Roadmap for increasing patient engagement in REiNS

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Response Evaluation In Neurofibromatosis Schwannomatosis
INTERNATIONAL COLLABORATION

Agenda

2:30 – 3:00 pm	Roadmap for increasing patient engagement in REiNS Scott Plotkin and Brigitte Widemann
3:00 – 3:45 pm	FDA's approach to patient engagement Steve Morin, R.N., B.S.N. CDR US Public Health Service
3:45 – 4:55 pm	REiNS working groups updates (with feedback from attendees)
3:45-4:05	Cutaneous neurofibromas (Dominique Pichard /Ashley Cannon)
4:05-4:25	Functional group (Srivandana Akshintala/David Stevenson)
4:25-4:40	Neurocognitive group (Bonnie Klein-Tasman)
4:40-4:55	Patient reported outcomes group (Ana-Maria Vranceanu)
4:55 – 5:00 pm	Plans for December meeting and closing comments

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REiNS International Collab...

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REiNS International Collaboration

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Mission Statement

REiNS is an international effort to develop new standardized response criteria for determining treatment response in patients with NF1, NF2, and schwannomatosis. Response criteria will continue to be modified as we gain experience in clinical trials for NF. We hope these criteria will be incorporated into future clinical trials and will improve our ability to determine and compare treatment efficacy.

History & Organization

The REiNS Collaboration was established in 2011 at the Children's Tumor Foundation annual NF Conference to achieve consensus within the NF community about future clinical trials and to accelerate the identification of agents which will benefit individuals with NF. Since its inception, the REiNS International Collaboration has played a key role in the creation and dissemination of outcome measures for clinical trials of neurofibromatosis and schwannomatosis.

The REiNS collaboration is organized around eight working groups that focus on the following topics: imaging of tumor response, functional outcomes, visual outcomes, patient -reported outcomes, neurocognitive outcomes, whole-body MRI, disease biomarkers, and cutaneous neurofibromas. Leaders of the eight working groups were identified based on their expertise. Membership in each working group is open to any interested party and representatives from patient advocacy groups and funding agencies have been invited to participate in the effort. Each REiNS group establishes a meeting schedule; the majority of meetings are held by teleconference. In-person meetings of the entire group are held twice per year to coordinate efforts among the working groups and to achieve consensus within the larger group for recommendations.

https://ccrod.cancer.gov/confluence/display/REINS/Home

What is REiNS?

Response Evaluation in NF and Schwannomatosis

- The REiNS working group is an international effort to develop standardized endpoints and response criteria for determining treatment response in patients with NF1, NF2, and schwannomatosis
- Collaboration across institutions, medical specialties; includes experts in NF and other areas
- The criteria are a work in progress and will continue to be modified as we gain experience in trials for NF
- We hope these criteria will be incorporated into clinical trials and will improve our ability to determine and compare treatment efficacy

Why does the NF community need REiNS?

- Previous trials used a variety of endpoints and response criteria
- REiNS focus on collaboration and consensus to unify clinical trials community
- Since 2015, many trials have adopted same endpoints/response criteria which has facilitated comparison
- New, meaningful endpoints have been developed by REiNS working groups
- Proactive discussion of endpoints with stakeholders will help facilitate approval of, and therefore access to, drugs for these rare conditions

Response Evaluation in Neurofibromatosis and Schwannomatosis (REiNS)

- Imaging response (Widemann, Dombi)
- Functional outcomes (Plotkin)
- Patient reported outcomes (Wolters)
- Whole body MRI (Ahlawat)
- Visual outcomes (Fisher)
- Neurocognitive outcomes (Walsh)
- Cutaneous neurofibroma
- (Cannon/Pichard)
- Biomarkers (Hanemann)

The REiNS working groups are open to all participants

- **7 working groups**
- **>60 active members**

How REiNS Works

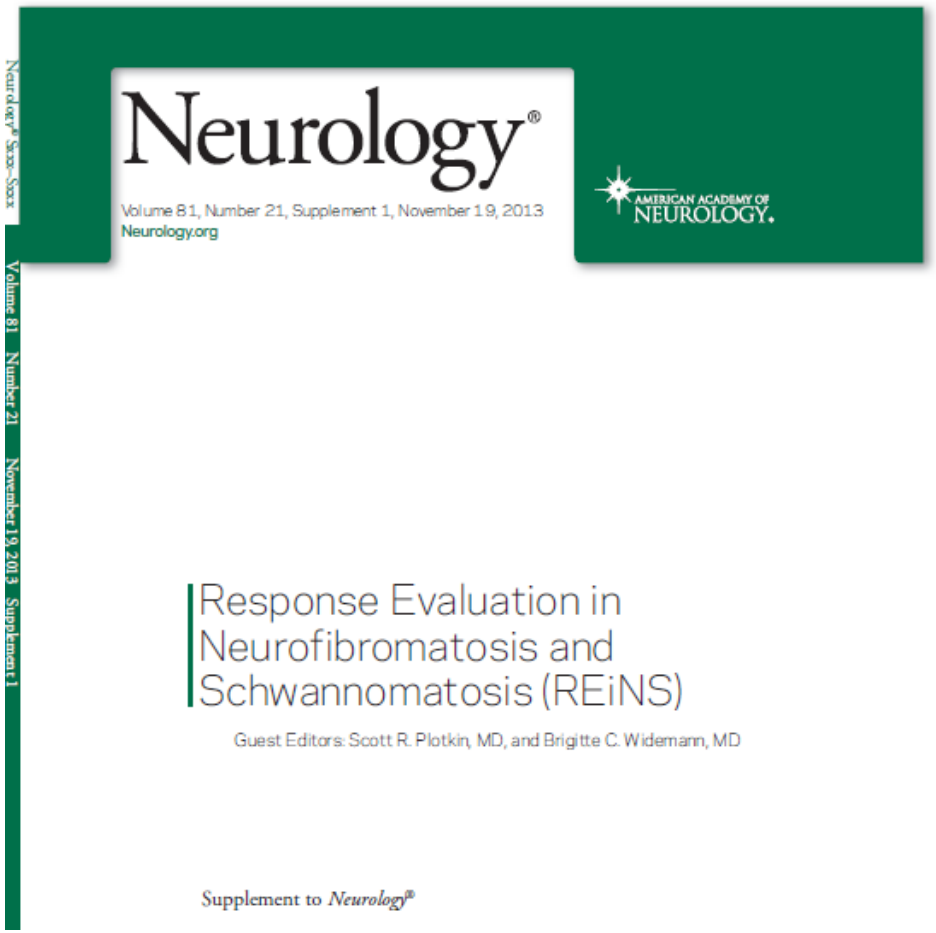
Endpoint development

- Meet semi-annually in June (CTF meeting) and December (NIH)
- Working groups set agenda and review literature on endpoints under discussion
- Working groups make recommendations to overall REiNS Collaboration
- Accepted endpoints are submitted for publication

Collaborations/Support

- Children's Tumor Foundation
- Food and Drug Administration
- Cancer Therapy Evaluation Program
- NIH
- Patient advocacy

REiNS publications 2013



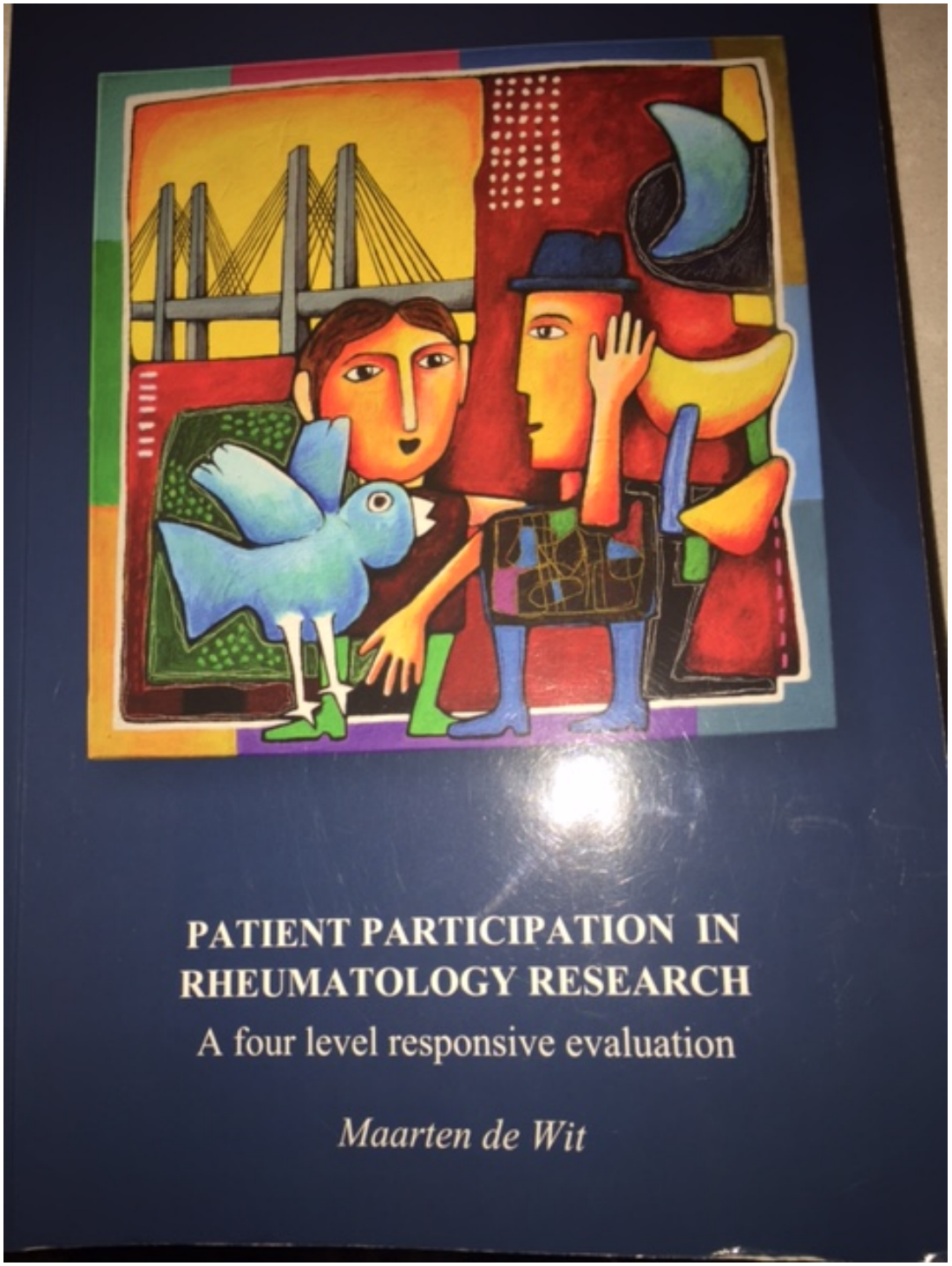
1. Achieving consensus for clinical trials: The REiNS International Collaboration
2. Patient-reported outcomes in neurofibromatosis and schwannomatosis clinical trials
3. Functional outcome measures for NF1-associated optic pathway glioma clinical trials
4. Hearing and facial function outcomes for neurofibromatosis-2 clinical trials
5. Recommendations for imaging tumor response in neurofibromatosis clinical trials
6. Conclusions and future directions for the REiNS International Collaboration

Response Evaluation in REiNS Neurofibromatosis & Schwannomatosis

CHILDREN'S TUMOR FOUNDATION
ENDING NF THROUGH RESEARCH

REiNS supplement 2016

1. Consensus for NF Clinical Trials: Recommendations of the REiNS Collaboration
2. Outcomes of Pain and Physical Functioning in NF Clinical Trials
3. Sleep and pulmonary outcomes for clinical trials of airway plexiform neurofibromas in NF1
4. Neurocognitive Outcomes in Neurofibromatosis Clinical Trials: Recommendations for the Domain of Attention
5. Current Whole-Body MRI Applications in the Neurofibromatoses: NF1, NF2 and Schwannomatosis
6. Current status and recommendations for biomarkers and biobanking in neurofibromatosis


PATIENT PARTICIPATION IN
RHEUMATOLOGY RESEARCH
A four level responsive evaluation
Maarten de Wit

Arguments for including patients in health research

- Patients have a right to have input in health research that affects their daily lives
- Patient engagement improves quality and relevance of research
  - Final outcomes will better meet needs and preferences of patients
  - Patient input on trial design will increase trial feasibility
- Patient engagement increases outreach, trial enrollment, trial completion, and dissemination of results
- Patient participation enhances chances for fund raising and implementation of results

Current state of patient engagement

- Patients' contribution to research is often limited to ad hoc or one-time events
  - Patient contributions are often limited
  - Knowledge/skills developed by patients are not optimally used
  - Established relationships with stakeholders are not maintained
  - Results of trials are many times not shared with participating patients

Barriers to incorporating patient partners

- Realizing importance of patient engagement
- Optimal incorporation of patients in research:
  - Researchers perceive that scientific training is required for participation
  - Partners may not be aware of time commitments required
  - Partners may not appreciate need for validated research methods
- Need to identify new and complementary tasks for partners

Barriers to incorporating partners

- Recognizing cultural barriers
  - Researchers value scientific knowledge and consider it “objective”
  - Patient partners have experiential knowledge which may be considered “subjective” and of less value
- Partners may feel insufficiently supported

FIRST model

- F(acilitate)
- I(dentity)
- R(espect)
- S(upport)
- T(raining)

Facilitate

- Create optimal circumstances for involvement of partners
  - Working in pairs (partners)
  - Divide workload and responsibility
  - Partners bring different experiences
- Partner and professional training is essential to promote collaboration
- Professionals must guide partners to enable supportive behavior and communication
  - Roles and responsibilities should be explicit
  - Can be junior researchers

Identity

- Identifying partners
  - Application process to select partners including evaluation of experience, letter of interest, and recommendation
  - Recruitment through clinics may be superior to recruitment through central organization as it strengthens bond for researcher-partner
- Identify projects
  - May be challenging to match interests with skills/knowledge
  - Standard lists of possible projects may help facilitate this process
- Identify and learn from successful examples of patient engagement

Respect

- Practical examples include training, support, and reimbursement
- Not recognizing partners as a valuable source of knowledge shows lack of respect
  - Not included in meetings
  - Input ignored
- Overt recognition is always helpful

Support

- Supporting partners is a key responsibility of researchers
- Enabling contribution = genuine dialogue to remove partners' internal barriers (eg, knowledge) and to strengthen intrinsic motivation
- Organize regular contact, direct communication, and individual learning
- Promote peer support from other partners
- Researchers may need support in working with partners to optimize their participation

Training

- Formal training of partners is essential
- Should include general information (e.g., research ethics and methods) and disease-specific information
- Training of professionals on how to conduct participative research and work optimally with partners is essential

Stages in clinical outcome assessment

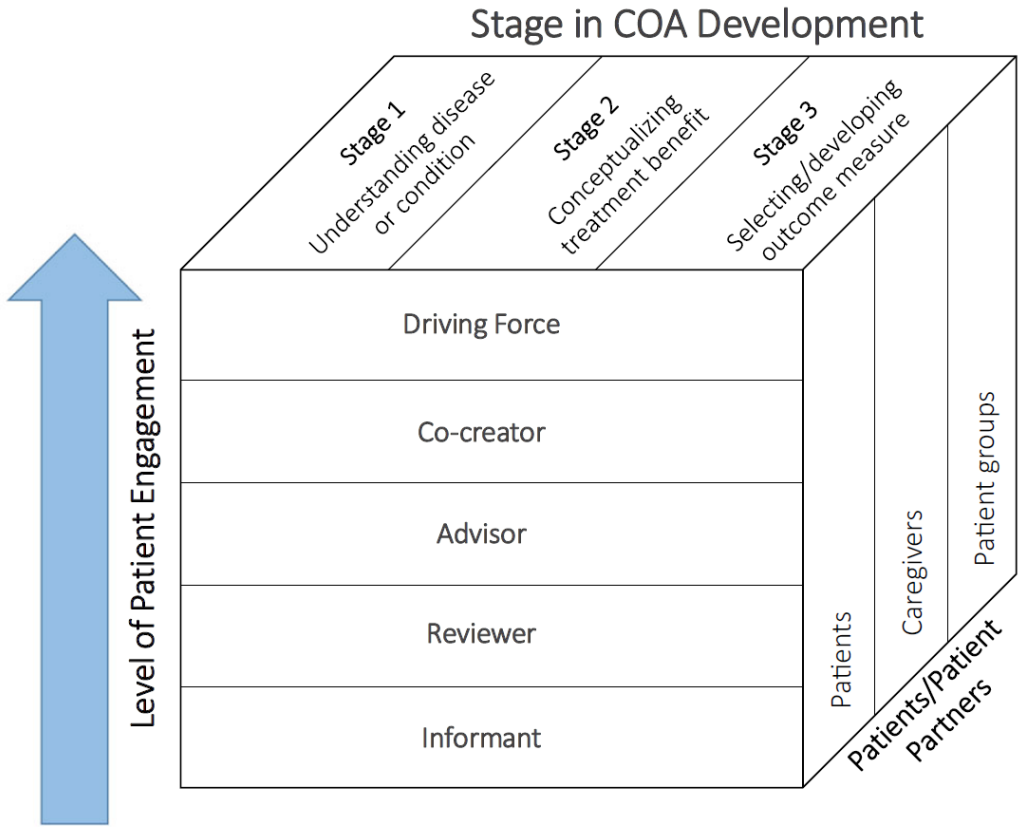


Fig. 1 Framework for engaging patients and patient partners in the selection and development of COAs

Wilson et al, Qual Life Res, 2017

Table 3 Level of patient engagement in the design and implementation of COAs

	Stage 1 Understanding Disease/Condition	Stage 2 Conceptualizing Treatment Benefit	Stage 3 Selecting/Developing the COA
Level 1 Informant	• Research participant in surveys, interviews, focus groups, and observational studies designed to inform COA activities. • Contribute information to publically available platforms (e.g., disease-specific forums, blogs, etc.) that may be used as supportive evidence to inform COA activities.	• Research participant involved in cognitive interviews to ask about hypothetical treatment benefits e.g. What "x" change would represent a meaningful treatment benefit to you? • Research participant in exit interview upon clinical trial completion to evaluate patient perceived treatment benefit	• Research participant in concept elicitation study to identify concept(s) of interest or; cognitive interview study to assess the comprehensiveness of the COA instrument and patient understanding of instrument content (e.g., items, response options, recall period); or quantitative validation study to evaluate the measurement properties of an instrument.
Level 2 Reviewer Level 3 Advisor	• Provide input on a conceptual disease model or design of study materials (e.g., study protocols, interview guides, conceptual frameworks, etc.). • Provide input on a research agenda designed to address gaps in current understanding of a disease or condition. • Identify alternative sources of information (e.g., grey literature, social media sources) that can inform the early stages of COA activities.	• Consult with medical product development teams on endpoint selection and development – what endpoints are most relevant to patients? • Provide advice on what constitutes meaningful treatment benefit.	• Provide input on the design of qualitative and quantitative instrument development studies. • Provide input on recruitment strategies and procedures. • Serve as patient liaison or study representative that can share study-related information with participants. • Disseminate instrument development research findings to patient communities. • Participate in regulatory meetings where COA strategy is discussed. • Communicate with payers about the interpretation and importance of patient-relevant endpoints.
Level 4 Co-creator Level 5 Driving Force	• Co-create/lead studies designed to understand a disease or condition. • Host interactive workshops with multiple stakeholders (e.g., externally lead patient-focused drug development meetings) to systematically document patient perspectives on their disease and related treatments, and/or the state of COA measurement in specific therapeutic areas. • Co-author publications from research activities related to understanding disease/condition	• Co-create/lead the development of guidance documents for industry that include recommendations for COA selection and development, endpoint selection and positioning, and other outcome measurement considerations. • Co-create/lead surveys, interviews, workshops, or consensus exercises to determine concepts of interest to patients and/or understand what constitutes a meaningful treatment benefit. • Co-author publications from research activities related to conceptualizing treatment benefit	• Co-create/develop a COA measure for use in disease specific population. • Lead efforts or collaborate with other stakeholders to qualify a COA for use in disease specific population. • Co-author publications from research activities related to selecting/developing a COA instrument

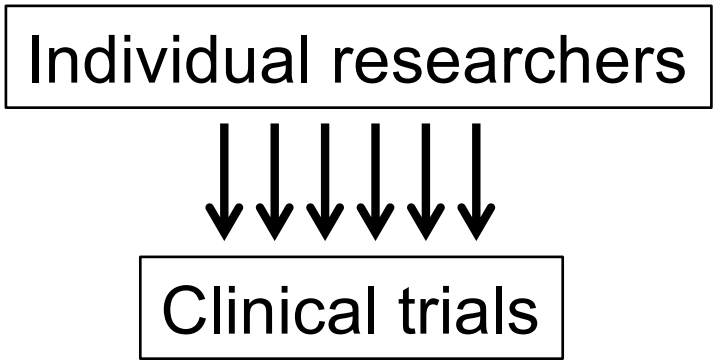
Wilson et al, Qual Life Res, 2017

June 2016	First REiNS discussion of patient engagement
December 2016	<u>REiNS Winter meeting</u> REiNS, foundation representatives Patient engagement researchers
January 2017	REiNS Steering committee planning
March – May 2017	Meetings with foundation leaders to discuss selecting patient partners

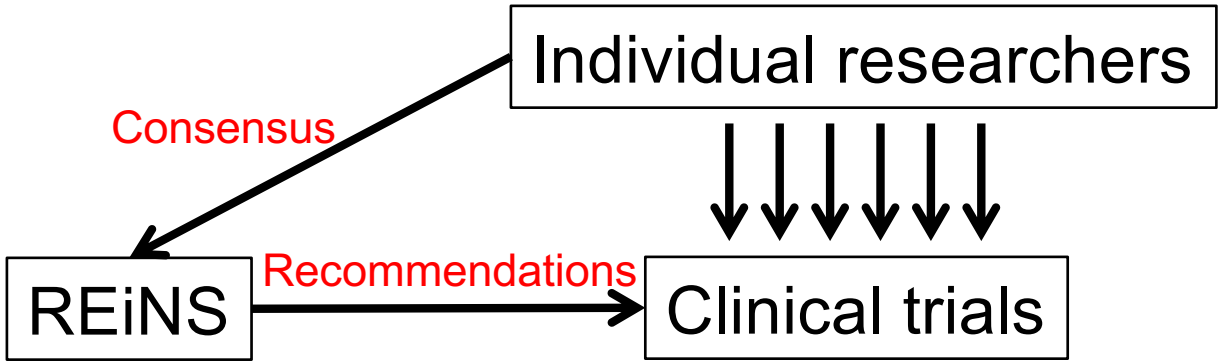
REiNS Meeting Timeline

June 2017	Summer REiNS meeting: outlining roadmap
July - August 2017	Open application for patient partners Design training for patient partners
September 2017	Select patient partners Training for REiNS working group leaders
October 2017	Training of patient representatives
November 2017	Patient representatives join working groups
December 2017	**Monday, 12/3/17: REiNS Winter Meeting** In person meeting with patient representatives Discuss possible FDA Patient-Focused Drug Development Meetings (PFDD)
May 4-6, 2018	Joint meeting: REiNS/NF Forum (Atlanta)

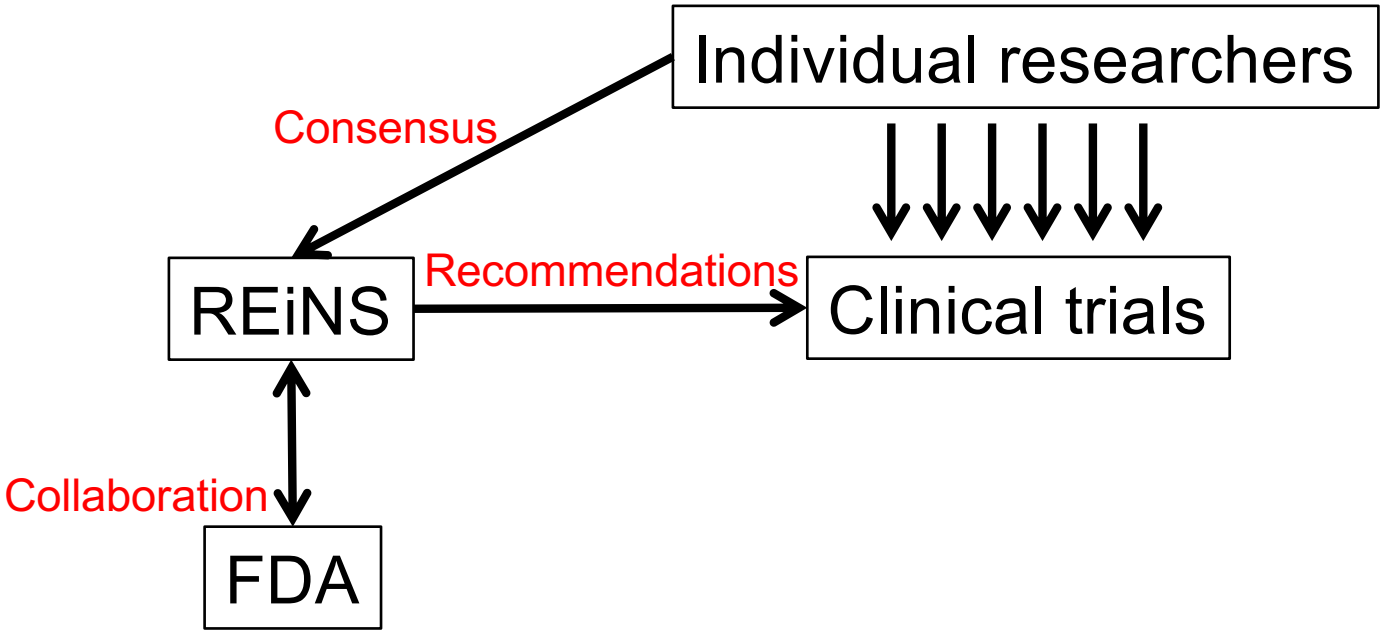
Clinical trials in 2000s



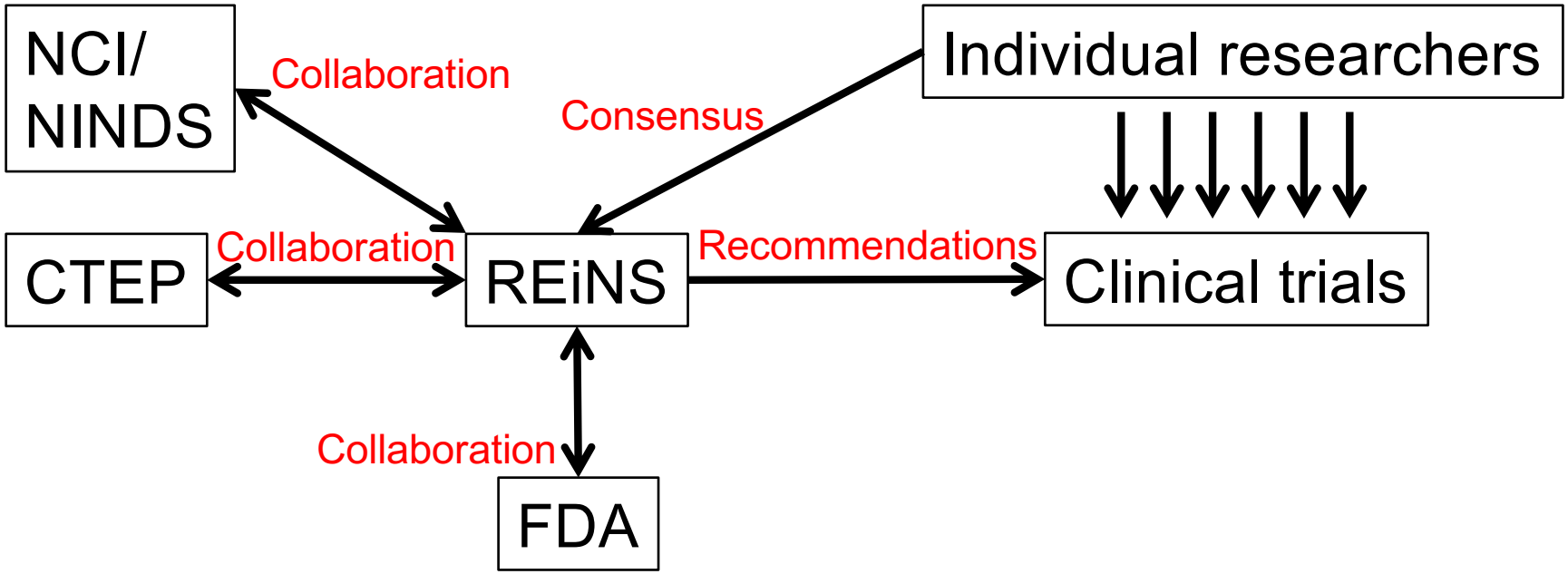
REiNS 2011: the Beginning



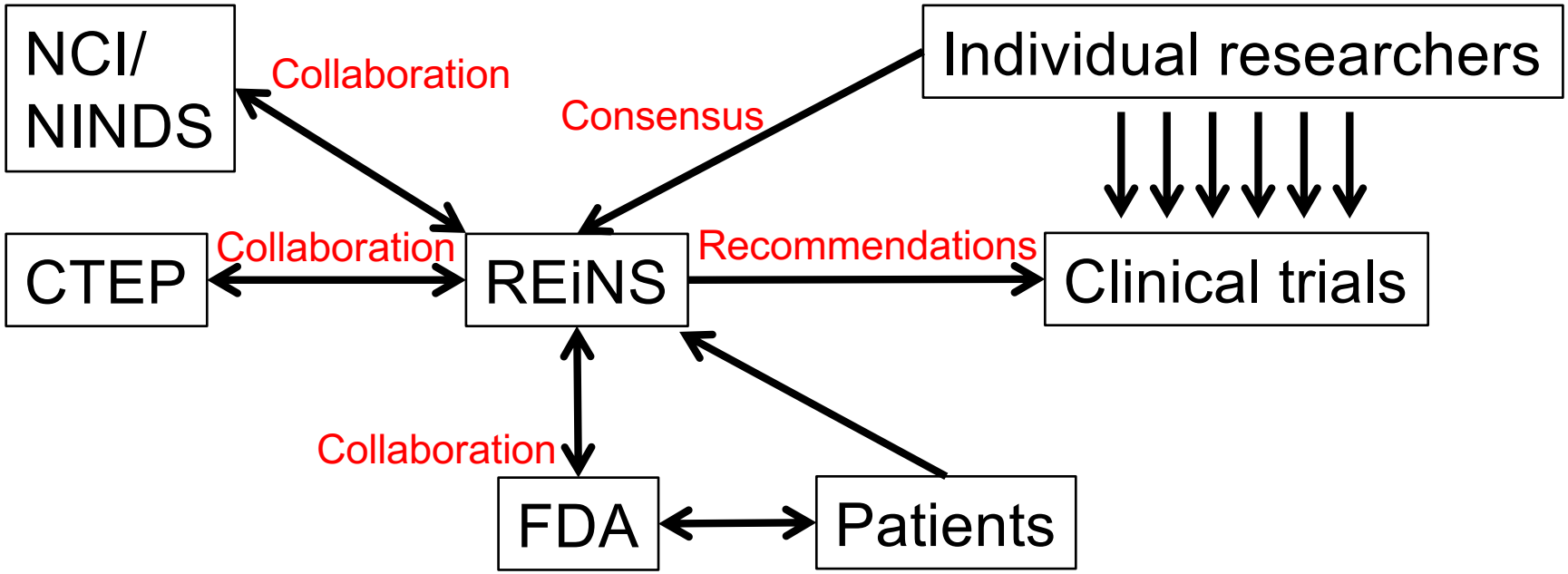
REiNS 2012: Engaging FDA



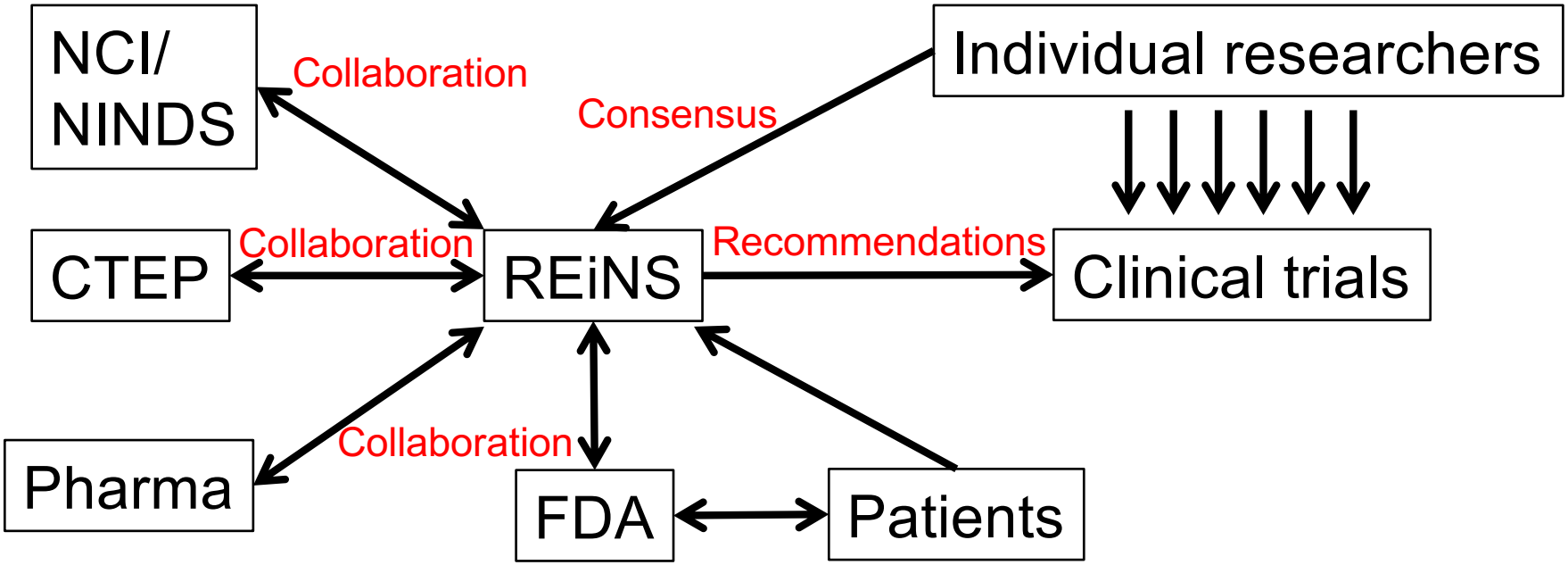
REiNS 2014: Enhancing collaboration



REiNS 2017: Engaging patient partners



REiNS post-2017: Strenghtening ties to industry



Acknowledgements

- REiNS members (Traceann Rose)
- REiNS steering committee
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- Neurofibromatosis Northeast, Neurofibromatosis Midwest, NF Texas, Neurofibromatosis Michigan, Littlest Tumor Foundation
- Patients and patient representative