

# Electronic Collection of ClinRO

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# Electronic Collection of PRO

Comparative study of electronic vs. paper VAS ratings:  
a randomized, crossover trial using healthy volunteers

Robert N. Jamison<sup>a,b,\*</sup>, Richard H. Gracely<sup>c</sup>, Stephen A. Raymond<sup>d</sup>, Jonathan G. Levine<sup>e</sup>,  
Barbara Marino<sup>d</sup>, Timothy J. Herrmann<sup>a</sup>, Margaret Daly<sup>a</sup>, David Fram<sup>e</sup>, Nathaniel P. Katz<sup>a</sup>

## Patient compliance with paper and electronic diaries

Arthur A. Stone, Ph.D.<sup>a,\*</sup>, Saul Shiffman, Ph.D.<sup>b,c</sup>,  
Joseph E. Schwartz, Ph.D.<sup>a</sup>, Joan E. Broderick, Ph.D.<sup>a</sup>,  
Michael R. Hufford, Ph.D.<sup>c</sup>

## Equivalence of Electronic and Paper-and-Pencil Administration of Patient-Reported Outcome Measures: A Meta-Analytic Review

Chad J. Gwaltney, PhD,<sup>1,5</sup> Alan L. Shields, PhD,<sup>2,5</sup> Saul Shiffman, PhD<sup>3,4,5</sup>

## Paper or Plastic? Data Equivalence in Paper and Electronic Diaries

Amie S. Green  
New York University

Eshkol Rafaeli  
Barnard College, Columbia University

Niall Bolger and Patrick E. Shrout  
New York University

Harry T. Reis  
University of Rochester



**Proving the  
eDiary Dividend**

Sara McKenzie, Jean Paty, Donna Grogan, Molly Rosano, Lisa Curry,  
Ken Sciarappa, and Michael Hufford

## COMMENTS

Paper and Electronic Diaries: Too Early for Conclusions on  
Compliance Rates and Their Effects—Comment on Green, Rafaeli,  
Bolger, Shrout, and Reis (2006)

Joan E. Broderick and Arthur A. Stone  
Stony Brook University

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# The PRO Guidance

## Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims

*Additional copies are available from:*

*Office of Communications, Division of Drug Information  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Ave., Bldg. 51, rm. 2201  
Silver Spring, MD 20993-0002  
Tel: 301-796-3400; Fax: 301-847-5714; E-mail: [druginfo@fda.hhs.gov](mailto:druginfo@fda.hhs.gov)  
<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>*

*or*

*Office of Communication, Outreach, and Development, HFM-40  
Center for Biologics Evaluation and Research  
Food and Drug Administration  
1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448  
Tel: 800-833-4709 or 301-827-1800; E-mail: [ocod@fda.hhs.gov](mailto:ocod@fda.hhs.gov)  
<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm>*

*or*

*Office of Communication, Education, and Radiation Programs  
Division of Small Manufacturers, International, and Consumer Assistance, HFZ-220  
Center for Devices and Radiological Health  
Food and Drug Administration  
1350 Piccard Drive, Rockville, MD 20850-4307  
DSMICA E-mail: [dsmica@cdrh.fda.gov](mailto:dsmica@cdrh.fda.gov)  
DSMICA Fax: 301-443-8818  
(Tel) Manufacturers Assistance: 800-635-2041 or 301-443-6597  
(Tel) International Staff: 301-827-3993  
<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm>*

**U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Drug Evaluation and Research (CDER)  
Center for Biologics Evaluation and Research (CBER)  
Center for Devices and Radiological Health (CDRH)**

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Clinical/Medical**

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# PRO Guidance: Page 16

We recommend that the user manual provided by a developer during the PRO instrument development process specify how to incorporate the instrument into a clinical trial in a way that **minimizes administrator burden, patient burden, missing data, and poor data quality.** The user manual should explain to investigators and interviewers critical principles of PRO administration.

## Minimize:

- **Administrator burden**
- **Patient burden**
- **Missing data**
- **Poor data quality.**

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# Administrator Burden



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# Organizing Clinician Questionnaires

## Visits and Questionnaires

Select a Visit

SitePad™



- Select a Visit from the list, then Choose the Questionnaire Type.

Visits	Status
Screening Visit	Completed
Baseline Visit	In Progress
Visit 3	Available
Visit 4	Available
Visit 5	Available
Visit 6	Available
Early Termination	Available

Subject: 0000001 (HLM)

▶ Subject Questionnaires (2)

▶ Site Questionnaires (3)

◀ Select Another Subject

🏠 Home

Site Questionnaires

SitePad™



- Select a Questionnaire, then Tap Start Questionnaire.

Questionnaire	Status
Disease Activity	Available
HAM-D	Available
Joint Assessment	Available

Subject: 0000001 (HLM)  
Visit: Baseline Visit

▶ Start Questionnaire

◀ Select Another Visit

🏠 Home

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# Missing Data

## THE HAMILTON RATING SCALE FOR DEPRESSION

(to be administered by a health care professional)

3

### 3. SUICIDE

0= Absent

1= Feels life is not worth living

2= Wishes he were dead or any thoughts of possible death to self

3= Suicidal ideas or gesture

4= Attempts at suicide (any serious attempt rates 4)

### 4. INSOMNIA EARLY

0= No difficulty falling asleep

1= Complains of occasional difficulty falling asleep—i.e., more than 1/2 hour

2= Complains of nightly difficulty falling asleep

### 5. INSOMNIA MIDDLE

0= No difficulty

1= Patient complains of being restless and disturbed during the night

2= Waking during the night—any getting out of bed rates 2 (except for purposes of voiding)

# No Missing Responses

CBI Conference

Subject: 0000001 (HLM)

HAM-D

eClinRO[T] V1.01 Site: 0001

Logged In: SWells

1/5



13:47

Depressed Mood (sadness, hopelessness, helplessness, worthlessness)

- 0=Absent
- 1=These feeling states indicated only on questioning
- 2=These feeling states spontaneously reported verbally
- 3=Communicates feeling states nonverbally (i.e. facial expression, posture, voice, tendency to weep)
- 4=Reports virtually only these feeling states in spontaneous verbal communication

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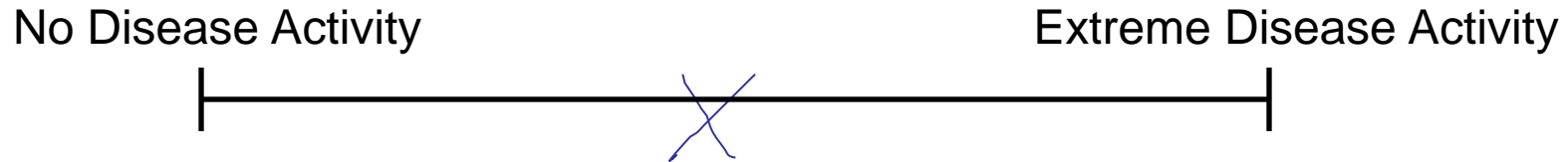
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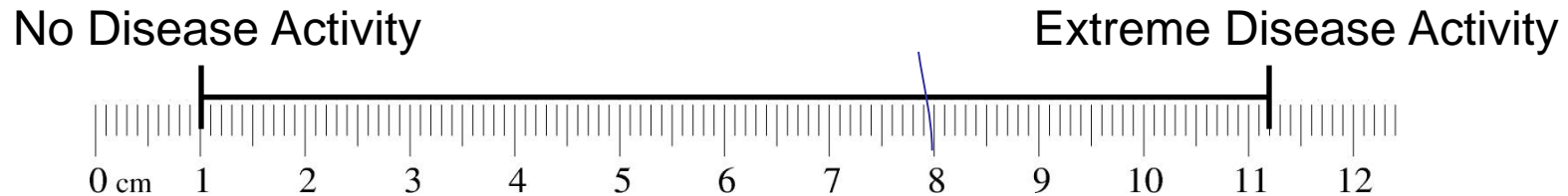
# Poor Data Quality

How would you assess the subject's current disease activity?

Use a vertical stroke. 



OR



**Result: 79??**

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# Electronic VAS

How would you assess the subject's current disease activity?



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# PRO Guidance: Timely Entry of Data

...FDA plans to review the protocol to determine what measures are taken to ensure that patients make entries according to the study design and not, for example, just before a clinic visit when their reports will be collected.



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# New DRAFT Guidance

## Guidance for Industry Electronic Source Documentation in Clinical Investigations

### *DRAFT GUIDANCE*

**This guidance document is being distributed for comment purposes only.**

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact Leonard Sacks at 301-796-8502.

U.S. Department of Health and Human Services  
Food and Drug Administration  
Office of the Commissioner

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# Encouragement of use of eSource

## INTRODUCTION

This guidance is intended to promote the capture of source data in electronic form, which will help to:

- Eliminate unnecessary duplication of data,
- Reduce the opportunity for transcription errors,
- Promote the real-time entry of electronic source data during subject visits, and
- Ensure the accuracy and completeness of data.

*“FDA recommends that clinical data be entered electronically by study site personnel at the time of the subject visit to avoid transcription from unnecessary paper records.”*

*(page 7)*

# Complex ClinRO Example

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## Quantitative joint assessment in rheumatoid arthritis

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T. Sokka<sup>1,2</sup>, T. Pincus<sup>1</sup>

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Please address correspondence to: Tuulikki Sokka, MD, PhD, Vanderbilt University School of Medicine, 203 Oxford House, Box 5, Nashville, TN 37232-4500, USA.

E-mail: [t.sokka@vanderbilt.edu](mailto:t.sokka@vanderbilt.edu)

*Clin Exp Rheumatol* 2005; 23 (Suppl. 39): S58-S62.

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**Key words:** Joint assessment, rheumatoid arthritis.

### ABSTRACT

*A count of swollen and tender joints is the most specific quantitative clinical measure to assess and monitor the status of patients with rheumatoid arthritis. Many methods have been described to quantitate joint abnormalities, including scoring various numbers of joints (with or without grading of abnormality) for different types of abnormalities, including swelling, tenderness, pain on motion, limited motion, and deformity. This article reviews selected methods for the performance of joint counts, with discussion of their advantages and limitations in the assessment of patients with rheumatoid arthritis.*

### Description of abnormalities in a quantitative joint evaluation

Abnormalities assessed in formal joint counts include swelling, tenderness, pain on motion, limited motion, and deformity. Joint swelling is defined as soft tissue swelling of the joint which is detectable along the joint margins. A synovial effusion invariably means that the joint is swollen. Fluctuance is a characteristic feature of swollen joints; neither bony enlargement nor deformity of the joint constitutes "swelling". Joint swelling may influence the range of joint motion, which can be useful to recognize the presence of swelling. Examples include decreased dorsiflexion

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# Joint Assessment (Paper)

Joints	Right Side		Left Side	
	Pain/Tenderness	Swelling	Pain/Tenderness	Swelling
	Yes/No	Yes/No	Yes/No	Yes/No
Temporomandibular				
Sternoclavicular				
Acromioclavicular				
Shoulder				
Elbow				
Wrist				
CMC				
MCP 1				
MCP 2				
MCP 3				
MCP 4				
MCP 5				
PIP 1				
PIP 2				
PIP 3				
PIP 4				
PIP 5				
DIP 2				
DIP 3				
DIP 4				
DIP 5				



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# Joint Assessment (Electronic)

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Subject: 0000001 (HLM)

Joint Assessment

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1/7



13:48

This questionnaire requires that 78 of the subject's joints be clinically assessed for the presence of pain/tenderness and the presence of swelling. The assessments will be recorded on this SitePad.

Please indicate below either that you will perform the assessments and record your own findings on the SitePad or that you will perform the assessments and a proxy recorder (such as a site coordinator) will record your findings on the SitePad.

- 
- I will both assess the joints and record my own assessments
- I will assess the joints and have a proxy recorder record my assessments on the SitePad

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# Joint Assessment (Electronic)

CBI Conference

Subject: 0000001 (HLM)

Joint Assessment

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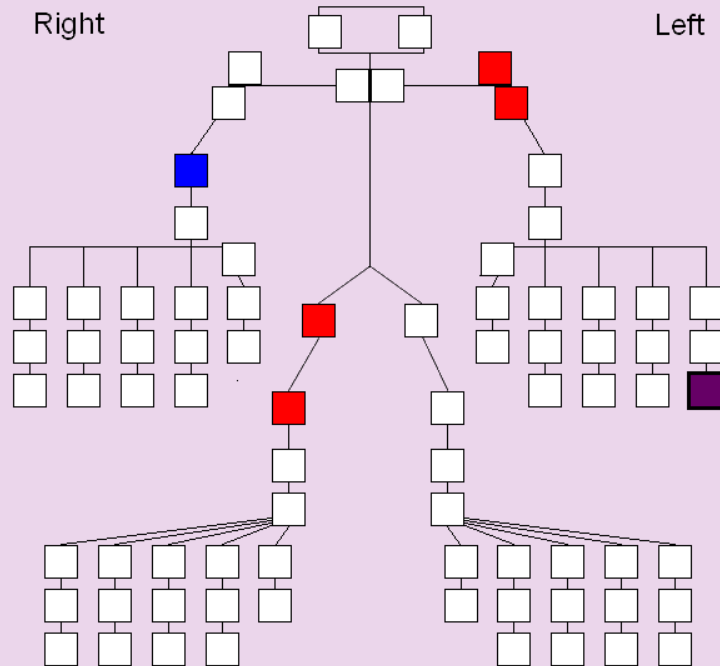
Logged In: SWells

4/7



13:51

Right



Left

## Left Hand Fifth Distal Interphalangeal

Please indicate the joints that have symptoms or are not assessable by tapping on the joint and tapping on the appropriate label below

- Pain/Tenderness Only
- Swelling Only
- Pain/Tenderness and Swelling (Both Symptoms)
- Temporarily not assessable
- Permanently not assessable
- Clear the Current Joint Label

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# Joint Assessment (Electronic)

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Subject: 0000001 (HLM)

Joint Assessment

eClinRO[T] V1.01 Site: 0001

Logged In: SWells

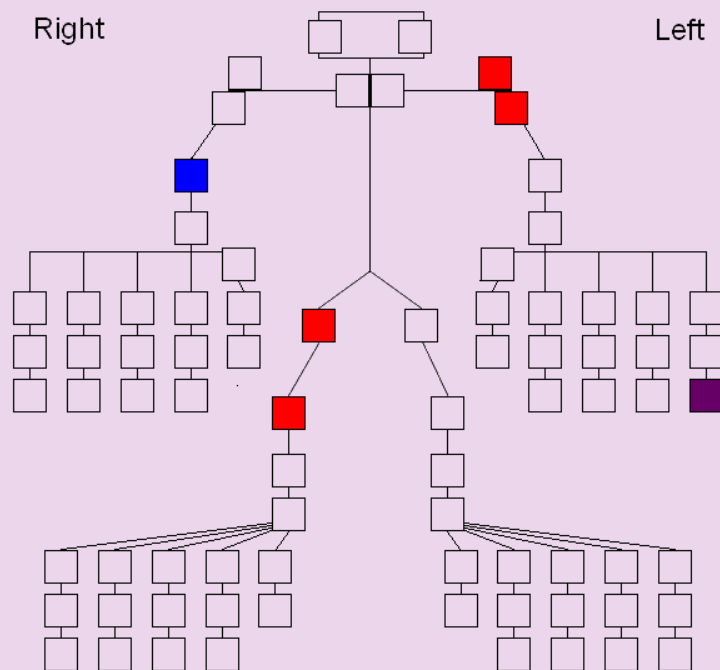
6/7



13:52

Right

Left



- |  |                      |  |                            |
|--|----------------------|--|----------------------------|
|  | Pain/Tenderness only |  | Asymptomatic               |
|  | Swelling Only        |  | Temporarily Not Assessable |
|  | Both Symptoms        |  | Permanently Not Assessable |

Please confirm that the display accurately represents the subject's symptomatic and asymptomatic joints, as well as the joints that could not be assessed.

To change the label of any joint, tap the Back button twice to return to the symptom screen. Then, change or clear appropriate joint labels on that screen.

- Confirm that all joints have been correctly labeled with the appropriate symptom(s) label, or labeled as asymptomatic or not assessable

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# Joint Assessment (Electronic)

CBI Conference

Subject: 0000001 (HLM)

Joint Assessment

eClinRO[T] V1.01 Site: 0001

Logged In: SWells



13:53

I have entered, cross-checked, and hereby confirm the preceding data.

**Signature:** Sarah Wells

A white rectangular box containing a handwritten signature in black ink that reads "Sarah Wells".



Clear Signature

**Back**

**Finish**



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# Feedback from Investigators



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# Summary

**Ease of Administration**

**+ Reduced Missing Data**

**+ Better Data Quality**

**+ FDA Support**

**+ Ease of Use**

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# eClinRO

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