Clinical Trials: What Every Patient Should Know

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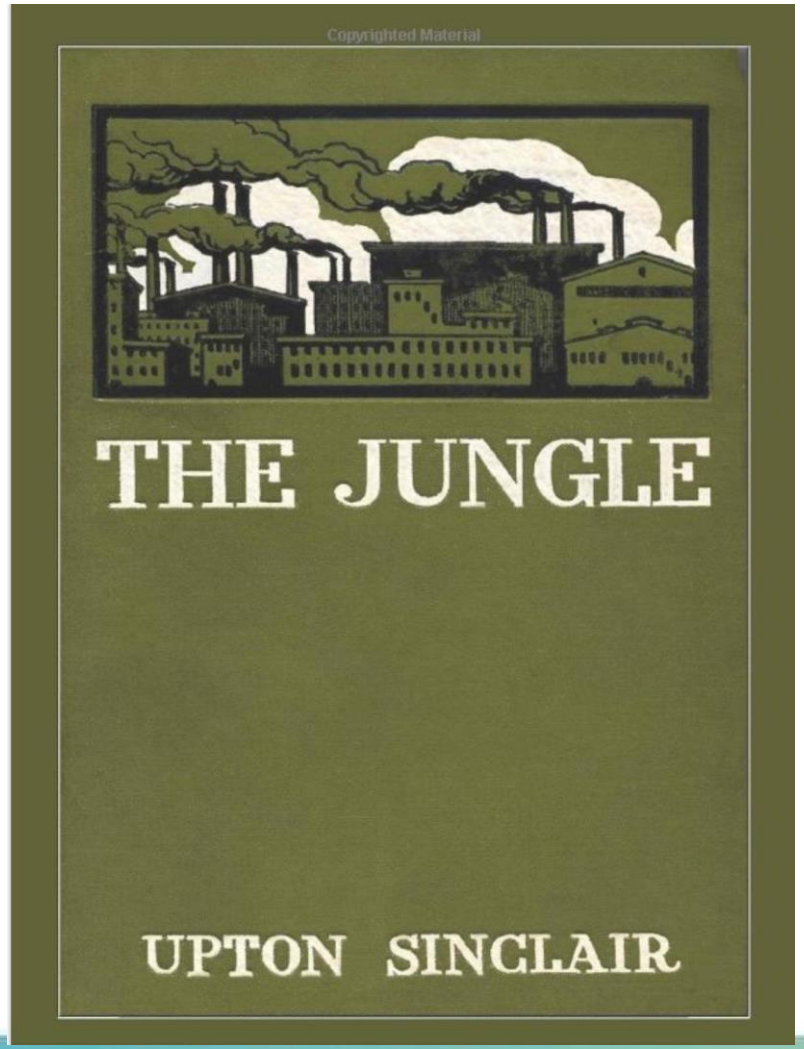
2022 Sjögren's Foundation
National Patient Conference

Personal Perspective


FDA
U.S. Department of
Health and Human Services
Food and Drug Administration

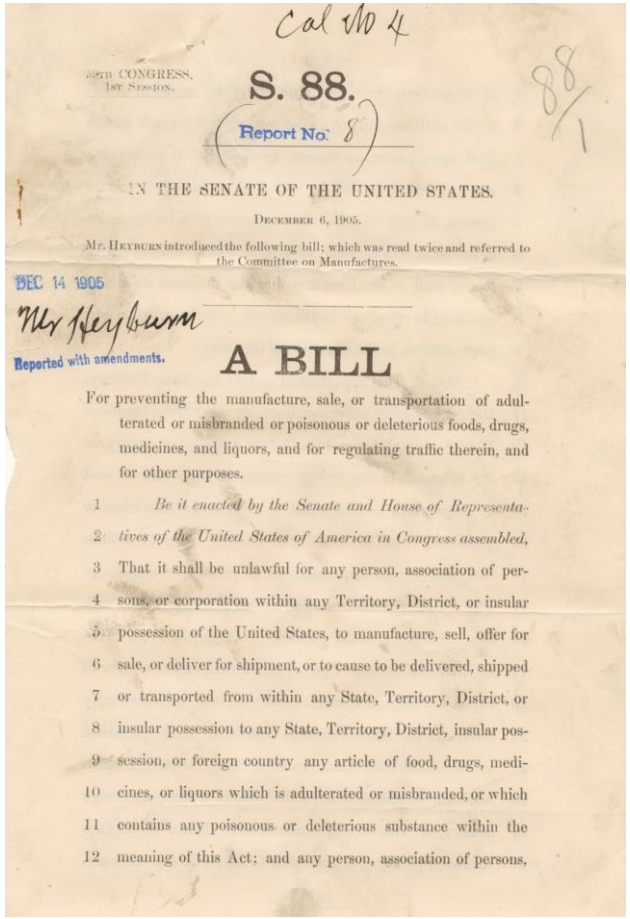
The FDA

- Upton Sinclair's 1906 book "The Jungle" revealed food adulteration and unsanitary practices in the meat production industry
- Public outrage prompted Congress to assume federal responsibility for public health and welfare
- The Pure Food and Drug Act and Meat Inspection Act were passed by Congress in 1906 empowering the USDA Bureau of Chemistry to enforce these laws



The FDA

- In 1927 the Bureau of Chemistry's regulatory powers were reorganized under the USDA's new "Food, Drug and Insecticide Administration"
- Name shortened to "Food and Drug Administration" in 1930
- Federal Food, Drug & Cosmetic Act of 1938 required a physician prescription for certain drugs



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59TH CONGRESS, 1ST SESSION.

S. 88.

Report No. 8

88/1

IN THE SENATE OF THE UNITED STATES.

DECEMBER 6, 1905.

Mr. HEYBURN introduced the following bill; which was read twice and referred to the Committee on Manufactures.

DEC 14 1905

Mr Heyburn

Reported with amendments.

A BILL

For preventing the manufacture, sale, or transportation of adulterated or misbranded or poisonous or deleterious foods, drugs, medicines, and liquors, and for regulating traffic therein, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That it shall be unlawful for any person, association of persons, or corporation within any Territory, District, or insular possession of the United States, to manufacture, sell, offer for sale, or deliver for shipment, or to cause to be delivered, shipped or transported from within any State, Territory, District, or insular possession to any State, Territory, District, insular possession, or foreign country any article of food, drugs, medicines, or liquors which is adulterated or misbranded, or which contains any poisonous or deleterious substance within the meaning of this Act; and any person, association of persons,

Bill Leading to the Pure Food and Drug Act

The FDA

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Daily Mirror

Bid to aid all Thalidomide victims

'DRUG BABY' PARENTS WILL SUE

Linked to Malformed Babies

'Heroine' of FDA Keeps Bad Drug Off of Market

By Morton Mintz
Staff Reporter

This is the story of how the skepticism and stubbornness of a Government physician prevented what could have been an appalling American tragedy, the birth of hundreds or indeed thousands of armless and legless children.

The story of Dr. Frances Oldham Kelsey, a Food and Drug Administration medical officer, is not one of inspired prophecies nor of dramatic research breakthroughs.

She saw her duty in sternly simple terms, and she carried it out, living the while with insinuations that she was a bureaucratic nitpicker, unsociable — even, she said, stupid. That such attributes could have been ascribed to her is, by her own acknowledgement, not surprising, considering all of the circumstances.

What she did was refuse to be hurried into approving an application for marketing a new drug. She regarded its safety as unproved, despite considerable data arguing that it was ultra safe.

It was not until last April, 19 months after the applica-

The Washington Post

DR. FRANCES O. KELSEY
. . . skepticism wins

standards and her belief that the drug was "peculiar" against these facts:

The drug had come into widespread use in other countries. In West Germany, where it was used primarily as a sedative, huge quantities of it were sold over the counter before it was put on a prescription basis. It gave a prompt, deep, natural sleep that was not followed by a hangover. It was cheap. It failed to kill even the would-be suicides who swallowed massive doses.

And there were the reports on experiments with animals. Only a few weeks ago the American licensee told of giving the drug to rats in doses 6 to 60 times greater than the comparable human dosage. Of 1110 offspring, none was delivered with "evidence of malformation."

In a separate study, one rat did deliver a malformed offspring, but the dosage had been 1200 times the usual one. Rabbits that were injected with six times the comparable human dose also were reported to have produced no malformed births.

Recently, the FDA publicly

that the terrible effects of the drug abroad were widely reported in this country. What remains to be told is how and why Dr. Kelsey blocked the introduction of the drug before those effects were suspected by anyone.

Giant firm faces a court fight

By TOM HEAD

THE £180,000,000 Distillers Company, British manufacturers of thalidomide, is to be sued by the parents of four babies deformed by the drug.

The parents plan to bring a High Court action on behalf of Richard, the eight-month-old armless son of Mr. Edward Sathirley.

Legal Aid?

'Not Liable'

Sjögren's FOUNDATION

The FDA

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- Name shortened to "Food and Drug Administration" in 1930 Federal Food, Drug & Cosmetic Act of 1938 required a physician prescription for certain drugs
- Following the thalidomide catastrophe a 1962 amendment to the FD&C Act led to a formal FDA drug approval process
- Safety and efficacy to be determined through a clinical trials process regulated by the agency

Emergency Use Authorization

vs

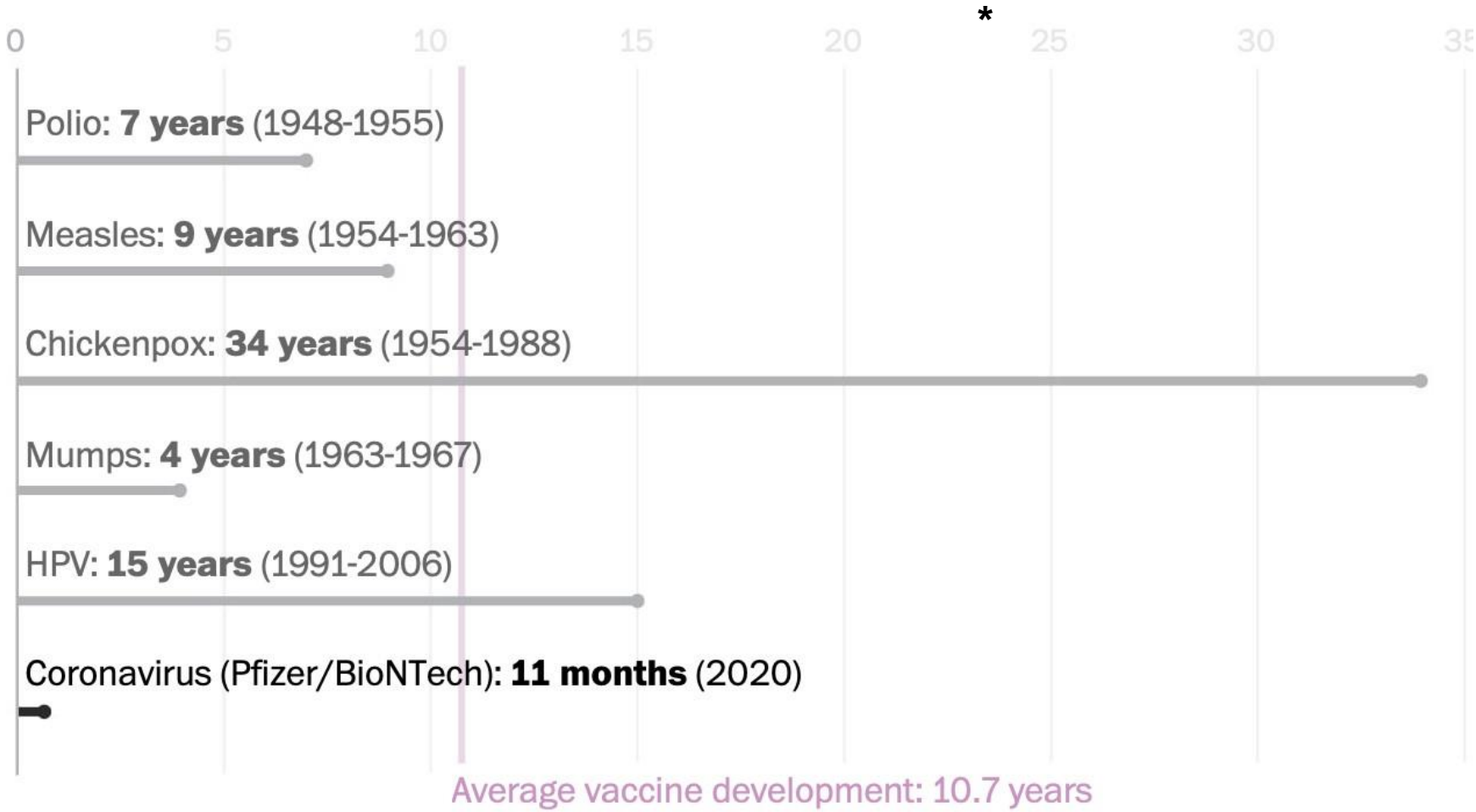
Standard FDA Approval Process


EMERGENCY USE
AUTHORIZATION

Emergency Use Authorization

- established in 2004 after the September 11 terrorist attacks
- rules created to fast-track development of drugs and vaccines during a public health emergency
- safety and efficacy data required but over shorter period than is standard
- data reviewed by outside advisory committee
- companies given EUA must continue performing clinical trials to ensure more longterm data
- FDA expects that companies will also file for standard approval

How long it took to develop other notable vaccines



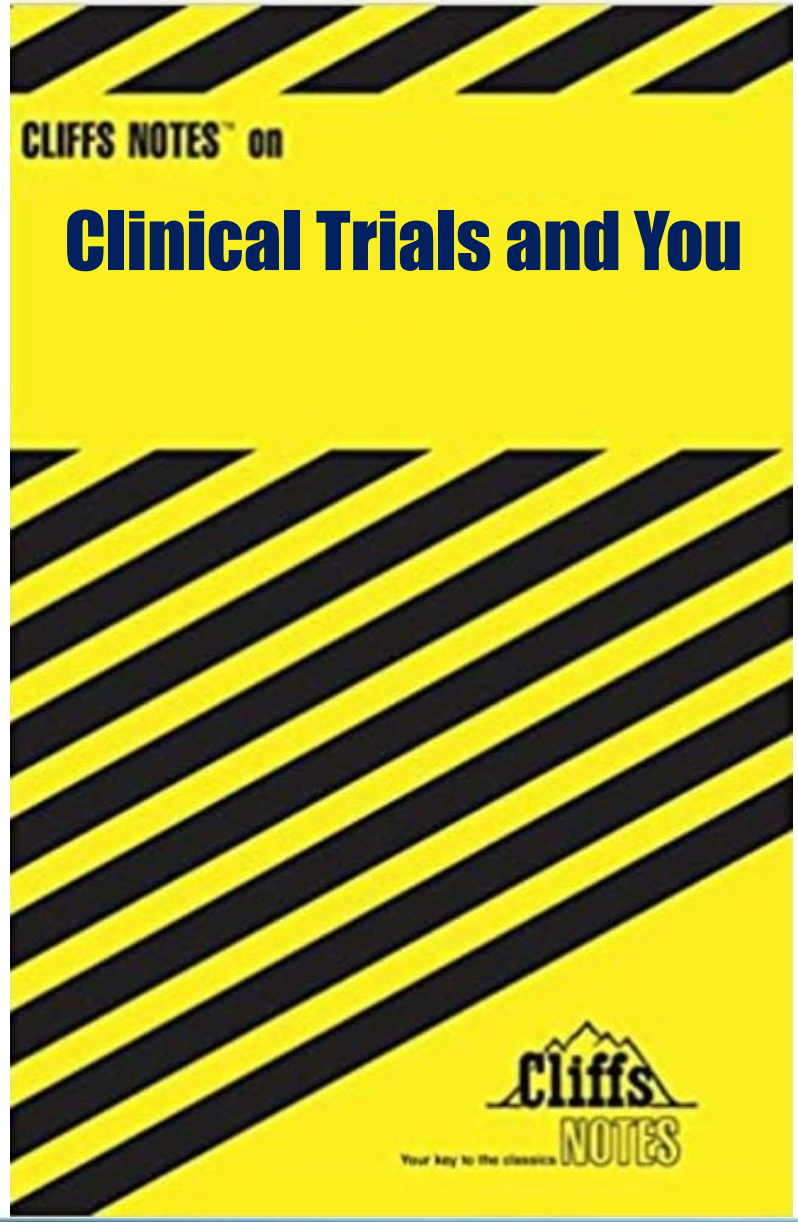
Sources: Center for Infection and Immunity; National Institutes of Health; Centers for Disease Control and Prevention

* during COVID PHE 4 monoclonal therapies, 3 oral antivirals & remdesovir were all granted EUA status

The standard drug approval process is rigorous and....

- slow - from pre-clinical testing of a drug to getting to market takes 12 years on average
- expensive - “the entire cost (of new drug development) may be in excess of 1 billion dollars”

Van Norman, G; Drugs, Devices and the FDA; JACC: Basic to Translational Science Vol. 1, No. 3, 2016 April 2016:170–9


CLIFFS NOTES™ on
Clinical Trials and You
Cliffs
NOTES

FDA Approval Process

- Slow, methodical and expensive
- All approvals require a clinical trials program
- Even after an FDA approval there is often additional testing or investigation needed
- The standard process is the focus of today's presentation

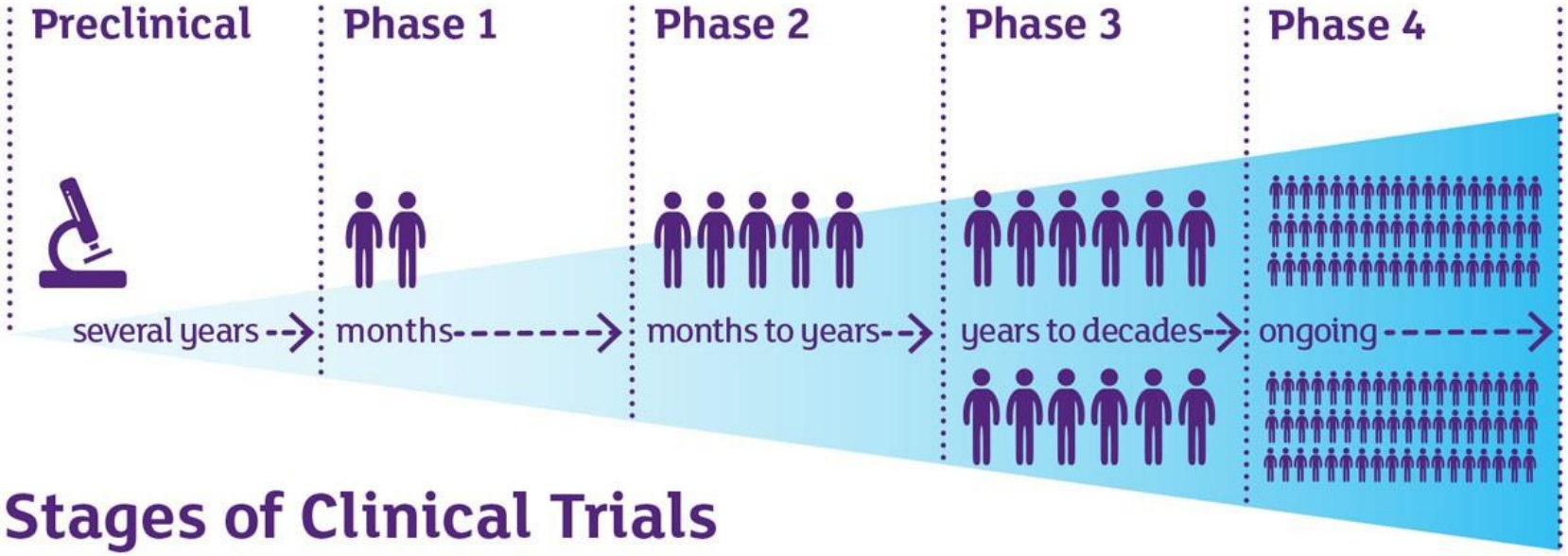
- Clinical trials are the means by which we evaluate a new drug or device for a particular disease or medical problem; or an old drug or device for a new application (e.g. methotrexate)

- New treatments are evaluated for safety and efficacy

- Data generated by a clinical trial provides the FDA with information necessary to determine if a drug should be approved

- Upon a drug's approval, *Prescribing Information* and patient labeling documents are generated that outline dosing and safety guidance

- Every step of this process is regulated by the FDA



Stages of Clinical Trials

- Pre-clinical: in the laboratory with animal subjects
- Phase 1 - healthy volunteers to determine “pharmacology” of a drug
- Phase 2 - to prove an effect, find the right dose and evaluate safety
- Phase 3 - to generate more meaningful data on safety and efficacy
- Phase 4 - primarily performed to evaluate long term safety


Randomised
Double-blind
Controlled

Controlled

New Drug - Pill “A” is Compared to *Something Else*

- itself in a different dose, or
- a drug with a known effect, and/or
- a placebo or “dummy pill” that has no expected effect

Randomized

Double-Blind

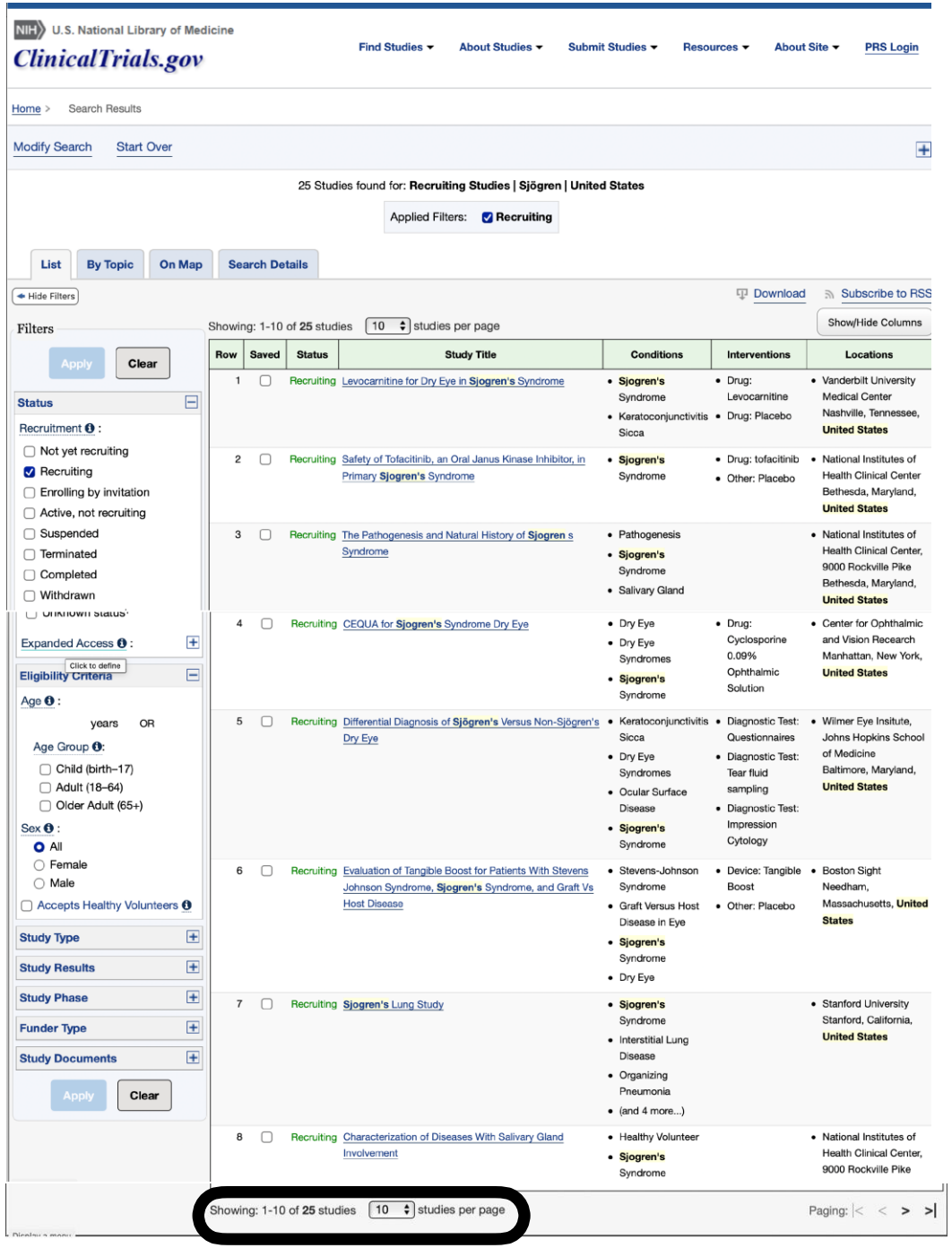
Double-Blind

- the patient is blinded to their treatment group assignment to lessen the chance that a preconception will affect outcome

- the clinician investigator is unaware of what the patient is getting to minimize bias which might influence results

Other Clinical Trial Jargon

- Dose finding
- Single or double-blind
- Placebo controlled *crossover* Open label
- Open label
- Long term follow-up - usually open label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Home > Search Results
Modify Search
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25 Studies found for: Recruiting Studies | Sjögren | United States
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List
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Download
Subscribe to RSS
Show/Hide Columns
Filters
Apply
Clear
Status
Recruitment :
Not yet recruiting
Recruiting
Enrolling by invitation
Active, not recruiting
Suspended
Terminated
Completed
Withdrawn
Expanded Access :
Eligibility Criteria
Age :
years OR
Age Group :
Child (birth–17)
Adult (18–64)
Older Adult (65+)
Sex :
All
Female
Male
Accepts Healthy Volunteers
Study Type
Study Results
Study Phase
Funder Type
Study Documents
Showing: 1-10 of 25 studies 10 studies per page
Row | Saved | Status | Study Title | Conditions | Interventions | Locations
1 Recruiting Levocarnitine for Dry Eye in Sjogren's Syndrome | Sjogren's Syndrome; Keratoconjunctivitis Sicca | Drug: Levocarnitine; Drug: Placebo | Vanderbilt University Medical Center Nashville, Tennessee, United States
2 Recruiting Safety of Tofacitinib, an Oral Janus Kinase Inhibitor, in Primary Sjogren's Syndrome | Sjogren's Syndrome | Drug: tofacitinib; Other: Placebo | National Institutes of Health Clinical Center Bethesda, Maryland, United States
3 Recruiting The Pathogenesis and Natural History of Sjogren s Syndrome | Pathogenesis; Sjogren's Syndrome; Salivary Gland | National Institutes of Health Clinical Center, 9000 Rockville Pike Bethesda, Maryland, United States
4 Recruiting CEQUA for Sjogren's Syndrome Dry Eye | Dry Eye; Dry Eye Syndromes; Sjogren's Syndrome | Drug: Cyclosporine 0.09% Ophthalmic Solution | Center for Ophthalmic and Vision Recearch Manhattan, New York, United States
5 Recruiting Differential Diagnosis of Sjögren's Versus Non-Sjögren's Dry Eye | Keratoconjunctivitis Sicca; Dry Eye Syndromes; Ocular Surface Disease; Sjogren's Syndrome | Diagnostic Test: Questionnaires; Diagnostic Test: Tear fluid sampling; Diagnostic Test: Impression Cytology | Wilmer Eye Insitute, Johns Hopkins School of Medicine Baltimore, Maryland, United States
6 Recruiting Evaluation of Tangible Boost for Patients With Stevens Johnson Syndrome, Sjogren's Syndrome, and Graft Vs Host Disease | Stevens-Johnson Syndrome; Graft Versus Host Disease in Eye; Sjogren's Syndrome; Dry Eye | Device: Tangible Boost; Other: Placebo | Boston Sight Needham, Massachusetts, United States
7 Recruiting Sjogren's Lung Study | Sjogren's Syndrome; Interstitial Lung Disease; Organizing Pneumonia; (and 4 more...) | Stanford University Stanford, California, United States
8 Recruiting Characterization of Diseases With Salivary Gland Involvement | Healthy Volunteer; Sjogren's Syndrome | National Institutes of Health Clinical Center, 9000 Rockville Pike
Showing: 1-10 of 25 studies 10 studies per page
Paging: |< < > >|

NIH U.S. National Library of Medicine

ClinicalTrials.gov

Current Sjögren's Trials

Showing: 1-50 of **61** studies 50 studies per page

Getting Involved in Clinical Trials

- Why participate?
- How do I get started?
- Am I eligible?
- Is it safe?
- What happens at my visits?

Why Participate?

- to gain access to a promising treatment not available elsewhere
- to obtain care at no cost or receive treatments that would otherwise be unaffordable
- to gain a better understanding of your disease
- to feel empowered and gain a sense of control of your disease
- to be involved in the development of a new treatment to help you and others who have your illness
- to contribute to scientific and medical knowledge

Why Participate?

Frequently stated patient concerns

- “I don’t want to be a guinea pig”
- time commitment
- complicated science and complicated protocols
- uncertainty about getting the active treatment
- trust

Why Participate?

Frequently stated physician investigator concerns

What's the potential benefit for the patient?

- is the duration of the study sufficient to provide a meaningful result to the patient
- is there a stipend for the patient if the study requires travel and significant inconvenience
- what percentage of patients will get the active treatment
- is there an opportunity for a long term open label extension

How Do I Get Started?

- it may come up at a visit with your physician
- you may see an advertisement on line, in your newspaper or on local or national broadcast media
- you may seek opportunities on www.clinical trials.gov

Am I Eligible?

- clinical trials are performed according to a plan design called a protocol which is unique to each project

- protocols define eligibility criteria such as age, gender, duration of illness, prior therapies, other medications you may be taking

- eligibility criteria fall into 2 categories:
  - inclusion: clinical and laboratory characteristics of your illness
  - exclusion: co-existent illness, prior treatments, history of allergy, etc

Is it Safe?

There is a significant, layered, complex infrastructure specifically developed to assure safe conduct of clinical trials in the United States.

Is it Safe?

- physicians and their coordinators are trained in “good clinical practice” principles (GCPs) and coordinators are likely certified
- before conducting a study the site must have the protocol reviewed by an Institutional Review Board (IRB); which then requires regular reporting of the site
- an independent data safety monitoring board is designated by the study sponsor to review all adverse events with the power to stop the study
- FDA regulations and auditing authority
- The informed consent

Informed Consent

"A process by which a subject *voluntarily* confirms…willingness to participate in a particular trial, after having been *informed* of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is *documented* by means of a *written, signed and dated* informed consent form."

-International Conference on Harmonization - Good Clinical Practice

Elements of Informed Consent

1. Description of the clinical trial
2. Potential risks and discomforts
3. Potential benefits
4. Alternative treatments available
5. Confidentiality
6. Compensation and medical treatment in event of injury
7. Contact information at the investigative site
8. Voluntary nature of participation and the right to withdraw

Is it Safe?

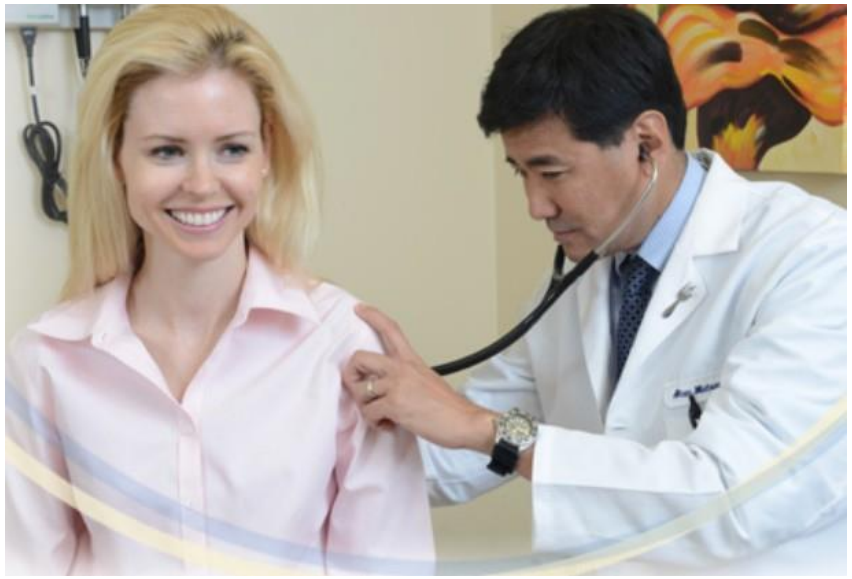
- has the drug been tested before or is it new
- has it been used in other diseases but is now being applied to your illness
- what is the safety of similar drugs in its class
- known risks should be spelled out in the informed consent

What Happens at My Visits?

- initially your clinical research coordinator will explain the nature of the program
- at a screening visit, the coordinator and investigator will provide you with the informed consent form, give you ample time to review it and answer any questions
- if all inclusion and exclusion criteria are met, randomization and treatment will begin at the baseline visit

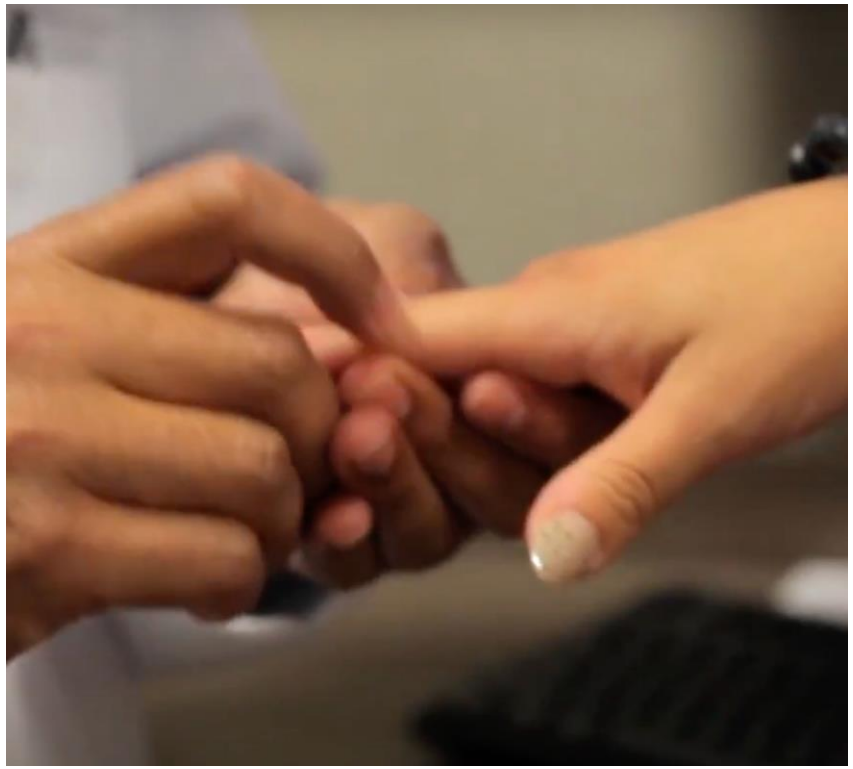
What Happens at My Visits?

- thereafter, the clinical research coordinator and investigator will closely monitor your progress at every visit
- you may be asked to fill out questionnaires to assess how you feel and determine your progress - your input is essential to this process
- the study team meticulously takes notes, records measurements and explains what is happening all along the way



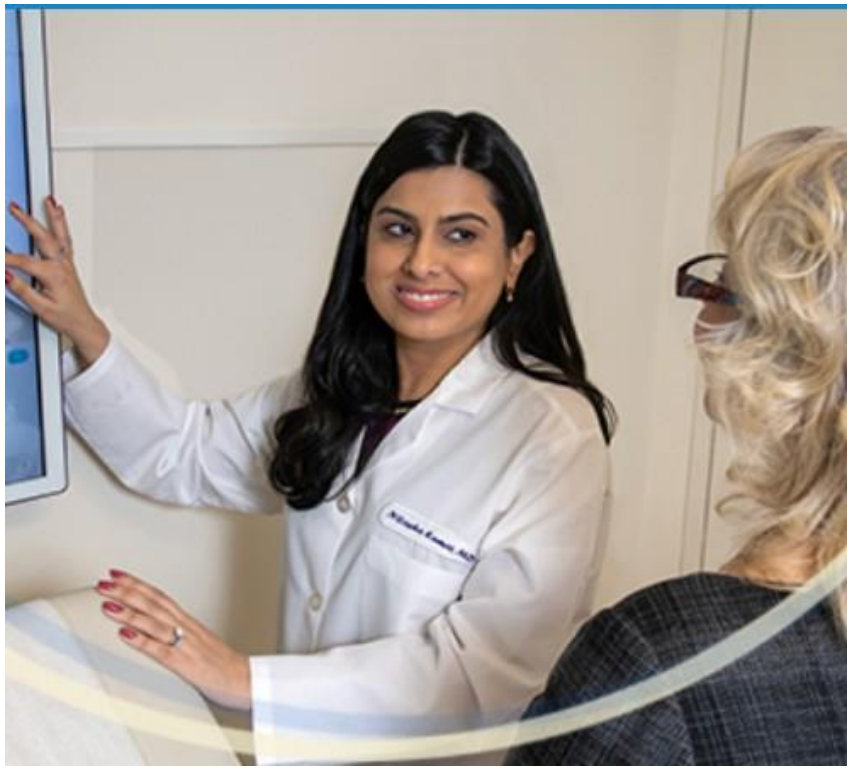
What Happens at My Visits?

- physical examinations will be performed at predetermined intervals
- testing will typically be required: blood work, x-rays, MRI's if part of the study design
- some studies in Sjogren's require measurements of tear or saliva production
- parotid ultrasound studies may required in others
- care will be at no cost to you



What Happens at My Visits?

- your safety is of paramount importance
- your compliance is critical to a good study outcome
- you may or may not notice improvement in the condition being treated
- some studies may have “open-label” extension periods and others “cross-over designs”



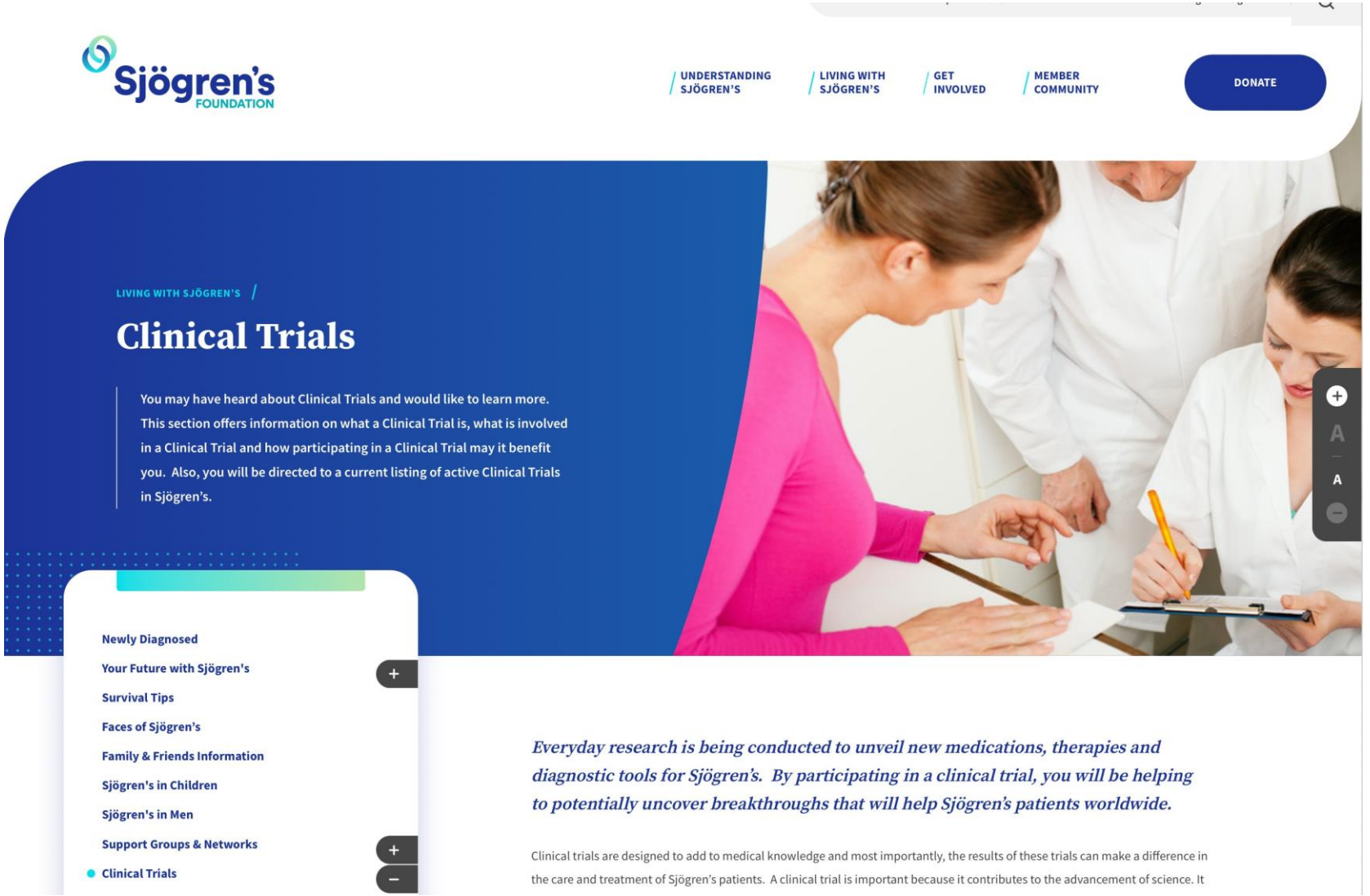
Trial Design in Sjögren's

Candidate Selection

- primary Sjögren's vs secondary
- early vs late disease
- specific symptom-focused
  - dry eye
  - dry mouth
  - fatigue
  - arthritis
- systemic disease-focused
  - e.g. hematologic, lung or kidney involvement
  - quality of life
  - outcome measures (ESSPRI, ESSDAI, SSI, PROFAD)

Trial Design in Sjögren's
Outcome Measures

- PROFAD - Profile of Fatigue and Discomfort
- SSI - Sicca Symptoms Inventory
- ESSPRI- EULAR Sjögren's Syndrome Patients Reported Index
- ESSDAI - EULAR Sjögren's Syndrome Disease Activity Index


Sjögren's FOUNDATION
UNDERSTANDING SJÖGREN'S
LIVING WITH SJÖGREN'S
GET INVOLVED
MEMBER COMMUNITY
DONATE
LIVING WITH SJÖGREN'S /
Clinical Trials
You may have heard about Clinical Trials and would like to learn more. This section offers information on what a Clinical Trial is, what is involved in a Clinical Trial and how participating in a Clinical Trial may it benefit you. Also, you will be directed to a current listing of active Clinical Trials in Sjögren's.
Newly Diagnosed
Your Future with Sjögren's
Survival Tips
Faces of Sjögren's
Family & Friends Information
Sjögren's in Children
Sjögren's in Men
Support Groups & Networks
Clinical Trials
Everyday research is being conducted to unveil new medications, therapies and diagnostic tools for Sjögren's. By participating in a clinical trial, you will be helping to potentially uncover breakthroughs that will help Sjögren's patients worldwide.
Clinical trials are designed to add to medical knowledge and most importantly, the results of these trials can make a difference in the care and treatment of Sjögren's patients. A clinical trial is important because it contributes to the advancement of science. It

Clinical Trials and This Practicing Rheumatologist

by Herbert S. Baraf, MD, FACP, MACR
Arthritis and Rheumatism Associates, P.C., Wheaton, Maryland

With a career spanning almost forty years, it's time for me to look back upon those things that have given me professional satisfaction and draw advice from those experiences to pass on to my younger colleagues.

I have worked in a private practice setting since completing a rheumatic disease fellowship at Duke University in 1978. Duke, a premier center for basic and clinical research for decades, was a great place to be. As a fellow, however, my goal was to take care of patients, eventually in a community practice setting, and not to

Continued on page 6 ▼

“From a humble start… I have participated in the struggle to make my patients’ lives better one at a time. By being part of the clinical trials process, a clinician’s reach extends beyond the lives of their patients to the lives of all patients with rheumatic disease. ”

–personal statement In Sjogren’s Quarterly Summer 2017