



## **NF Clinic Network (NFCN) Application Form\***

**Clinic Name:**

Children's Hospital Boston Multidisciplinary Neurofibromatosis Center

**Affiliated Hospital:**

Children's Hospital Boston

**Affiliated University or Institution:**

Harvard Medical School

**Clinic Address:**

Children's Hospital Boston  
Clinical Genetics Program  
Fegan 10  
300 Longwood Avenue  
Boston, MA 02115

**Clinic Director:**

Mira Irons, MD

**Clinic Coordinator Name:**

Danielle Cataldo, MSN

*\*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 Children's Hospital Boston Multidisciplinary Neurofibromatosis Center is a multidisciplinary clinic in its 24th year of operation at Children's Hospital Boston and Dana-Farber Cancer Institute, two adjoined buildings with shared faculty and facilities.

NF1 is a genetic disease with a wide range of phenotypic expression; as a result of many factors, the clinical manifestations take on many forms and respond in a variety of ways to an array of treatments. The concepts in dealing with NF1, in the same way, require many kinds of expertise, a broad range of abilities, experience, and points of view.

The philosophy of collegiality is the foundation on which the Neurofibromatosis Program has been established. In every aspect of our program, we stress the strength that comes from working together: even in our relations with patients' parents/guardians, we emphasize the effectiveness of the coordinated approach. This is not new for us: many of the same specialists already collaborate in other treatment consortia; the center involves world-renowned neurosurgeons, neurologists, geneticists, oncologists, radiologists and pathologists. An essential part of our commitment to excellence involves working with other people and other institutions in order to maximize the potential of everything we do.

In addition to our long-standing role as a major referral center for Massachusetts, Rhode Island, New Hampshire, Maine, Vermont and upstate New York, we see patients from all over the United States and throughout the world. The resources of the entire group and of the individual departments highlight the extensive multidisciplinary character of the Children's Hospital Neurofibromatosis Program.

The NF clinic at Children's Hospital Boston is comprised of 3 physicians and one pediatric nurse practitioner. The clinic meets for 5 sessions offered at different times during the week. There are also sessions available within satellite locations in communities north, west, and south of the city of Boston. These satellite locations include: Children's Hospital Waltham, and Children's Hospital at South Shore Hospital.

In order to meet patient needs, we have assembled a large multi-disciplinary team of experts to provide diagnostic, therapeutic and follow-up care of these patients. At the Center's clinical meetings, treatment decisions are made for all patients. There are three weekly meetings. The first includes the core members of the NF clinic. The second meeting involves the departments of Neurology, NeuroOncology, Genetics, Oncology, Radiology, Radiation Oncology and Pathology. The third meeting takes place as part of the Pediatric Brain Tumor Program, for ongoing management of patients with symptomatic optic pathway gliomas, or on experimental treatment protocols. This latter group includes the above, as well as Endocrinology, Neuropsychology and Social Work.

## 2. CLINIC DIRECTOR and STAFF EXPERTISE

### a. CLINIC DIRECTOR: Please describe:

#### i. Your experience to date with NF care

Dr. Irons is board certified in Pediatrics, Clinical Genetics, and Biochemical Genetics. She has cared for patients with NF and allied disorders for the last 24 years, initially at New England Medical Center, and currently at Children's Hospital Boston. She was the Director of the NF Program at New England Medical Center for 10 years. She returned to Children's Hospital Boston in 1998, and became the Director of the NF Program here shortly thereafter, upon the departure of Dr. Bruce Korf from Children's Hospital.

The already sizeable program has continued to grow steadily under her direction and currently includes 3 physicians and 1 nurse practitioner and three clinical sites. Dr. Irons has a vast amount of experience treating large numbers of patients with NF and allied disorders of all degrees of severity and with all reported clinical and developmental problems.

#### ii. Your past and current association with NF clinical trials

##### Multicenter studies

1. Department of Defense Phase II Trial of R115777 in children and young adults with NF1, who have progressive, plexiform neurofibroma(s).  
PI: Widemann (NCI), site PI: Kieran. Ongoing study.
2. Department of Defense Phase II Trial of Pirfenidone in children and young adults with NF1, who have progressive plexiform neurofibroma(s).  
PI: Widemann (NCI), site PI: Kieran. Ongoing study.
3. Multi-centered study of tibial dysplasia in NF1 patients.  
PI: Carey (Utah), local PI: Miller. Currently enrolling patients.
4. Natural history of plexiform neurofibromas.  
PI: Korf (UAB), site PI: Irons. Study completed.

##### Local clinical studies

5. Moyamoya after cranial irradiation for primary brain tumors in children.  
PI: Ullrich. CHB protocol #:03-10-217. Completed study.
- Brainstem gliomas in children with NF1.  
PI: Ullrich (CHB). Study completed.

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

Children's Hospital Boston Neurofibromatosis Center has a major clinical and preclinical research effort directed at children with neurofibromatosis and associated malignancies. Combining one of the premiere specialized tertiary pediatric hospitals in the country with an internationally renowned cancer center has allowed us to build a major focus in this field. Within neuro-oncology, we have successfully piloted a large number of phase I/II protocols with an extensive patient population. We have developed a large support staff, which will provide the infrastructure for future trials in NF1. CHB/DFCI is an active member of the Children's Oncology Group and Pediatric Brain Tumor Consortium and serves as one of the Phase I contract institutions that provide patients and pharmacology samples for these important studies. We have acted as the reference laboratories and served crucial roles on many integral committees. For example, during the calendar year 2006, we have accrued over 30 patients on experimental phase I and phase II protocols, which required pharmacokinetics, biologic samples and novel methods.

We currently have the expertise and the mechanisms in place, along with a dedicated office, for the collection of Phase I and Phase II biological samples. This full time staff ensures that samples are collected and processed in a timely manner according to existing protocols. We have also built a dedicated phase I/II laboratory so that samples are kept separate; this laboratory is responsible for processing of pharmacokinetics and analysis of biological samples. We have the ability to establish tumor cell lines from specimens of patients treated on consortium-sponsored studies. The tissue bank and pathology review will be made available for use by the scientific community, provided IRB approval is obtained, in order to collect more information on the pathology, genetics, and cell biology of NF1.

- 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.

**W81XWH-06-1-0025 (Irons)**  
**Department of Defense**  
**10/15/05-11/14/06**  
**Amount was \$30, 000.00**  
**Children's Hospital Multidisciplinary Neurofibromatosis Center**  
**The purpose of the project was to work with other funded centers to create a clinical trials consortium for NF1.**

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

Rahbar R, Litrovnik BG, Vargas SO, Robson CD, Nuss RC, Irons MB, McGill TJ, Healy GB: The biology and management of laryngeal neurofibroma. Archives of Otolaryngology: Head and Neck Surgery, 1004:130:1400-1406.

Ullrich NJ, Raja A, Kieran MW, Irons MB, Goumnerova L. Brainstem lesions in children with neurofibromatosis type I. Neurosurgery, in press.

- c. Who are the key staff in your NF clinic facility? Provide Name; Title; Degree/Qualifications; Role in Clinic.

Mira Irons, M.D.  
Director, Neurofibromatosis Program  
Associate Chief, Division of Genetics, Children's Hospital Boston

Nicole Ullrich, M.D, Ph.D.  
Pediatric Neurologist  
Associate Director, Neurofibromatosis Program  
Director, Neuro-Oncology, Children's Hospital Boston

David Miller, M.D., Ph.D.  
Attending Physician, Genetics  
Assistant Director, Neurofibromatosis Program

Danielle Cataldo, MSN, CRNP  
Pediatric Nurse Practitioner  
Clinic Coordinator, Neurofibromatosis Program

- d. Who within this core staff currently coordinates NF patient services? Describe this individual's NF clinic related duties.

Danielle Cataldo is the clinic coordinator. Current duties include: Coordination of patient care. The clinic coordinator works with administrative staff to ensure that all patients are scheduled in an appropriate time frame based on their individual needs. The clinic coordinator is also a member of the multidisciplinary team and assists with coordination and referrals for specialty services for NF patients. The coordinator is actively involved in NF clinic sessions and ensures that appropriate follow-up for each patient occurs as recommended. The clinic coordinator is the first point of contact for NF patients and their families within the NF program. The coordinator is available for all questions regarding the diagnosis of NF and evaluation process, as well as concerns regarding NF-related complications, including both medical and developmental/learning issues.

- 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.

Our expertise encompasses all areas of NF care due to the long history of the NF Program here at Children's Hospital, the large number of patients that we have cared for over the years, and the multiple specialists who have been involved in NF care here over the years. Our expertise includes caring for patients with optic gliomas, central nervous system tumors, plexiform neurofibromas, and malignant peripheral nerve sheath tumors with our colleagues in the Pediatric Brain Tumor Program (Drs. Kieran, Ullrich, Chi, Turner), and Solid Tissue Tumor Program (Drs. Albritton and Grier) at the Dana Farber Cancer Institute (DFCI) and the Department of Neurosurgery (Drs. Scott, Goumnerova, Smith, Black, Proctor); head, vestibular, and neck tumors with our colleagues in the Department of Otolaryngology (Dr. Rahbar), skeletal complications of NF1 (scoliosis, extremity plexiform neurofibromas, tibial dysplasia) with our colleagues in the Department of Orthopaedics (Drs. Kasser, Karlin, Emans, Bae, and Waters), visual disturbances with our colleagues in the Department of Ophthalmology (Drs. Fulton, Vanderveen, Dagi), learning disabilities with our colleagues in the Developmental Medicine Center at the Children's Hospital and the Neuropsychology Program at the DFCI, and disturbances of growth and pubertal development with our colleagues in the Division of Endocrinology (Drs. Cohen and Stafford).

### 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 are scheduled for an evaluation within 3 - 4 weeks. All patients are appropriately triaged and can be seen sooner based on individual need. Patients with an acute need can be seen within 3-5 days, or even sooner based on need.

- b. Provide details of those specialists to whom (either within or outside your own clinic facility) your clinic refers NF patients for the following specialty care. These should be 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 617- 355- ext	EMAIL (if available)
Genetics	Mira Irons, MD David Miller, MD, PhD	Children's Hospital Boston Division of Genetics 300 Longwood Avenue, Boston, MA 02115	4697 4697	mira.iron@childrens.harvard.edu david.miller2@childrens.harvard.edu
Neurology	Nicole Ullrich, MD, PhD Scott Pomeroy, MD, PhD Mustafa Sahin, MD	Children's Hospital Boston Department of Neurology 300 Longwood Avenue Boston, MA 02115	2067 6386 2711	nicole.ullrich@childrens.harvard.edu scott.pomeroy@childrens.harvard.edu mustafa.sahin@childrens.harvard.edu
Orthopedics	John Emans, MD Peter Waters, MD James Kasser, MD Lawrence Karlin Donald Bae, MD	Children's Hospital Boston Department of Orthopaedics 300 Longwood Avenue Boston, MA 02115	7132 4849 6617 7132 6808	john.emans@childrens.harvard.edu peter.waters@childrens.harvard.edu james.kasser@childrens.harvard.edu lawrence.karlin@childrens.harvard.edu donald.bae@childrens.harvard.edu
Developmental pediatrics/ learning disabilities	Leonard Rappaport, MD Lisa Albers, MD	Children's Hospital Boston Developmental Medicine Center 300 Longwood Avenue Boston, MA 02115	7030 4125	leonard.rappaport@childrens.harvard.edu lisa.albers@childrens.harvard.edu
Ophthalmology	Linda Dagi, MD Deborah Vanderveen, MD Anne Fulton, MD	Children's Hospital Boston Department of Ophthalmology 300 Longwood Avenue Boston, MA 02115	8531 8761 5685	linda.dagi@childrens.harvard.edu deborah.vanderveen@childrens.harvard.edu anne.fulton@childrens.harvard.edu
Neurosurgery	Peter Black, MD, PhD Liliana Goumnerova, MD Edward Smith, MD Michael Scott, MD Mark Proctor, MD	Children's Hospital Boston Department of Neurosurgery 300 Longwood Avenue Boston, MA 02115	7795 6364 8414 6011 2403	peter.black@childrens.harvard.edu liliana.goumnerova@childrens.harvard.edu Edward.smith@childrens.harvard.edu michael.scott@childrens.harvard.edu mark.proctor@childrens.harvard.edu

<b>Plastic surgery</b>	Gary Rogers, MD John Meara MD, DMD	Children's Hospital Boston Department of Plastic Surgery 300 Longwood Avenue Boston, MA 02115	8509 4401	garry.rogers@childrens.harvard.edu john.meara@childrens.harvard.edu
<b>Neurooncology</b>	Mark Kieran, MD, PhD Susan Chi, MD Christopher Turner, MD Karen Albritton, MD	Dana Farber Cancer Institute 44 Binney Street Boston, MA 02115	617-632- 4907 4386 4386 2545	mark_kieran@dfci.harvard.edu susan_chi@dfci.harvard.edu christopher.turner@childrens.harvard.edu karen_albritton@dfci.harvard.edu
<b>Medical Oncology/ Radiation Oncology</b>	Karen Marcus, MD	Children's Hospital Boston Radiation Oncology 300 Longwood Avenue Boston, MA 02115	8399	
<b>Endocrinology</b>	Laurie Cohen, MD Diane Stafford, MD	Children's Hospital Boston Division of Endocrinology 300 Longwood Avenue Boston, MA 02115	7476 5066	laurie.cohen@childrens.harvard.edu diane.Stafford@childrens.harvard.edu
<b>Audiology/ENT</b>	Reza Rahbar, MD	Children's Hospital Boston Department of Otolaryngology 300 Longwood Avenue Boston, MA 02115	6460	reza.rahbar@childrens.harvard.edu
<b>Radiology/ Neuroradiology</b>	Tina Young Poussaint, MD Kirsten Ecklund, MD	Children's Hospital Boston Department of Radiology 300 Longwood Avenue Boston, MA 02115	6450 8825	tina.poussaint@childrens.harvard.edu kirsten.ecklund@childrens.harvard.edu
<b>General Surgery/Surgical Oncology</b>	Robert Shamberger, MD Craig Lillehei, MD	Children's Hospital Boston Department of General Surgery 300 Longwood Avenue Boston, MA 02115	8326 3039	robert.shamberger@childrens.harvard.edu craig.lillehei@childrens.harvard.edu
<b>Dermatology</b>	Stephen Gellis, MD Peter Lio, MD	Children's Hospital Boston Division of Dermatology 300 Longwood Avenue Boston, MA 02115	6126 6117	stephen.gellis@childrens.harvard.edu peter.lio@childrens.harvard.edu
<b>Cardiovascular Disease</b>	Mark Alexander, MD Ronald Lacro MD	Children's Hospital Boston Department of Cardiology 300 Longwood Avenue, Boston, MA 02115	6328	mark.Alexander@childrens.harvard.edu ronald.lacro@childrens.harvard.edu
<b>Oral and Maxillofacial Surgery</b>	Nalton Ferraro, MD Bonnie Padwa, MD	Children's Hospital, Boston Department of Oral- Maxillofacial Surgery 300 Longwood Avenue Boston, MA 02115	7687 6259	nalton.ferraro@childrens.harvard.edu bonnie.padwa@childrens.harvard.edu
<b>Neuropsychology</b>	Celiane Rey-Casserly PhD Susan Waisbren, PhD	Children's Hospital Boston Department of Psychiatry 300 Longwood Avenue, Boston, MA 02115	6708 7346	celiane.rey-casserly@childrens.harvard.edu susan.waisbren@childrens.harvard.edu

## ADULT CARE

The Children's Hospital Boston Multidisciplinary Neurofibromatosis Center generally evaluates patients from infancy to young adulthood. We begin to transition patients to adult facilities when they are approximately 22 years of age. We have a good working relationship and meet regularly with the adult programs at Brigham and Women's Hospital (BWH), Beth Israel Deaconess Medical Center (BIDMC), and Massachusetts General Hospital (MGH). Other institutions in our city generally see more of the adult population (see below on transitioning to adult care).

### 4. NUMBER OF NF PATIENTS YOUR CLINIC SEES

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

The table below includes patients that were seen for evaluation in the NF program during the last year. This does not include the subspecialty programs, which are included in the table that follows.

	NF1	NF2	SCHWANNOMATOSIS	OTHER
NUMBER OF FOLLOW UP PATIENTS SEEN IN PAST 12 MONTHS	325	9		
NUMBER OF <u>NEW</u> PATIENTS SEEN IN PAST 12 MONTHS	165	2	1	
TOTAL	490	11	1	

### NF patients evaluated in specialty clinics at CHB in the past year

Neurology	135
Neurosurgery	52
Oncology	167
Orthopaedics	574
Ophthalmology	304
Developmental Medicine / Neuropsychology	41
Endocrinology	61
Dermatology	42
Otolaryngology	22
Plastic Surgery	20

Total 1418

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

Under 18 \_\_\_\_\_ 18+ \_\_\_\_\_ (give numbers - if data available)

OR estimate

Under 18 (%) 90-95%

18+ (%) 5-10%

##### 5. TRANSITIONING PEDIATRIC TO ADULT NF CARE

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

An adult NF program has been established at the Brigham and Women's Hospital by Drs. Michael Murray and Natasha Frank. Drs. Murray and Frank are both internists and geneticists and trained in the Harvard Medical School Genetics Training Program under Dr. Irons' direction. The Brigham and Women's Hospital is adjacent to Children's Hospital and many physicians at Children's also have privileges there so that continuity of care is possible for many of the patients' providers. Patients are generally transitioned to the BWH program at approximately 21-22 years of age. Some patients older than this continue to be seen in the CHB program if they are still being followed by CHB surgeons or other providers. There are also some patients that may choose to be followed at the MGH or BIDMC programs.

Those patients followed by the pediatric oncologists at the DFCI are transitioned to the adult oncologists at the DFCI as determined by protocol.

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

See above.

## 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.)

Neurooncology Conference is held weekly. Participants of this conference include Neurooncology, Neurosurgery, Radiation Oncology, Genetics, Neuroradiology, Neurology, Endocrine, Neuropsychology, and Social Work.

NF clinic case management meeting is held weekly. Participants include Drs. Irons, Ullrich, and Miller and Danielle Cataldo, nurse practitioner and clinic coordinator.

Brain tumor clinic conference (for patients with symptomatic optic pathway gliomas, other intracranial gliomas, or on investigational agents) is held weekly. Dr. Ullrich participates in this meeting and sees patients here as part of the multidisciplinary clinic.

## 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.

Department of Defense Phase II Trial of R115777 in children and young adults with NF1, who have progressive, plexiform neurofibroma(s).

PI: Widemann (NCI), site PI: Kieran. Ongoing study.

Department of Defense Phase II Trial of Pirfenidone in children and young adults with NF1, who have progressive plexiform neurofibroma(s).

PI: Widemann (NCI), site PI: Kieran. Ongoing study.

## 8. PATIENT REGISTRY

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

Yes  No

If 'yes', please describe.

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

Yes  No

This will be contingent upon local institutional research board approval.

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.

Rahbar R, Litrovnik BG, Vargas SO, Robson CD, Nuss RC, Irons MB, McGill TJ, Healy GB: The biology and management of laryngeal neurofibroma. Archives of Otolaryngology: Head and Neck Surgery, 1004:130:1400-1406.

Ullrich NJ, Robertson R, Kinnamon D, Scott RM, Kieran MW, Turner CW, Chi SN, Goumnerova L, Proctor M, Tarbel N, Marcus K, Pomeroy SL. Moyamoya following cranial irradiation for primary brain tumors in children. Neurology 2007;68:932-938.

Ullrich NJ, Raja A, Kieran MW, Irons MB, Goumnerova L. Brainstem lesions in children with neurofibromatosis type I. Neurosurgery, in press.

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

1. Genetics and molecular studies of Neurofibromatosis, Harvard NF center.  
PI: Irons. CHB protocol #: 04-05-066. Ongoing study.
1. Measurement of angiogenic growth factors in the blood and urine of patients with Neurofibromatosis type I and plexiform neurofibromas.  
PI: Irons. CHB protocol #: 04-10 113R. Ongoing study.
2. Use of Matrix Metalloproteinases as non-invasive biomarkers of central nervous system disease.  
PI: Smith. CHB protocol #:04-12-138. Ongoing study.
3. Multi-centered study of tibial dysplasia in NF1 patients.  
PI: Carey (Utah), local PI: Miller. Currently enrolling patients.
4. Growth and Development of Children with NF1.  
PI: Cohen (CHB). Ongoing study
5. Failure to thrive and NF1.  
PI: Ullrich (CHB). Ongoing study
6. Learning Disabilities in Segmental NF1.  
PI: Ullrich (CHB). Ongoing study

#### 10. PATIENT SUPPORT

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

No, although we recently hosted a patient/family centered symposium on Learning Disabilities in children with NF1, co-hosted with CTF.

If 'yes' provide details.

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

What resources would help you to do this?

We would be interested in starting a NF support group in association with our clinic.

There are some resources available through the division of genetics for funding, and there is staff available to help with the organization of such a group. Children's Hospital Boston can provide the needed space and facilities for this.

## 11. OTHER INFORMATION

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

The Children's Hospital Boston Neurofibromatosis Center has a major clinical and preclinical research effort directed at children with NF1 and associated malignancies. Combining one of the premiere specialized tertiary pediatric hospitals in the country with an internationally renowned cancer center has allowed us to build a major focus in this field. The clinical program is currently in its 24<sup>th</sup> year and encompasses a clinical team that includes all pediatric subspecialties, many of whom have worked together and cared for patients for over 15-20 years. Major efforts in molecular biology and genomics as well as adult and pediatric neuro-oncology, based on innovative neurosurgical and oncologic advances, have made our program extremely successful. Within neuro-oncology, we have successfully piloted a large number of phase I/II protocols. We have developed a large support staff, which will provide the infrastructure for future trials in NF1. An extensive basic and applied research section has resulted in an extremely active and productive center. We feel that this expertise combined with innovative approaches gives our center a unique ability to meet the goals of the CTF Clinic Network and our patients and to provide leadership in many areas it has been designed to pursue.