefly describe why.

Do you currently refer patients to clinical trials?

Yes No

If 'yes', provide details of current clinical trial protocols in which you currently or have had patients involved in the past 5 years.

- 1) Our own phase II study of imatinib for treatment of plexiform neurofibromas in adults and children with NF1.
- 2) Call for NF1 Tumor Donations (Research Call), Dr. Peggy Wallace, University of Florida

8. PATIENT REGISTRY

Do you currently have an NF specific patient database/registry?

Yes No

If 'yes', please describe.

We have a paper formatted database including patient identifying information, vitals, clinical criteria and common complications of neurofibromatosis. We have been compiling this database for the last 3 years and include all patients during new and follow-up appointments.

Would you be willing to transfer this data to a centralized CTF NF Database?

Yes No

We have initiated the process of transferring this paper database to electronic format using the database template by Dr. Friedman that we received at the 2006 NF Conference. We have a graduate student who will be starting this transfer and working to enter new data at each clinic session. We have found it difficult to keep up with more than minimal information while seeing patients in the clinic and have recognized that we need someone dedicated to collecting and verifying this information if we are to have a searchable database that will allow us to participate more in local and national clinical trials. We hope that this new system we are starting is a step in the right direction.

If 'no', explain your limitations.

9. PUBLICATIONS and RESEARCH (IF APPLICABLE)

- a. Please list any relevant NF publications from your clinic in the past 5 years. Include Journal, Citation and Title.

Smith LH, Christensen CK, Walsh LE, **Hingtgen CM**. Pain in patients with neurofibromatosis type 1. Submitted to *Pain*.

- b. Please provide information on NF-related research ongoing in your clinic or performed by personnel affiliated with your clinic.

We have two active studies related to NF1. The first involves characterizing pain associated with NF1 and using quantitative electrodiagnostic testing to evaluate sensory responses. The second is a limited phase II study of imatinib for treatment of plexiform neurofibromas in adults and children with NF1.

10. PATIENT SUPPORT

Do you have an NF patient support group that meets in association with your NF Clinic?

Yes. Kim Bebley, the mother of one of our patients is the Affiliate Representative for Indiana for the CTF support network. She has only taken on this position in the last

couple of years. The clinic, itself, has not been very involved in outreach or support group activities. This is a deficit that we hope to remedy in the next year. To do this, we will need to dedicate some of the time of our clinic coordinator to interacting with Ms. Bebley and other interested volunteers in the other parts of the state, we are attempting to find funds to support this time.

If 'yes' provide details.

If 'no', are you interested in starting such a group?

What resources would help you to do this?

11. OTHER INFORMATION

Please provide any additional information that is pertinent to your request to join the CTF NF Clinic Network.