NF Clinic Network (NFCN) Application Form*

Clinic Name:
Trans-NIH Intramural NF Clinic

Affiliated Hospital:
NIH Clinical Center

Affiliated University or Institution:
N/A

Clinic Address:
Trans-NIH Intramural NF Clinic
10 Center Drive
Clinical Research Center
Bethesda, MD 20892

Clinic Director:
Douglas R. Stewart, MD
Brigitte Widemann, MD

Clinic Coordinator Name:
Jennifer Sloan
Andrea Gillespie

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

Children's Tumor Foundation™
Ending Neurofibromatosis Through Research

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): The Trans-NIH Intramural NF Clinic is located at the Clinical Center of the National Institutes of Health.

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

The Trans-NIH Intramural NF Clinic is co-directed by Drs. Stewart and Widemann. The Clinic is protocol-driven, meaning that patients are enrolled in one of a variety of NF1-related clinical protocols open at the NIH Clinical Center. Dr. Widemann of the National Cancer Institute (NCI) evaluates primarily children and young adults (< 25 years) with plexiform neurofibromas and individuals with MPNST (no upper age limit) in treatment protocols. Dr. Stewart of the National Human Genome Research Institute (NHGRI) evaluates primarily adults in one of two natural history protocols.

The NIH Clinical Center provides the infrastructure required for the conduct of clinical trials and the care of children and adults with NF1 entered on clinical trials. This includes departments for clinical microbiology, anesthesia and surgical services, critical care, pharmacy, rehabilitation medicine, transfusion medicine, imaging sciences (radiology, nuclear medicine, PET), bioethics, hospital epidemiology, nursing, nutrition, pain and palliative care services, social work, clinical research informatics, and medical records. In addition, a wide range of consult services is available to patients treated at the NIH Clinical Center.

CLINIC DIRECTOR and STAFF EXPERTISE

b. CLINIC DIRECTOR: Please describe:

i. Your experience to date with NF care

Dr. Widemann has been directly involved with the care of individuals with NF1 since 1999. She trained in pediatrics at the University of Cologne, Germany and in and pediatric hematology and oncology at the NCI Pediatric Oncology Branch in Bethesda, MD.

Dr. Stewart has been directly involved with care of individuals of NF1 since 2004 when he joined NHGRI. He is boarded in internal medicine and clinical genetics and received all of his medical training at the University of Pennsylvania.

ii. Your past and current association with NF clinical trials

Dr. Widemann has been involved with NF1 clinical trials since 1999. She currently has four active trials investigating plexiform neurofibromas (n=3) and MPNST (n=1).

Dr. Stewart has two natural history studies open at NIH. The first, open since 2005, investigates NF1 in adults and uses a novel approach to find modifier genes. The second, open since 2006, investigates the natural history and biology of dermal neurofibromas.

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

Dr. Widemann has been involved with oncology trials since 1993.

c. 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.

Dr. Widemann is a tenure-track investigator in the Center for Cancer Research at NCI and thus receives NIH intramural funding for her work. She joined NCI in 1992 after completing her pediatric residency in Cologne, Germany, and has been a tenure-track investigator since June 2000.

Dr. Stewart is in the Physician Scientist Development Program (PSDP) at NHGRI and receives NIH intramural funding for his work. The PSDP is a non-tenure track position akin to an intramural K-23. Dr. Stewart is involved with the PSDP until November 2009.

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

Dr Widemann:

Widemann, B. Merlin PAKs a punch. Cancer J 2004; 10: 8-11

Widemann B, Salzer W, Arceci R, et al: Phase I trial and pharmacokinetic study of the farnesyltransferase inhibitor tipifarnib (R115777) in children with refractory solid tumors or neurofibromatosis type I and plexiform neurofibromas. J Clin Oncol 2006:24:507-516

Babovic-Vuksanovic D, **Widemann B**, Dombi E, Gillespie A, Wolters P, Toledo-Tamula M, O'Neil B, Fox E, Steinberg S, MacDonald T, Beck H, Packer R. Phase I Trial of Pirfenidone in Children with Neurofibromatosis Type 1 (NF1) and Plexiform Neurofibromas (PN). Pediatr Neurol 2007; 36:293-300.

Dombi E, Solomon J, Gillespie A, Fox E, Balis F, Patronas N, Korf B, Babovic D, Packer R, Belasco J, Goldman S, Jakacki R, Kieran M, Steinberg S, **Widemann B**. Plexiform neurofibroma growth rate by volumetric MRI and relationship to age and body weight. Neurology 2007; 68:643-647.

Dr. Stewart:

Stewart DR, Corless CL, Rubin BP, Heinrich MC, Messiaen LM, Kessler LJ, Zhang PJ, Brooks DG. Mitotic recombination as evidence of alternative pathogenesis of gastrointestinal stromal tumors (GISTs) in neurofibromatosis type 1. *Journal of Medical Genetics,* 44: e61, 2007.

Stewart DR, Cogan JD, Kramer MR, Miller WT Jr., Christiansen LE, Pauciulo MW, Messiaen LM, Tu GS, Thompson WH, Pyeritz RE, Ryo JH, Nichols WC, Kodama M, Meyrick BO, Ross DJ. Is pulmonary arterial hypertension in neurofibromatosis type 1 secondary to a plexogenic

arteriopathy? *Chest* Papers In Press, prepublished online June 15, 2007; DOI:10.1378/chest.06-3017.

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

Dr Widemann:

Eva Dombi, MD. Responsible for image analysis of NF1-related tumors.
Andrea Gillespie, RN. Research Nurse Specialist and coordinator for NF1 clinical trials.
Tatiana Petrosyan. Data manager.

Dr. Stewart:
Jennifer Sloan, Ph.D, M.S. Dr. Sloan is a certified genetic counselor and is the protocol coordinator for Dr. Stewart.

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

For Dr. Widemann, Ms. Gillespie primarily coordinates patient inquiries, scheduling and visits.

For Dr. Stewart, Dr. Sloan is the primary coordinator. She answers inquiries, coordinates scheduling, is the primary contact during a patient visit and provides genetic counseling. She has also presented NF1-related scientific posters at national meetings.

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.

Dr. Widemann has special expertise in 1) management of plexiform neurofibromas and malignant peripheral nerve sheath tumors and, 2) development of clinical trial designs and endpoints for NF1-related tumors.

Dr. Stewart has special interest and expertise in 1) imaging methods of dermal neurofibomas and 2) the adult phenotype of NF1, especially the more uncommon manifestations of the disorder (glomus tumors, dental anomalies, pulmonary hypertension).

2. 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.

For both Drs. Stewart and Widemann, a patient inquiry is typically answered within 1-7 days, depending upon medical urgency. Priority is given to acute patient management and enrollment in clinical trials.

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	Douglas Stewart	49 Convent Drive Bldg 49 Rm 4A62 Bethesda, MD 20892	301-451-7716	drstewart@mail.nih.gov
Neurology	NIH Consult Service			
Orthopedics	Scott Paul, MD	10-CRC - Hatfield Clinical Research Center, 1-1424 10 Center Dr Bethesda, MD 20892	301-496-4733	spaul@mail.cc.nih.gov
Developmental pediatrics/learning disabilities	Pamela Wolters, Ph.D	Center for Cancer Research National Cancer Institute Bethesda, MD 20892	301-496-0562	woltersp@mail.nih.gov
Ophthalmology	Edmont FitzGibbon	Building 49, 2A50 49 Convent Dr Bethesda, MD 20892	301-496-7144	ejf@nei.nih.gov
Neurosurgery	John Heiss, MD	Building 10 - Magnuson CC, 5D37 10 Center Dr Bethesda, MD 20892	301-594-8112	heissj@ninds.nih.gov
Plastic surgery	NIH Consult Service			

Neurooncology	Kathy Warren, MD Roger Packer, MD	Dr. Warren: 10-CRC - Hatfield Clinical Research Center, 1-3940 10 Center Dr Bethesda, MD 20892 Dr. Packer: Children's National Medical Center 111 Michigan Avenue, NW Washington, DC 20010	Dr. Warren: 301-435-4683 Dr. Packer: 202-884-2652	Dr. Warren: warrenk@mail.nih.gov Dr. Packer: rpacker@cnmc.org
Medical Oncology/Radiation Oncology	Deborah Citrin, MD	10-CRC - Hatfield Clinical Research Center, B2-3500 10 Center Dr Bethesda, MD 20892	301-496-5457	citrind@mail.nih.gov
Endocrinology	Constantine Stratakis, MD	10-CRC - Hatfield Clinical Research Center, 1-3330 10 Center Dr Bethesda, MD 20892	301-402-1998	stratakc@mail.nih.gov
Audiology/ENT	NIH Consult Service			
Radiology/ Neuroradiology	Nicholas Patronas, MD	Building 10 - Magnuson CC, 1D27 10 Center Dr Bethesda, MD 20892	301-402-5726	npatronas@mail.cc.nih.gov
General Surgery/Surgical Oncology	NIH Consult Service *and* Robert Henshaw, MD	Washington Cancer Institute 110 Irving St., NW Room CI-2158 Washington DC 20010	202-877-3970	robert.m.henshaw@medstar.net
Dermatology	Thomas Hornyak, MD, Ph.D	Building 10 - Magnuson CC, 12N242 10 Center Dr Bethesda, MD 20892	301-451-1926	hornyakt@mail.nih.gov

Cardiovascular Disease	NIH Consult Service			
Oral and Maxillofacial Surgery	Carter Van Waes, MD	10-CRC - Hatfield Clinical Research Center, 4-2732 10 Center Dr Bethesda, MD 20892	301-402-4216	vanwaesc@nidcd.nih.gov
Behavioral Issues	Maryland Pao, MD	10-CRC - Hatfield Clinical Research Center, 6-5340 10 Center Dr Bethesda, MD 20892	301-435-5770	paom@mail.nih.gov

ADULT CARE

SPECIALTY	DOCTOR	CLINIC ADDRESS	PHONE	EMAIL (if available)
Genetics	Douglas Stewart	49 Convent Drive Bldg 49 Rm 4A62 Bethesda, MD 20892	301-451-7716	drstewart@mail.nih.gov
Neurology	NIH Consult Service			
Orthopedics	Scott Paul, MD	10-CRC - Hatfield Clinical Research Center, 1-1424 10 Center Dr Bethesda, MD 20892	301-496-4733	spaul@mail.cc.nih.gov
Developmental pediatrics/learning disabilities	N/A			
Ophthalmology	Brian Brooks, MD, Ph.D	Building 10 - Magnuson CC, 10B16 10 Center Dr Bethesda, MD 20892	301-451-2238	BrooksB@mail.nih.gov
Neurosurgery	John Heiss, MD	Building 10 - Magnuson CC, 5D37 10 Center Dr Bethesda, MD 20892	301-594-8112	heissj@ninds.nih.gov
Plastic surgery	NIH Consult Service			

Neurooncology	Howard Fine, MD	Building 82 - Bloch Intl Cancer Ctr, 225 9030 Old Georgetown Rd Bethesda, MD 20892	301-402-6383	hfine@mail.nih.gov
Medical Oncology/Radiation Oncology	Deborah Citrin, MD	10-CRC - Hatfield Clinical Research Center, B2-3500 10 Center Dr Bethesda, MD 20892	301-496-5457	citrind@mail.nih.gov
Endocrinology	Constantine Stratakis, MD	10-CRC - Hatfield Clinical Research Center, 1-3330 10 Center Dr Bethesda, MD 20892	301-402-1998	stratakc@mail.nih.gov
Audiology/ENT	NIH Consult			
Radiology/ Neuroradiology	Nicholas Patronas, MD	Building 10 - Magnuson CC, 1D27 10 Center Dr Bethesda, MD 20892	301-402-5726	npatronas@mail.cc.nih.gov
General Surgery/Surgical Oncology	NIH Consult Service Robert Henshaw, MD	Washington Cancer Institute 110 Irving St., NW Room CI-2158 Washington DC 20010	202-877-3970	robert.m.henshaw@medstar.net
Dermatology	Thomas Hornyak, MD, Ph.D	Building 10 - Magnuson CC, 12N242 10 Center Dr Bethesda, MD 20892	301-451-1926	hornyakt@mail.nih.gov
Cardiovascular Disease	NIH Consult Service			
Oral and Maxillofacial	Carter Van Waes, MD	10-CRC - Hatfield	301-402-4216	vanwaesc@nidcd.nih.gov

Surgery		Clinical Research Center, 4-2732 10 Center Dr Bethesda, MD 20892		
Behavioral Issues	NIH Psychiatry Consult			

Note: Patients evaluated at the NIH come from all over the United States. Specific questions may be addressed during an NIH evaluation, but patients are typically referred to their primary local physician. Care is often referred to physicians who are local to the patient. In this case, referrals are typically made to the local academic medical center.

3. 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?

Insert numbers below

	NF1	NF2	SCHWANNOMATOSIS	OTHER
NUMBER OF PATIENTS SEEN IN PAST 12 MONTHS				
Widemann	**80**	**None**	**None**	
Stewart	**70**	**None**	**None**	
NUMBER OF NEW PATIENTS SEEN IN PAST 12 MONTHS				
Widemann	**20**	**None**	**None**	
Stewart	**50**	**None**	**None**	
TOTAL				
Combined Total Patients Widemann and Stewart	**150**	**None**	**None**	
Combined New Patients Widemann and Stewart	**70**	**None**	**None**	

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

For Dr. Widemann:

Under 18: 70/80 18+ 10/80 (give numbers – if data available)

For Dr. Stewart:
Under 18: 10/70 18+ 60/70 (give numbers – if data available)

OR estimate

Under 18 (%)___ 18+ (%)___

4. TRANSITIONING PEDIATRIC TO ADULT NF CARE

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

In Dr. Widemann's plexiform neurofibroma studies, the upper age limit is 25 years. Newer studies on this tumor will have no upper limit. In her study for MPNST, there is no upper or lower age limit.

Dr. Stewart primarily sees adults. Families with affected children are encouraged to be evaluated by an NF center convenient to them and are counseled on the importance of transitioning to adult care.

Drs. Stewart and Widemann are in the process of developing a longitudinal natural history study of NF1, which will be open to children and adults.

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

In Dr. Widemann's clinic, emphasis is made on proper communication with the referring physician.

In Dr. Stewart's clinic, appropriate referrals and copies of medical records from an NIH evaluation are provided to families of younger patients.

5. 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.)

In Dr. Widemann's clinic, a weekly meeting is held to discuss active patients. Tumor boards are held with multi-disciplinary input to discuss complex patients.

In Dr. Stewart's clinic, an NHGRI-wide pre- and post-clinic conference is held weekly to discuss patients.

6. 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 X ☐ No

If 'no', briefly describe why.

Do you currently refer patients to clinical trials?

Yes X No

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

Dr. Widemann has four active trials in which she enrolls patients. She has also referred patients to Dr. Stewart (Gene modifier study, natural history of dermal neurofiborma study), Children's Hospital of Philadelphia (for plexiform neurofibroma, PI Jean Belasco) and Indiana University (for plexiform nerurofibroma, PI Kent Robertson).

In his adult population, Dr. Stewart sees many patients with plexiform neurofibromas. Some of these patients he has referred to Dr. Widemann. In addition he has referred patients to the Gleevec study at Indiana University.

7. PATIENT REGISTRY

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

Yes X No X

If 'yes', please describe.

Dr. Widemann tracks patient information in protocol-specific electronic database. Dr. Stewart uses a LabMatrix database to track clinical and research data.

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

Yes X No

A limited amount of patient data could be transferred to a centralized CTF NF Database. This would need to be approved by the appropriate NIH IRB.

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.

Dr Widemann:

Widemann, B. Merlin PAKs a punch. Cancer J 2004; 10: 8-11

Widemann B, Salzer W, Arceci R, et al: Phase I trial and pharmacokinetic study of the farnesyltransferase inhibitor tipifarnib (R115777) in children with refractory solid tumors or neurofibromatosis type I and plexiform neurofibromas. J Clin Oncol 2006:24:507-516

Babovic-Vuksanovic D, **Widemann B**, Dombi E, Gillespie A, Wolters P, Toledo-Tamula M, O'Neil B, Fox E, Steinberg S, MacDonald T, Beck H, Packer R. Phase I Trial of Pirfenidone in Children with Neurofibromatosis Type 1 (NF1) and Plexiform Neurofibromas (PN). Pediatr Neurol 2007; 36:293-300.

Dombi E, Solomon J, Gillespie A, Fox E, Balis F, Patronas N, Korf B, Babovic D, Packer R, Belasco J, Goldman S, Jakacki R, Kieran M, Steinberg S, **Widemann B**. Plexiform neurofibroma growth rate by volumetric MRI and relationship to age and body weight. Neurology 2007; 68:643-647.

Dr. Stewart:

Stewart DR, Corless CL, Rubin BP, Heinrich MC, Messiaen LM, Kessler LJ, Zhang PJ, Brooks DG. Mitotic recombination as evidence of alternative pathogenesis of gastrointestinal stromal tumors (GISTs) in neurofibromatosis type 1. *Journal of Medical Genetics*, 44: e61, 2007.

Stewart DR, Cogan JD, Kramer MR, Miller WT Jr., Christiansen LE, Pauciulo MW, Messiaen LM, Tu GS, Thompson WH, Pyeritz RE, Ryo JH, Nichols WC, Kodama M, Meyrick BO, Ross DJ. Is pulmonary arterial hypertension in neurofibromatosis type 1 secondary to a plexogenic arteriopathy? *Chest* Papers In Press, prepublished online June 15, 2007; DOI:10.1378/chest.06-3017.

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

Dr. Widemann has been involved with NF1 clinical trials since 1999. She currently has four active trials investigating plexiform neurofibromas (n=3) and MPNST (n=1).

Dr. Stewart has two natural history studies open at NIH. The first, open since 2005, investigates NF1 in adults and uses a novel approach to find modifier genes. The second, open since 2006, investigates the natural history and biology of dermal neurofibromas.

10. PATIENT SUPPORT

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

No, but referrals to regional support groups are regularly made.

If 'yes' provide details.
If 'no', are you interested in starting such a group?

At this time we rely on, and regularly refer, our patients to appropriate regional support groups throughout the United States.

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.

At this time, there is an active clinical and research program in NF1 at NIH. Since research programs in the intramural program at NIH are investigator dependent, NF2 and Schwannomatosis studies may be available in the future and would be a

welcome addition to the Trans-NIH Intramural NF Clinic. Both Drs. Stewart and Widemann refer the occasional inquiry about NF2 and Schwannomatosis to an appropriate regional clinic.