

# **Clinical Investigation of Neurological Channelopathies (CINCH) Landmarks**

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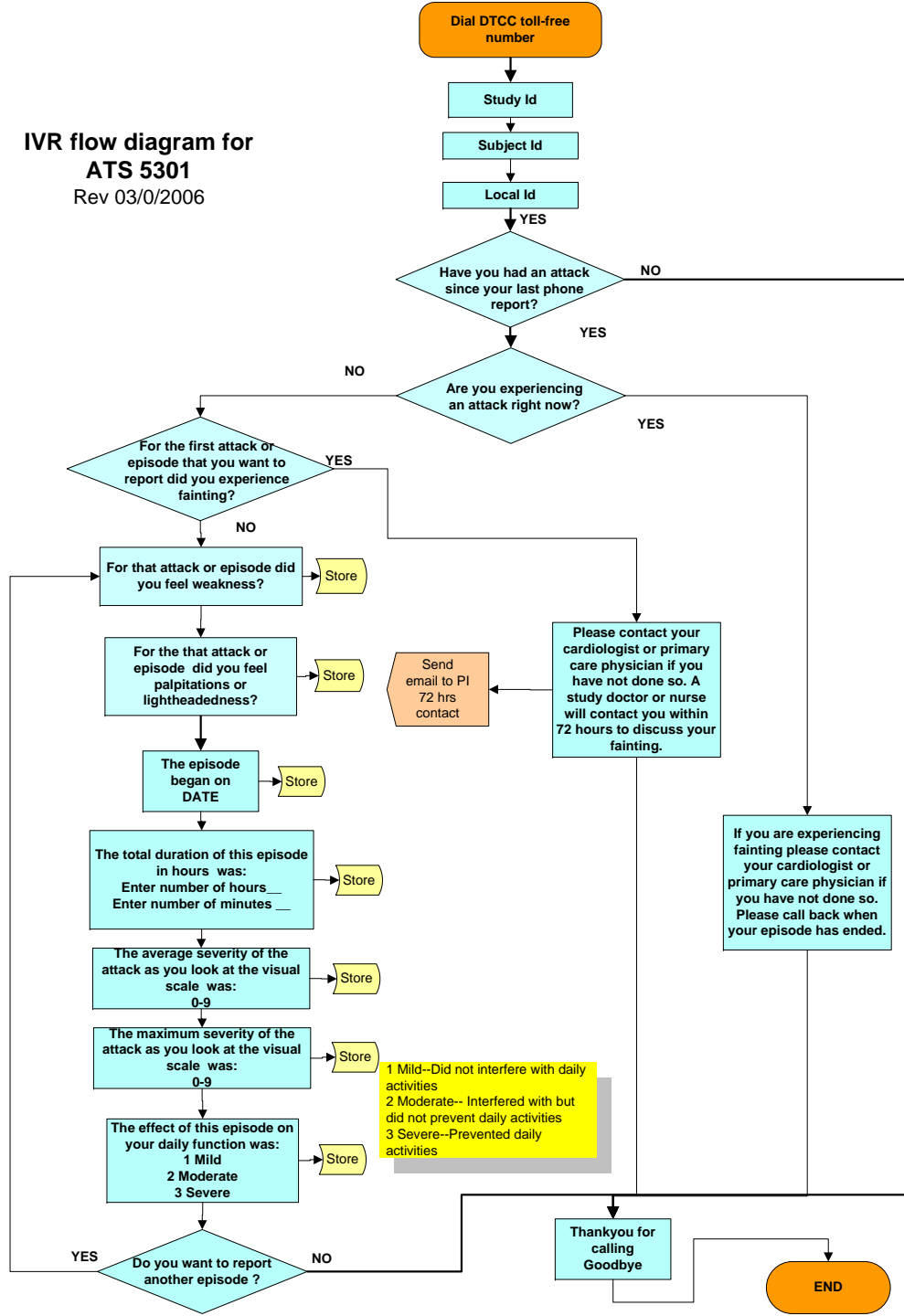
**Richard Barohn, M.D.**

# CINCH Landmarks

- **Patient-reported outcomes: interactive voice response system for**
  - **NDM**
  - **Periodic paralysis**
  - **Cardiac arrhythmias**
- Clinical trial in NDM (Richard Barohn)
- Clinical Trial in the periodic paralysis, Andersen-Tawil Syndrome
- Training Program
  - 22 Fellows
  - 4 medical Students
- 16 additional grants for CINCH studies
- 94 publications

# IVR flow diagram for ATS 5301

Rev 03/0/2006



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# Phase II Therapeutic Trial of Mexiletine in Non-Dystrophic Myotonia (IND #77,021; 1R01- FD003454)

- Principal Investigator: Richard J. Barohn, MD, Co-I: Yunxia Wang, M.D. University of Kansas Medical Center
- FDA Orphan Drug Division - Funding: May 2008 - April 2011
  - 3 years total \$949,028
- 60 patients; randomized, placebo controlled crossover study
  - NDM subjects from Natural History Study
  - 4 wks on mexiletine or placebo; 1 wk washout; crossover
  - 1° endpoint – patient report of stiffness on IVR (interactive voice response)
  - 2° endpoints – quantitative myotonia, electrophysiologic tests,
- DTCC data management and biostatistical support
  - Funded by NINDS supplement to CINCH – 1<sup>st</sup> meeting 5/28/08
- Study initiation meeting Oct. 25 Tampa, FL

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# Supplemental Grants (16)

Examples:

- (1) Mexilatine in nondystrophic myotonia
- (2) Potassium/acetazolamide in the periodic paralysis Andersen Tawil syndrome
- (3) Bringing dichlorphenamide to registration for periodic paralysis – with Taro Pharmaceuticals



# Taro funded by MDA to bring Dichlorphenamide to Market

- PAG (Periodic Paralysis Association) – President Jacob Levitt works for Taro
- MDA has awarded funding (\$1 million) to enable Taro Pharmaceuticals U.S.A., Inc to provide DCP commercially to patients with the periodic paralyses.
- Taro has purchased the NDA from Merck
  - Will develop a synthetic method for the manufacture of pharmaceutically pure DCP to 2008 standards.
  - Will develop a formulation in which DCP is sufficiently bioavailable
  - Will perform clinical studies to establish bioavailability of DCP
  - Rochester will support the clinical arm of the project and provide safety and outcome data necessary for FDA filings
- Plan to bring the drug to the marketplace soon after the Phase III trial is complete.

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# Representative Publication (1)

“Pivotal Studies of Orphan Drugs Approved for Neurological Diseases.”

Authors: J Mitsumoto (CINCH medical student), ER Dorsey, CA Beck, J Thompson, T Nguyen, K Kieburtz, RC Griggs

Comparing orphan drugs with non-orphan drugs

# Publication Conclusion:

“Orphan drugs for neurological diseases have been approved by the FDA without randomized, doubled-blind, placebo-controlled clinical trials. As therapeutic development for orphan diseases is increasing, the design of alternative clinical studies will likely become more important.”

# Representative Publication (2)

- S. L. Venance, S. C. Cannon, D. Fialho, B. Fontaine, M. G. Hanna, L. J. Ptacek, M. Tristani-Firouzi, R. Tawil and R. C. Griggs and the CINCH Investigators. The primary periodic paralyses: diagnosis, pathogenesis and treatment. *Brain*. 2006;129(Pt 1):8-17
- J. C. Jen, T. D. Graves, E. J. Hess, M. G. Hanna, R. C. Griggs and R. W. Baloh and the CINCH Investigators. Primary episodic ataxias: diagnosis, pathogenesis and treatment. *Brain*. 2007;130(Pt 10):2484-93
- E. Matthews and the CINCH Investigators: Non-dystrophic myotonia. (In preparation for submission to *Brain*.)