RECRUITING PATIENTS WITH RARE DISEASES AND THEIR CAREGIVERS

JACQUELYN WAN
Senior User Experience Researcher
Radius Innovation & Development

BETH LORING
Principal
Loring Human Factors, LLC

March 7th, 2017

Overview

- Rare disease overview
- Increasing interest in treatments for rare diseases
- Impacts on human factors studies
- Case study
- Project overview
- Recruiting challenges and solutions

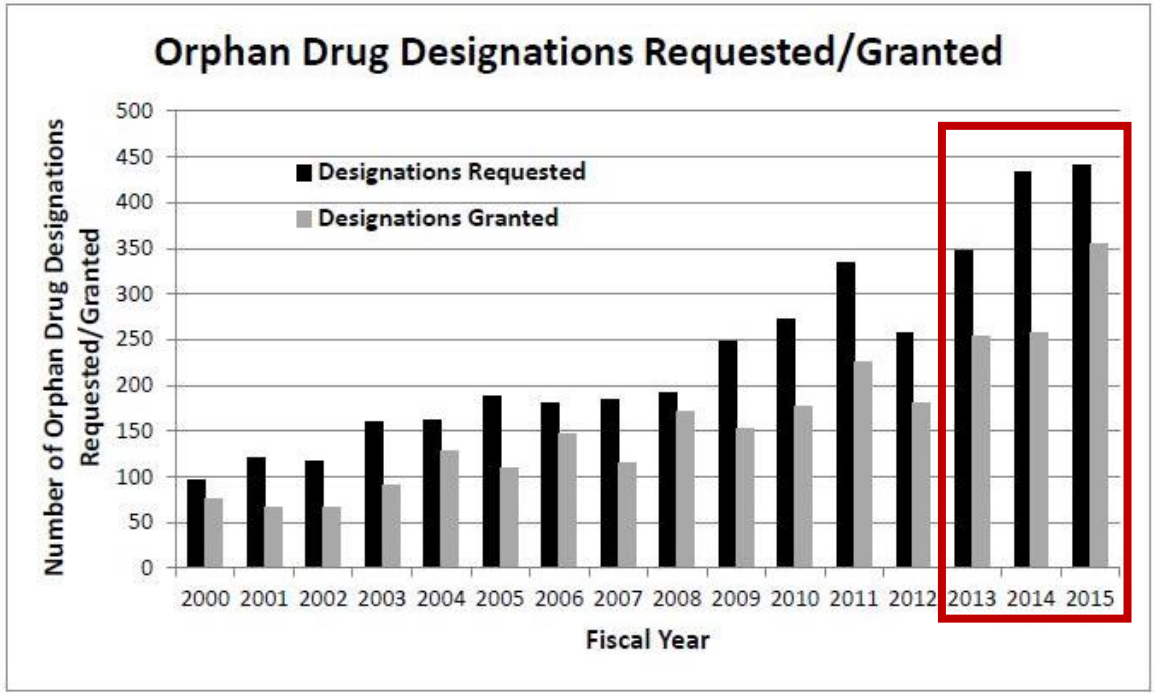
What constitutes a “rare disease?”

- A rare disease—also referred to as an orphan disease—as defined by the US Food and Drug Administration (FDA) and Orphan Drug Act (ODA):

> A disease/condition that affects **fewer than 200,000 people** in the US.

- There are about 7,000 known rare diseases afflicting about 30 million Americans.

Increasing trend in orphan drug applications



Office of Orphan Products Development:
http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/BudgetReports/UCM488554.pdf

Why is the number of drugs and biologics for treating orphan diseases increasing?

- **Expedited Process:**
  - Upon request by a sponsor, the FDA can grant special status or designation to expedite the development and review of a drug or biologic to treat an orphan disease/ condition.
    - Breakthrough Therapy Designation
    - Fast Track
    - Orphan Designation

Why is the number of drugs and biologics for treating orphan diseases increasing?

- **Incentives:**
  - Special grants to fund orphan drug research
  - Tax credit covering 50% of clinical trial cost
  - 7 years of market exclusivity

Why is the number of drugs and biologics for treating orphan diseases increasing?

- **New Draft Guidance/ Grants program:**
  - **2013:** Pediatric Device Consortia (PDC) Grant Program
  - **2014:** Rare Pediatric Disease Priority Review Vouchers: Draft Guidance for Industry
  - **2016:** Orphan Products Natural History Grants Program

Office of Orphan Products Development:

http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/RarePediatricDiseasePriorityVoucherProgram/default.htm

http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/DesignatingHumanitarianUseDevicesHUDS/default.htm

http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/OrphanProductsNaturalHistoryGrantsProgram/ucm487336.htm

Why is the number of drugs and biologics for treating orphan diseases increasing?

- **Changes to Existing Programs:**
  - **2016:** Humanitarian Use Device (HUD) (established in 1990)
    - Qualifying population changed from “fewer than 4,000” to “not more than 8,000” individuals in the US per year.

Office of Orphan Products Development:

http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/RarePediatricDiseasePriorityVoucherProgram/default.htm

http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/DesignatingHumanitarianUseDevicesHUDS/default.htm

http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/OrphanProductsNaturalHistoryGrantsProgram/ucm487336.htm

How does this increasing demand impact human factors studies?

- Standard recruiting methods are often unsuitable.
- Difficult to find and locate patients and caregivers.
- Rare diseases constitute a very small and select population
  → Challenging to satisfy participant quotas per FDA guidance.
    - Example:

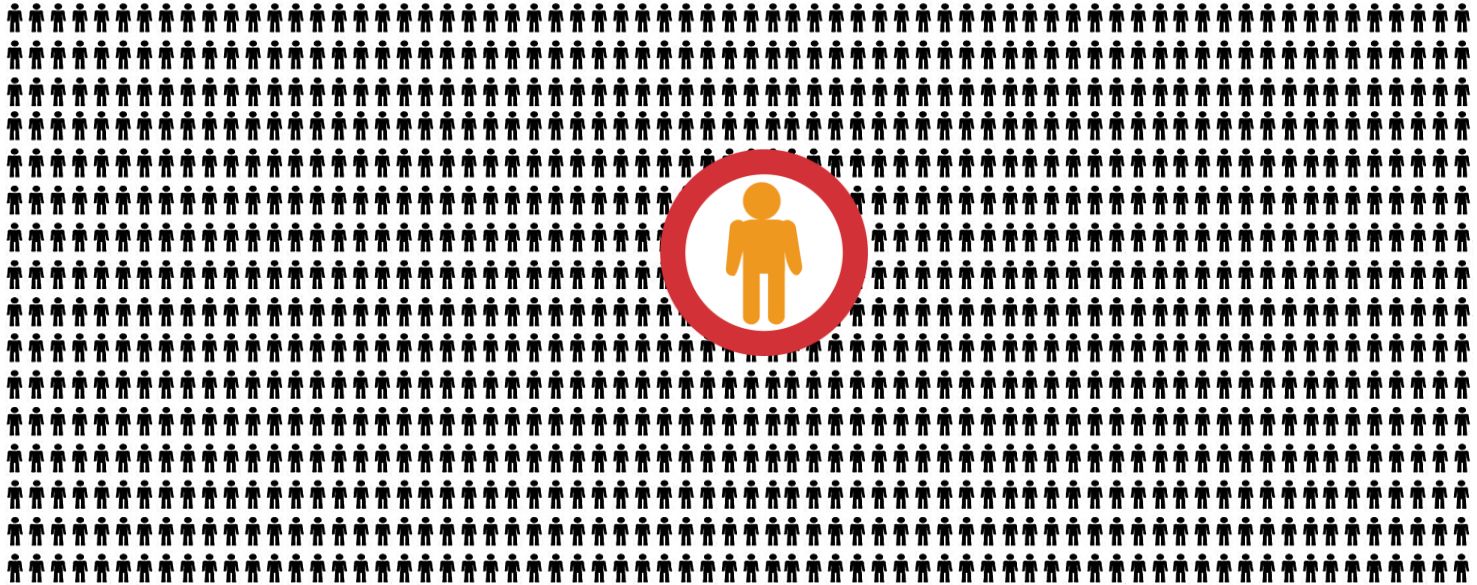
VALIDATION STUDY PARTICIPANT QUOTA		
User Group	**Naïve User**	**Experienced User**
Nurse	15	15
Adult Patient	15	15
Juvenile Patient	15	15
Caregiver	15	15
Participant Total = 120		

What makes recruiting patients with rare diseases difficult?

- One rare disease may affect only a handful of patients, and another could affect as many as 200,000.
- Relatively common symptoms can hide underlying diseases leading to misdiagnosis and delayed treatment.
- Patients with rare diseases may not be willing or physically able to participant in studies due to their health conditions.

What makes recruiting patients with rare diseases difficult?

- A large database and/or creative recruiting methods are required.



CASE STUDY: Recruiting Patients with Rare Diseases and Their Caregivers

OVERVIEW

CASE STUDY

Project Overview:

- Formative (2014) and validation (2016) studies on a new delivery system for a drug that is currently available in the market.
- A combination device that delivers drug through subcutaneous infusion therapy to over 10,000 patients with this rare autoimmune disease.
- Demographic included 50% naïve and 50% experienced users:

VALIDATION STUDY PARTICIPANT QUOTA		
User Group	**Naïve User**	**Experienced User**
Nurse	15	15
Adult Patient (age 18 +)	15	15
Juvenile Patient (ages 2 to 17)	15	15
Caregiver	15	15
Participant Total = 120		

CASE STUDY: Recruiting Patients with Rare Diseases and Their Caregivers

CHALLENGES

CASE STUDY

Challenge # 1: Setting the Right Expectations for Program Planning

	TYPICAL STUDY	RARE DISEASE STUDY
Participant Recruit	Relatively Easy	Extremely Difficult
Testing Location	Single US City (Boston)	Multiple US Cities (Boston, Atlanta, Houston, Chicago)
Project Timeline	Standard Project Timeline (2-3 weeks for recruiting)	Extended Project Timeline (8-12 weeks for recruiting)
Project Budget	Standard Budget	Increased Budget

CASE STUDY

Challenge # 2: Finding the Right Recruiters *(Don't underestimate this effort!!!)*

PROBLEM	SOLUTION	CHALLENGE
• Major national recruiting companies lacked confidence in fulfilling the full quota. • Rejected by majority of recruiting vendors. (Contacted 25+ vendors, only 7 accepted the project)	• Hired multiple recruiting vendors. • Increased participant database and wider outreach.	• Vetting the right recruiters to get the job done right. • Managing multiple recruiting vendors and recruiting quotas.

Case Study

Challenge # 3: Study Location(s)

PROBLEM	SOLUTION	CHALLENGE
• Difficult for any one city to fulfill the total number of participants needed per study that satisfies the quotas per FDA guidance.	• Conducted the study in multiple cities.	• Managing participant quotas and travel schedule. *(We never made it to Houston due to flooding!)* • Extended project timeline.

CASE STUDY: Recruiting Patients with Rare Diseases and Their Caregivers

OPPORTUNITIES

Case Study

Opportunity # 1: Work with Your FDA Reviewer

OPPORTUNITY	RATIONALE
• Get your protocol reviewed. • Raise project challenges to your FDA reviewer as early as possible. • Notify your reviewer and present different options to narrow down the best solutions.	• The FDA reviewer will be able to provide guidance on the proposed study approach and suggestions on how to solve foreseen challenges.

Case Study

Opportunity # 2: Learn from the Formative Study

OPPORTUNITY	RATIONALE
• Recognize challenges and address them early on (such as difficult recruiting, use errors and study artifacts.)	• Use the information learned from the formative study to inform and guide you for a successful validation study.

Case Study

Opportunity # 3: Leverage the Drug Sales Organization Database

OPPORTUNITY	RATIONALE
• Reach out to the drug sales team for guidance. • Identify geographic areas with the highest sales and the highest concentrations of patients. • Identify physicians treating patients with the disease.	• Increase probability of finding potential recruits. • Physician outreach = Patient referral. • Potential connections to local non-profit organizations and charities through local events and sponsorships.

Case Study

Opportunity # 4: Consider Non-Profit Organizations and Charities

OPPORTUNITY	RATIONALE
• Reach out to charitable organizations and foundations dedicated to the specific disease.	• Some may provide links to blogs and online communities for patient outreach programs. • With a donation, some may offer to post study details on their site or patient blog.

Case Study

Opportunity # 5: Transform Participants into an Army of Recruiters

OPPORTUNITY	RATIONALE
• Offer referral incentives to pre-recruited participants to reach out to their friends and families. • Word of mouth!	• Many patients are a part of a local support group or national online community. • Many rare diseases are inherited genetically. • This is a powerful method that can increase recruit on both local and national levels.

When All Else Fails…

When All Else Fails…

Reuse Formative Study Participants

SOLUTION	RATIONALE
• Formative participants may be recruited for validation study to fulfill the total number of participants needed as required by FDA (but confirm with your FDA reviewer).	• These participants are the true representation of the patient population. • Due to a 2-year delay between formative and validation, FDA felt that learning had decayed sufficiently. • Some of the pediatric/ adolescent patients had shifted into another user group.

When All Else Fails…

Use Surrogate Patients

SOLUTION	RATIONALE
• Recruit patients diagnosed with similar disease characteristics (but confirm with your FDA reviewer.) • Comorbidities should be taken into account.	• While these patients may not be diagnosed with the prescribed disease, they may share similar disease characteristics, such as hereditary diseases, life long conditions.

When All Else Fails…

Use Surrogate Patients- Examples

	POPULATION NEEDED	REPLACED WITH	JUSTIFICATION
Example #1	• Bariatric, gastric ulcer and gastric cancer patients	• Additional bariatric patients	• Gastric cancer patients were hospitalized or too ill to participate. • No difference in intended use of treatment device.
Example #2	• Pediatric and juvenile patients with a particular autoimmune disease	• Pediatric and juvenile patients with diabetes	• Life-long disease that requires frequent treatment. • No difference in physical comorbidities.

Conclusion

- Increase the success rate of your program and be better equipped to mitigate recruitment challenges by:
  - Identifying and acknowledging how difficult the recruit will be
  - Working with your FDA reviewer to address the challenge
  - Coming up with different options and narrowing down the best solutions
  - Using a combination of tactics

THANK YOU.

JACQUELYN WAN
Senior User Experience Researcher
Radius Innovation & Development

Jacquelyn.Wan@RadiusInnovation.com

BETH LORING
Principal
Loring Human Factors, LLC

Beth@Loring-HF.com