BIOCLINICA®
SEE MORE CLEARLY

bioclinica.com

Samumed SM04690-OA-06
Version 1.0

HOLOGIC DXA Procedure Manual

Version 7.0_20180815

INTRODUCTION

ADDITIONAL SECTIONS

LIST OF FIGURES

LIST OF FLOWCHARTS

List of Terms and Abbreviations

Abbreviation/Term/Acronym	Definition
Baseline (visit)	The first clinical trial visit to which all subsequent visits are compared
BMD	Bone Mineral Density
CRF	Case Report Form
DCF	Data Clarification Form (Query)
DXA	Dual X-ray Absorptiometry
Follow-up visit	All visits after Baseline
GCP	Good Clinical Practice
DXA Facility	Facility where DXA images are acquired
Inv Site	Investigator Site
IQC	Instrument Quality Control
PTQ	Pre-Trial Questionnaire
QC	Quality Control
QRG	Quick Reference Guide
ROI	Region of Interest
TF	Transmittal Form
UD	Ultra-distal

1 INTRODUCTION TO BIOCLINICA

Bioclinica

Bioclinica works with sponsors who conduct clinical trials that require medical imaging, biochemical marker and clinical research services. Bioclinica's team of scientists, radiologists, operations and software specialists work closely with sponsors, investigators, imaging technologists and monitors to ensure that study objectives and quality standards are met throughout each clinical trial.

Imaging

Bioclinica's medical imaging services are designed to reduce the variability inherent to multisite, international clinical trials, thereby maximizing the accuracy of efficacy and safety imaging assessments. Bioclinica helps design study procedures that accommodate the various DXA machine types that exist across sites in a clinical trial, optimizing the consistency and quality of the images produced and the accuracy and precision of the image analyses performed by Bioclinica's specialized in-house radiologists and technologists.

Why Bioclinica works closely with DXA Technologists

The quality of work of DXA Technologists directly affects a sponsor's ability to determine the effectiveness and safety of a study drug. Variability of BMD measurement increases due to acquisition issues such as differences in subject positioning, changes in scan mode, subject movement in the scan or the presence of an external artifact. The purpose of this manual is to standardize the procedures used by all DXA Facilities participating in this clinical trial; the issues addressed in this manual may differ slightly from what each DXA Facility is accustomed to. Consistency by DXA Technologists in subject preparation, positioning, scan mode, scan acquisition and analysis at both baseline and follow-up visits is the key to obtaining reliable bone density data.

2 PROCEDURE MANUAL

2.1 Purpose of the Procedure Manual

The purpose of this manual is to standardize the DXA scanning procedures among the DXA Facilities participating in studies for which DXA data is managed by Bioclinica. Success will depend on several factors, including the qualifications and dedication of the DXA technologists, clear understanding of the study requirements and good communication between Bioclinica, the Investigator Sites, the DXA Facilities and the Sponsor.

This manual is intended to build upon, not replace, the Operator's Manual for each DXA machine. It is expected that all staff that perform scan acquisition have expert knowledge of their DXA machine. The material in this manual should be read and understood prior to scanning study subjects.

2.2 Procedure Manual Content

This manual contains instructions for some procedures that are not necessary for all studies. Users should refer to the relevant sections as needed and may disregard sections that do not apply to a particular study. All study-specific DXA information is provided to the DXA Facilities by Bioclinica along with this training manual.

2.3 DXA Scanners in this Procedure Manual

This manual contains instructions specific to Hologic scanner models running on Windows software. It is important for DXA Technologists to know how to use their DXA equipment to ensure all instructions are understood.

3 STUDY ROLES AND RESPONSIBILITIES

Bioclinica

- Training all DXA Technologists who will be scanning study subjects.
- Collecting and performing quality control and analysis of Instrument Quality Control (IQC) data from each DXA scanner being used in a study.
- Collecting and performing quality control and analysis of images collected for study subjects.
- The following responsibilities apply for some studies, refer to study-specific materials for details:
    - Providing results of central image analysis at the screening visit to the Investigator Site and the Sponsor.
    - Reporting subjects with excessive bone change to the Sponsor and the Principal Investigator per Sponsor's requirements.
    - Providing interim DXA analysis results to the Sponsor per the Sponsor's requirements.
- Providing final DXA analysis results to the Sponsor for their regulatory submission of study results.

DXA Facility

- Completing Bioclinica's study start-up procedures.
- Acquiring DXA images in accordance with the guidelines detailed in this manual and in study-specific materials.
- Performing daily and monthly Instrument Quality Control (IQC) procedures.
- Submitting DXA images to Bioclinica in an appropriate and timely manner; refer to study-specific materials for details.
- Performing cross calibration scans (for some studies).
- Completing end of study/interim analysis procedures as detailed in this manual.
- Securely backing up study data in the event of a computer failure.

Study Coordinator at the Investigator Site

The Study Coordinator serves as a liaison to help resolve issues between Bioclinica and the DXA Facility.

Monitor

The Monitor helps to resolve issues that cannot be resolved between Bioclinica and the Investigator Sites; the Monitor is typically only involved when there is no assigned Study Coordinator at the Investigator Site.

4 GOOD CLINICAL PRACTICE & ARCHIVING

4.1 Good Clinical Practice

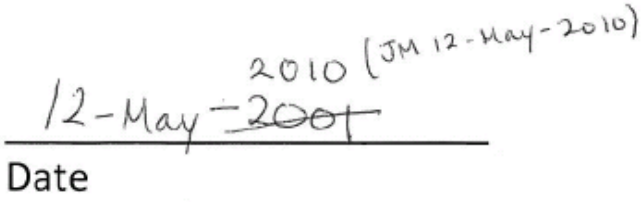
Good Clinical Practice (GCP) is a universal standard that outlines the quality processes required in the conduct of clinical trials. Regulatory agencies determine the reliability of clinical data based on adherence to this standard.

Studies that adhere to GCP standards:

- Are well designed
- Are conducted in accordance with the protocol and outlined procedures
- Follow proper data collection, analysis and documentation procedures
- Ensure safety and privacy of study subjects

GCP standards relating to DXA:

- Maintain study protocol and subject confidentiality.
- Use the forms and electronic media labels provided by Bioclinica.
- Accurately complete all forms.
- Write clearly and legibly.
- Draw a single line through any mistakes so the original entry is still readable. Initial and date all corrections.



- DO NOT use post-it notes, pencil, or white-out.
- Make comments on Transmittal Forms to convey information or clarify an issue.
- Always include the study site number and protocol name in all correspondence and phone contact regarding a protocol-specific issue.
- Always include the DXA Machine Scanner ID number in correspondence and phone contact regarding IQC; IQC is not protocol specific--it is tracked per DXA Machine.
- Keep copies of all forms and correspondence.

If Bioclinica identifies a GCP violation, a Data Clarification Form will be sent to the DXA Facility to identify and aid in the correct documentation of any errors to ensure quality data. The goal is to practice good science and to work as a team.

DXA Facilities should contact Bioclinica with any questions regarding GCP.

4.2 Archiving DXA Images and Documentation

At any time throughout a study, or after a study has closed, Bioclinica may identify missing data or discrepancies in the provided data that require clarification. To ensure that the data are retrievable, please follow these guidelines:

- Keep copies of all study related forms and correspondence in an organized binder.
- Copy all subject scans to secure electronic media for long term storage at the DXA Facility. Secure media is defined as a CD, optical disk or network directory backed up on tape.
- Maintain study related materials in compliance with Sponsor requirements and in an environment that is safe, secure and accessible.

Sponsors will provide instructions to Principal Investigators at study start on how to retain records after a study is complete.

5 DXA FACILITY STUDY START-UP

Prior to scanning any subjects for a study, a DXA Facility must be authorized by Bioclinica for the particular study. There are four steps to DXA Facility Study Start-up:

1) Submission of a Pre-Trial Questionnaire listing all involved DXA Technologist(s) at the DXA Facility
2) Completion of study-specific training by at least one DXA Technologist who will be acquiring scans for the study
3) Submission of acceptable Baseline IQC data
4) Receipt of an Authorization letter from Bioclinica listing the DXA Technologist(s) and scanner(s) that may begin scanning study subjects

Details about these steps are outlined below.

5.1 Pre-Trial Questionnaire

The Pre-Trial Questionnaire form will be provided to the Investigator Sites by Bioclinica. The Investigator Site or the DXA Facility must complete this form including all DXA Technologists per DXA Facility and return the form to Bioclinica.

- Technologists must be included on the study specific Pre-Trial Questionnaire for each Bioclinica study they participate in, even if they have completed one or more Pre-Trial Questionnaires for Bioclinica studies in the past.
- Upon approval of the DXA Pre-Trial Questionnaire, Bioclinica will provide:
  - The DXA Procedure Manual (this manual)
  - Materials for DXA training
  - Data submission materials (forms, labels, airway bills)
- Changes in site personnel, contact information or DXA machines are to be documented on a new PTQ and submitted to Bioclinica.

5.2 DXA Technologist Training

At least one technologist must attend a study-specific Bioclinica training. Bioclinica will schedule these trainings prior to the first subject visit. DXA training may be remote (by phone), centralized, on-site or web-based; refer to study-specific materials for details. It may be acceptable for a DXA Technologist at the site who has completed the study-specific Bioclinica training to train other DXA Technologists. If your site has previously worked with Bioclinica, some requirements may be waived per sponsor approval. Each site and DXA technologist is assessed individually.

- Upon completion of remote (by phone) training, each technologist must sign the completed DXA Training Sign-Off form and submit to Bioclinica.
- For centralized and on-site trainings, the Bioclinica trainer will ensure all participants sign a DXA Training Sign-Off form.
- For web-based training each technologist must print and file their Training Certificate.
- For DXA Technologists trained by a previously trained DXA Technologist at the site, send a completed DXA Training Sign-Off form to Bioclinica. A blank DXA Training Sign-Off form is located in the DXA Study Binder.

5.3 Submission of Baseline IQC Data

Prior to scanning study subjects, a DXA Facility must complete the Baseline IQC requirements (instructions can be found starting on page I-5) and send the appropriate data and forms to Bioclinica:

1) Two reports of analyzed spine phantom scans
2) Spine Phantom database file

Submission of Baseline IQC is not required if a DXA machine is currently being monitored by Bioclinica and the IQC is current.

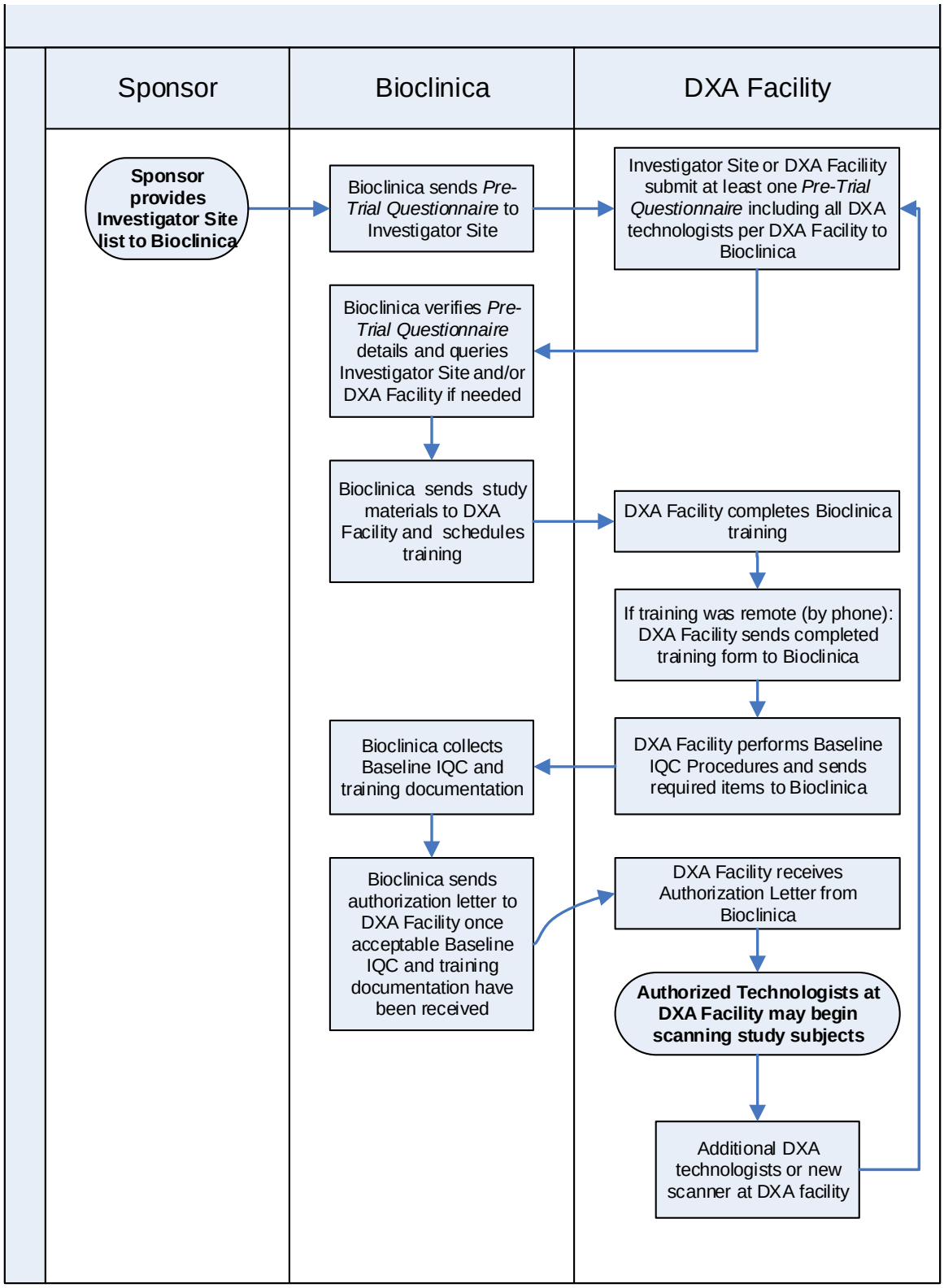
5.4 DXA Facility Authorization

Once Bioclinica verifies:

1) Receipt of completed Pre-Trial Questionnaire
2) Proper documentation of at least one DXA Technologist having been trained at a DXA Facility
3) Submission of acceptable Baseline IQC data

Bioclinica will send the DXA Facility an Authorization letter indicating that the DXA Facility may begin scanning study subjects and collecting study data.

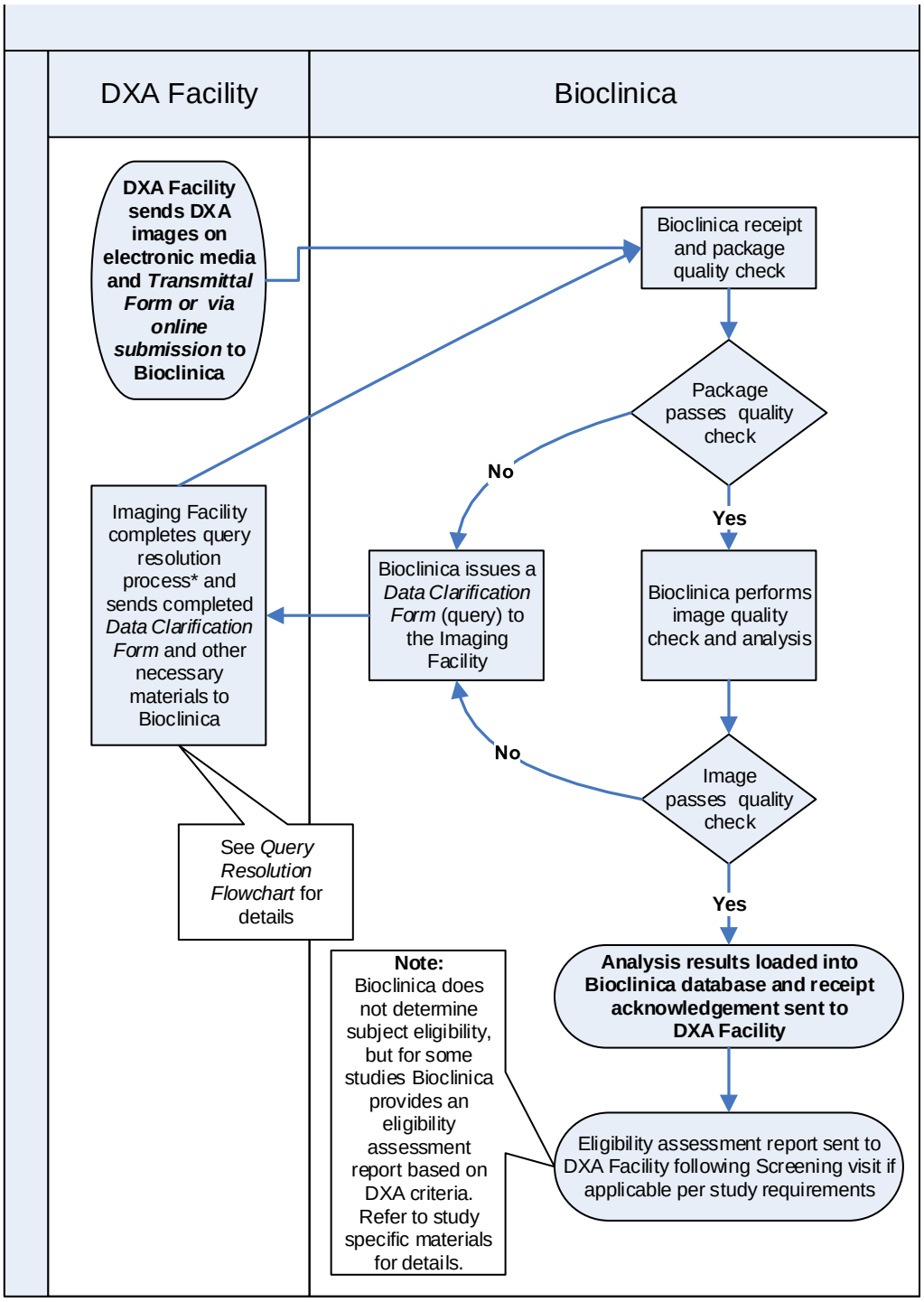
Flowchart 5-1: DXA Facility Study Start-up Procedures



6 STANDARD STUDY DXA DATA FLOW

The flowchart below outlines the standard flow of data between DXA Facilities and Bioclinica.

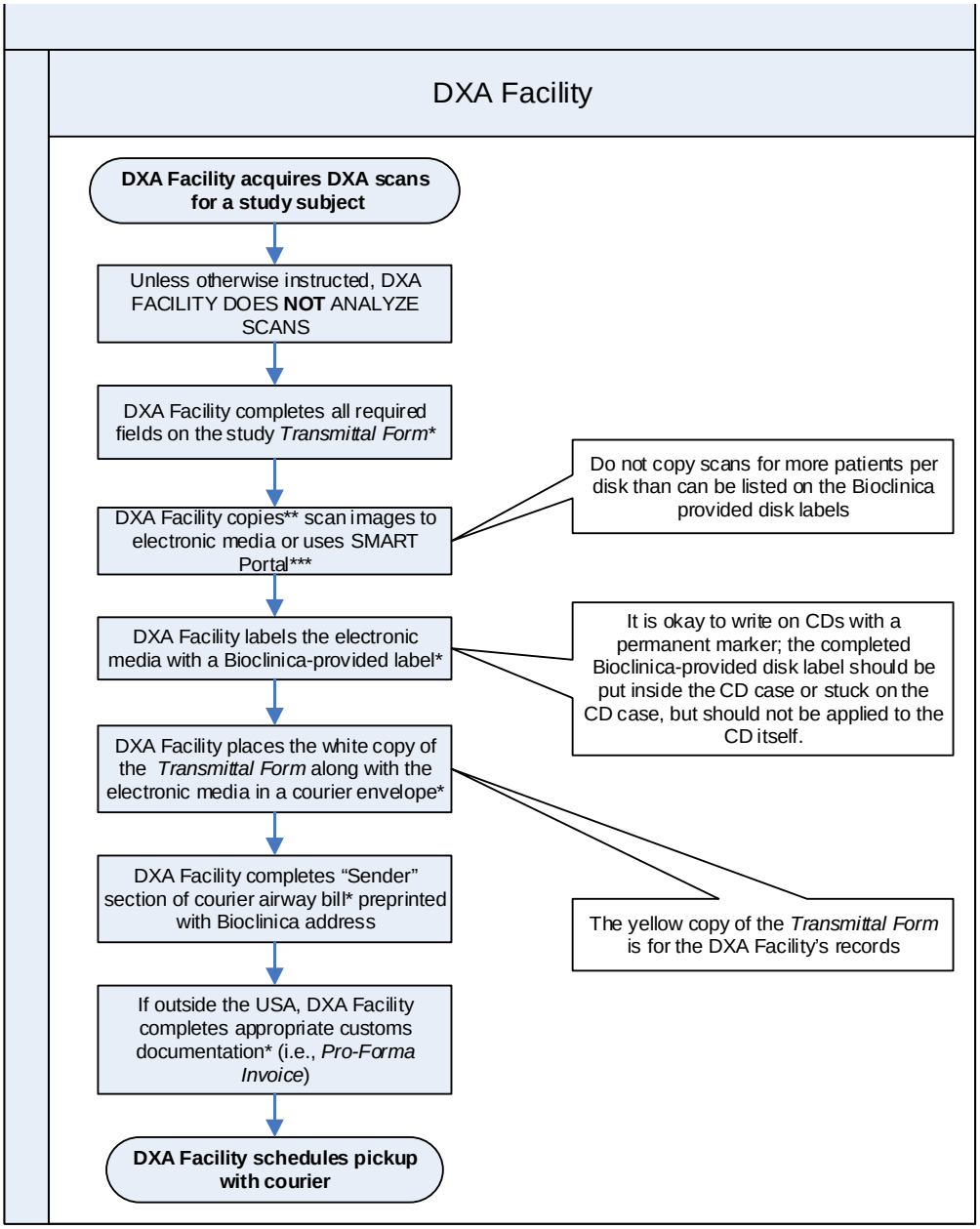
Flowchart 6-1: Standard Study DXA Data Flow



* See page 16 for details on the query resolution process.

7 DXA DATA SUBMISSION

Flowchart 7-1: DXA Data Packaging and Shipping to Bioclinica



***Where to acquire supplies (please find Supply Order Form in Study Binder):**

- Disks and CDs are provided by each DXA Facility or by other arrangements with the Sponsor for a particular study.
- Supplies to be ordered from Bioclinica (these are study-specific):
  - Transmittal Forms
  - Disk labels
  - Airway bills
- Supplies to be acquired from the courier:
  - Shipping envelopes
  - Customs documentation; see example on page 15.

** See page X-4 Appendix B for instructions on copying subject images to electronic media.

*** Please contact your Bioclinica Study Team to acquire your instructions and online password to utilize the SMART Portal. It is not necessary to send any hardcopy materials to Bioclinica when submitting data online. Patient data should be uploaded under the study code and site number, while IQC data should be entered under the DXA IQC Submission or IQCS-0003 study and scanner ID (unless alternate study specific procedures have been provided)

7.1 DXA Transmittal Form

Complete one transmittal form for each subject. Send the white copy to Bioclinica along with scans on electronic media in a courier envelope or use web based submission. The yellow copy is for the DXA Facility's records.

Figure 7-1: Example DXA Transmittal Form

Complete all fields provided in this section, which usually include: Site Number, Patient ID, Patient Initials, Date of Birth, Exam Date

Indicate visit by checking the appropriate box

Check as appropriate if data are submitted in response to a Bioclinica DCF for a repeat or bone loss repeat scan

Describe anything unusual about the scan here, especially internal artifacts

Record forearm length at baseline only (unless specified to do differently in protocol specific requirement)

If your site is using more than one machine, record scanner number here

Print the name of the DXA Technologist who acquired the scans and enter initials

This area is completed by Bioclinica upon receipt

Note: Transmittal Forms are customized for each protocol, the form shown here is a generic example

BIOCLINICA

<SPONSOR> Protocol <Protocol Number>
Transmittal Form for DXA

Site, Subject, and Visit Information — To be completed at study site or by DXA Technologist

Site Number: ☐☐☐☐ Subject ID Number: ☐☐☐☐☐☐☐☐ Subject Initials: ☐☐☐ (F M L)

Date of Birth: ☐☐ / ☐☐☐ / ☐☐☐☐ (D D / M M M / Y Y Y Y)

Randomization Number: ☐☐☐☐☐☐

Exam Date: ☐☐ / ☐☐☐ / 2 0 ☐☐ (D D / M M M / Y Y Y Y)

DXA Visit:
- ☐ [Visit #1 ID]
- ☐ [Visit #2 ID]
- ☐ [Visit #3 ID]
- ☐ [Early Termination]
- ☐ [Unscheduled]

☐ Repeat Scan (select visit)

☐ Bone Loss Repeat Scan (select visit)

DXA Scan Information — To be completed prior to submission to BioClinica

DXA Scan	Scan Filename	Comments
Spine		
Femur		
Whole Body		
Forearm		Forearm Length*:_____cm *Only recorded at baseline
VFA		

Record scan filenames of scans submitted, must match filenames of scans sent on disk

DXA Scanner Information

If your site is using more than one DXA machine for this study, please indicate the DXA machine serial number used for this subject, as displayed on a DXA analysis printout, here: _____

Printed Name of DXA Technologist Acquiring Scans: _____ Initials of DXA Technologist Acquiring Scans: ☐☐☐ (F M L)

Data Shipment MUST include: Completed DXA Transmittal Form and correctly labeled transfer media containing measurements listed.
Distribution: File YELLOW page at study site. Send (Original) White page to BioClinica

Comments

Use this area for additional comments

Do not write below this line. For BioClinica use only

Data Receipt: BioClinica Study Code <Study Code>

(BioClinica Stamp with Date and Initials)

Final

BioClinica Tracking Number: 9 9 9 9 0 1 Y Y Y Y M M D D ☐

S4-FOR-0005-V4.0 CONFIDENTIAL Page 1 of 1

7.2 Customs Documentation

DXA Facilities outside the United States shipping data to Bioclinica who are not using web based submission will need to complete appropriate customs documentation available from the courier company. The Pro-Forma Invoice below is an example of the types of information often required.

Figure 7-2: Example Customs Documentation, Pro-Forma Invoice

Commercial Invoice

Date Bill of Lading/Air Waybill No. Invoice Number Purchase Order Number. Terms of Sale (Incoterm) Reason for Export	**SHIPPER** Tax/VAT No. Contact Name Company Name Company Address City State/Province Postal Code Country Telephone No. Email ID
SHIP TO Tax/VAT No. Contact Name Company Name Bioclinica Company Address City Portland State/Province Oregon Postal Code Country USA Telephone No. 1-503-528-7800 Email ID	**SOLD TO** Tax/VAT No. Contact Name Company Name Company Address City State/Province Postal Code Country Telephone No. Email ID

No.Units	Unit of Measure	Description of Goods (Include Harmonized Tariff Number if known)	Country Of Origin	Unit Value	Total Value
	Each				
	Each				
	Each				
	Each				

Additional Comments NLR	Invoice Line Total	
	Discount/Rebate	
	Invoice Sub-Total	
	Freight Charges	
Declaration Statement I hereby certify that the information on this invoice is true and correct and the contents and value of this shipment are as stated.	Insurance	.
	Other (Specify Type)	
	Invoice Total Amount	
	Currency Code	
Shipper Signature/Title — Date	Total Number of Packages	
	Total Weight (indicate LBS or KGS)	

the Export Administration Regulations. Diversion contrary to U.S. laws is prohibited.

8 QUERY RESOLUTION

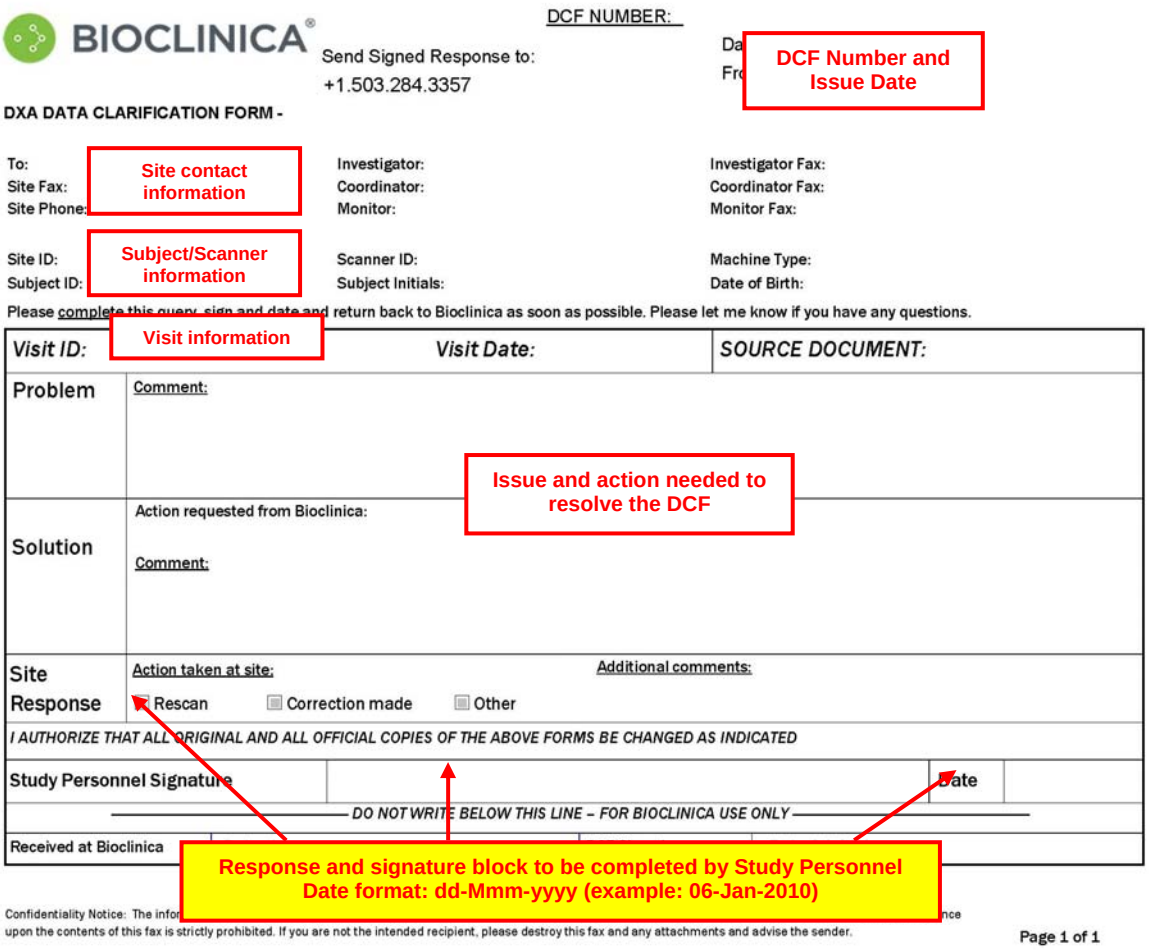
There will be instances when Bioclinica receives data that cannot be processed because they are incomplete, incorrect or simply need clarification. Examples include:

- Incorrect Transmittal Form completion
- Date of birth or subject ID questions
- DXA images missing from electronic media
- Repeat examination needed
- Visit date/designation questions

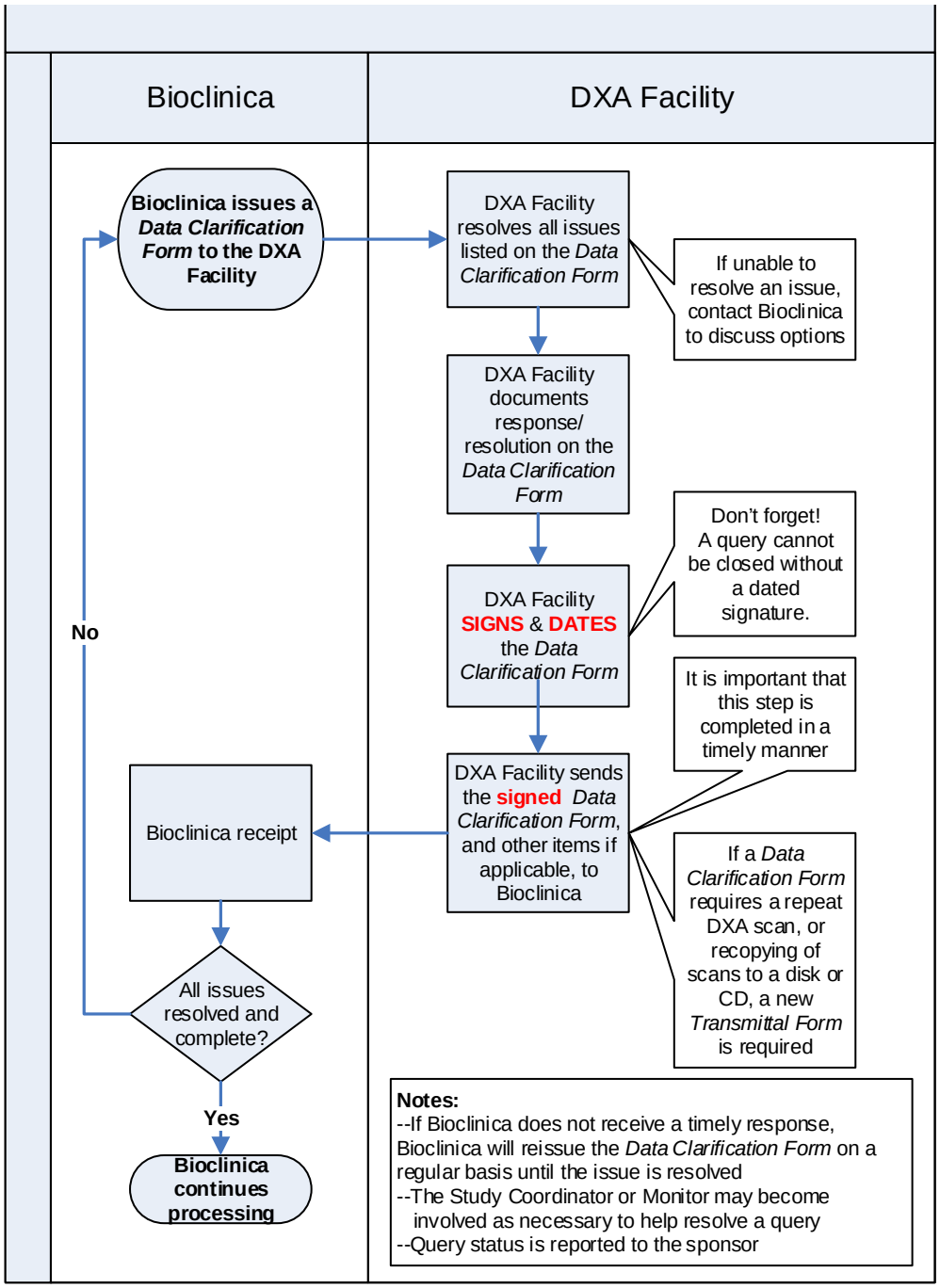
Bioclinica utilizes Data Clarification Forms (DCFs) to communicate with DXA Facilities about these issues. DCFs also serve as GCP documentation ensuring that someone reviewing study data in the future will be able to determine what was changed, when it was changed, why it was changed and who changed it.

It is important that DXA Facilities provide accurate information in a timely manner to clarify the issues listed on a DCF and to sign and date the DCF before returning it to Bioclinica.

Figure 8-1: Example Data Clarification Form



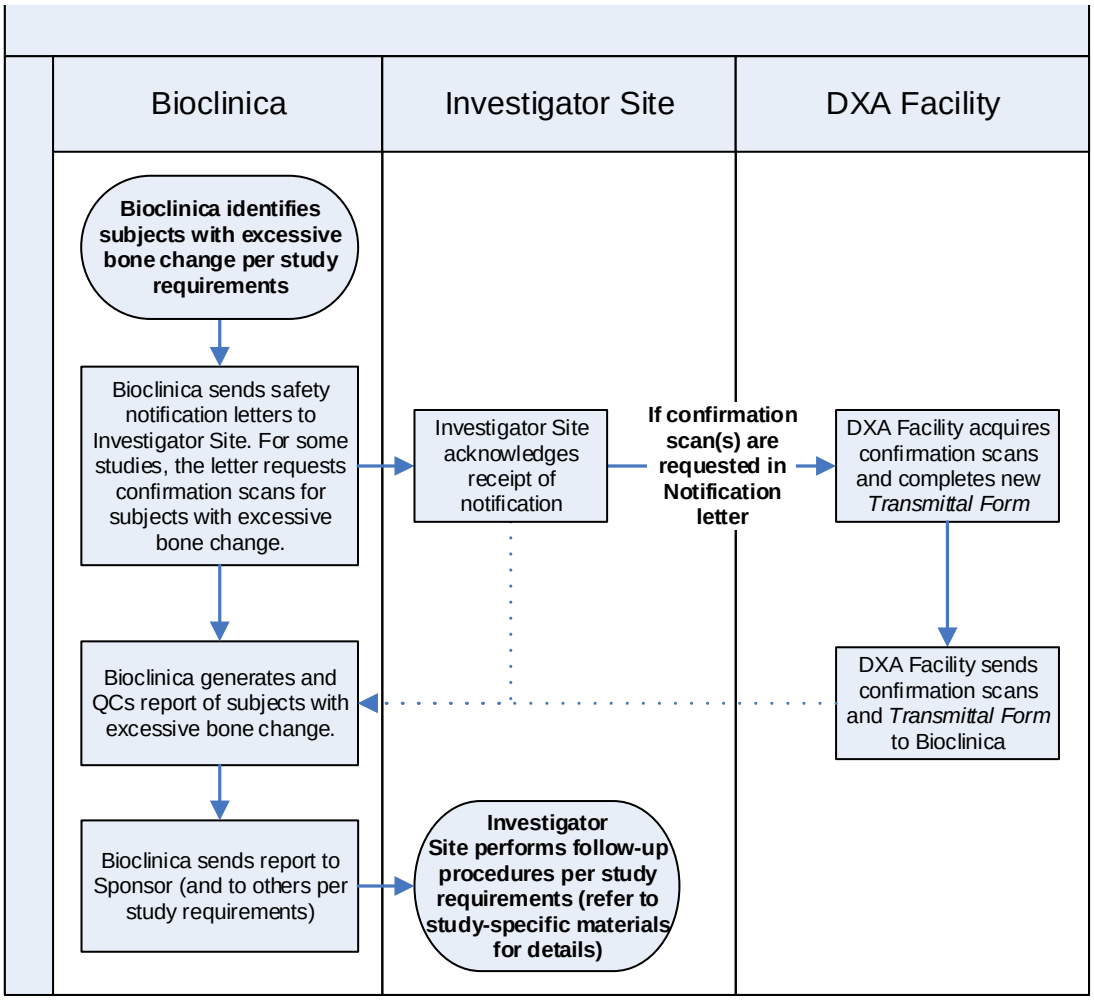
Flowchart 8-1: Query Resolution Process



9 SAFETY EVALUATION

Excessive bone change is defined as a Bone Mineral Density (BMD) loss or gain compared to baseline at any point in a trial. If Bioclinica is responsible to report subjects with excessive bone change per protocol requirements (refer to study-specific materials for details about this), the flowchart below displays the process flow between the DXA Facility, Investigator Site and Bioclinica.

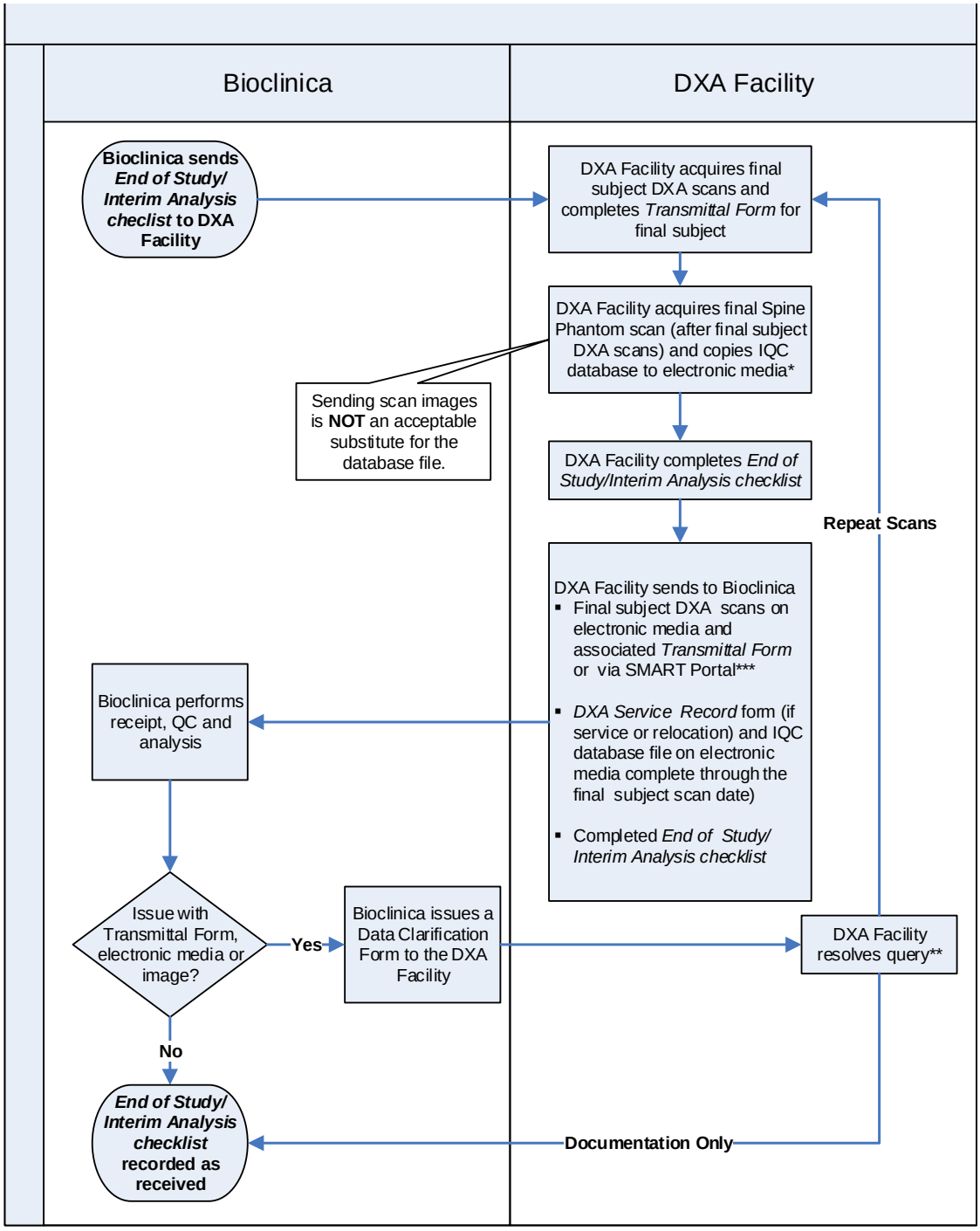
Flowchart 9-1: Safety Evaluation Process



10 END OF STUDY/INTERIM ANALYSIS

Bioclinica is responsible for collecting certain information at the end of a study and/or at interim time points identified by the Sponsor. The flowchart below displays the process flow between the DXA Facility and Bioclinica for this event.

Flowchart 10-1: End of Study/Interim Analysis Process



*Instructions for copying the IQC database to electronic media can be found beginning on page X-5.

**The process for resolving queries can be found beginning on page 16.

***Instructions for submission of data can be found on page 13.

11 DXA SCAN ACQUISITION AND ANALYSIS

11.1 Overview

The quality of work of DXA Technologists directly affects a sponsor's ability to determine the effectiveness and safety of a study drug. Variability of BMD measurement increases due to acquisition errors like a difference in subject positioning, a change in scan mode, and subject movement in the scan or presence of an external artifact. Consistency by DXA Technologists in subject preparation, positioning, scan mode, scan acquisition and analysis at both baseline and follow-up visits is the key to obtaining reliable bone density data.

11.2 Data Entry of Subject Biography

Data must be entered correctly into the fields of the subject biography in order to exactly match the information contained on the Case Report Form (CRF) and to comply with the format designated by Bioclinica and the Sponsor.

- Enter data as received from the study coordinator.
- Enter data prior to scanning a subject.
- Enter data prior to copying scans to electronic media or entering for online submission.
- Create only one biography per subject.
    - Enter gender at birth.
- Update the biography at follow-up visits before scanning subjects.
- Distinguish between the number 0 and the letter O (Use 0 for numbers and O for letters).
- Do not add additional characters or spaces.

Be sure to enter data as defined per scanner type; refer to your study-specific materials for details.

11.3 General DXA Image Acquisition Guidelines

Subject Preparation

- Describe the procedure to the subject.
- Remove all external artifacts from the scan field.

Baseline Scan

Acquisition of a good quality baseline scan is critical as all follow-up images must match the subject positioning and scan mode used at baseline.

Baseline Subject Positioning

- Center the subject on the scanner table (except for forearm scans).
    - Use the centerline as a reference to align the whole body: head, trunk and legs
- Use positioning devices in a correct and consistent manner as required by the scan type.
- Ensure that the subject is comfortable and remains still.
- Avoid unnecessary conversation with the subject.

- If duplicate scans are being acquired in a study, ensure the subject gets up from the scanner and is repositioned between scans.

Baseline Scan Acquisition

- Always ensure the Auto-Analysis feature is disabled (see Appendix D on page X-7).
- Use the correct scan mode and positioning method for each scanner model. Bioclinica recommends certain scan modes be used for clinical trials. These are listed in Appendix A on page X-2. Bioclinica-recommended scan modes may be different from what you use every day.
  - Never use the Quickview, Fast, Turbo, Survey or Express modes.
- Always use the positioning methods outlined in this manual.
- Use the repositioning tool to ensure accurate acquisition (applicable for lumbar spine, femur and forearm scans.)
- Make sure that the body part to be scanned is correctly positioned within the scan field.
- Reposition the detector or subject to improve the scan image if necessary.
- Document variations to normal procedure and presence of internal artifacts in the comment section of the DXA Transmittal Form.
- Keep a paper copy of the baseline scan images in the DXA QA binder for reference at follow-up.

Baseline Image Quality Checklist

- Correct scan mode is used.
- There are no external artifacts in the scan field.
- There is no evidence of subject motion in the scan.
- The entire region is acquired.
- The image is of good quality.
- **Reposition and rescan if necessary. Catching and correcting mistakes early while the subject is still on the scanner will save time and energy.**

Baseline Scan Analysis

- Do not analyze baseline images unless instructed to do so in study-specific materials.
- Instructions on disabling the auto-analysis feature can be found in Appendix D on page X-7.

Follow-up Scans

Follow-up Subject Positioning

- Refer to a printout of the baseline DXA image taken to ensure that the follow-up positioning is the same.
  - **Always** match the baseline positioning of subjects at follow-up; this is crucial to reliable measurement of changes in BMD.
- If duplicate scans are being acquired in a study, ensure the subject is repositioned between scans.

Follow-up Scan Acquisition

- Instructions on disabling the auto-analysis feature can be found in Appendix D on page X-7.
- **Always** use the same scan mode used at baseline.
- Use the repositioning tool to ensure accurate acquisition (applicable for lumbar spine, femur and forearm scans.)
- Document variations to normal procedure and presence of internal artifacts in the comment section of the DXA Transmittal Form.

Follow-up Image Quality Checklist

- The scan mode used at follow-up matches the scan mode used at baseline.
- The follow-up positioning matches the positioning at baseline.
- There are no external artifacts in the scan field.
- There is no evidence of subject motion in the scan.
- The image is of good quality.
- **Reposition and rescan if necessary.**

Follow-up Scan Analysis

- Do not analyze follow-up images unless instructed to do so in study-specific materials; it is not a common practice.
- Instructions on disabling the auto-analysis feature can be found in Appendix D on page X-7.

Common Problems with Scans

- Incorrect subject positioning
- Subject motion
- Incomplete acquisition
- Poor centering within the scan field
- Presence of external artifacts
- Follow-up scan positioning and/or scan mode are inconsistent with baseline

(Page intentionally left blank)

LUMBAR SPINE

SECTION S

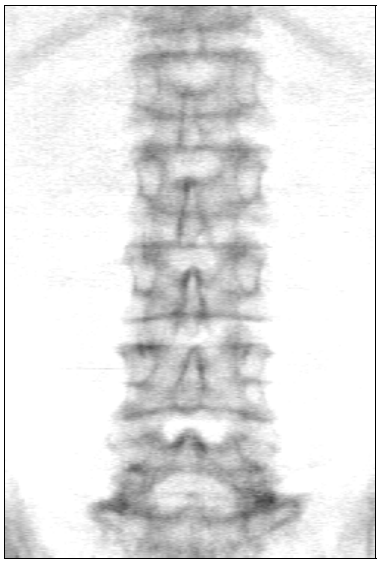
TABLE OF CONTENTS

LIST OF FIGURES

LUMBAR SPINE

1 Example of a good quality Spine scan

Figure 10-1: Example of a good quality Spine scan



- The image is of good quality.
- The spine is straight and centered in the scan field.
- The entire L1-L4 region is visible.
- The pelvis/L5 and ribs/T12 are visible.
- There are no internal or external artifacts visible.
- There is no evidence of subject motion.

2 Subject Preparation

- Describe the procedure to the subject.
- Ensure the subject has not had any nuclear medicine procedures or medical procedures involving contrast media within 10 days prior to the scan.
  - Examples of compounds include (but not limited to): barium, iodine, and barium sulfate, as well as all contrast media used in various diagnostic imaging procedures.
- Ensure the subject has **NOT** taken a calcium tablet within 2 hours prior to the scan.
- Remove all external artifacts from the scan field
  - Examples: bras, jewelry (naval rings), zipper, buttons, snaps, belt, thick elastic waistband.

3 Baseline Scan

3.1 Baseline Subject Positioning

Figure 10-2: A well-positioned subject for a spine scan

AP Lumbar Spine Scan Parameters screen from Hologic QDR Users Guide

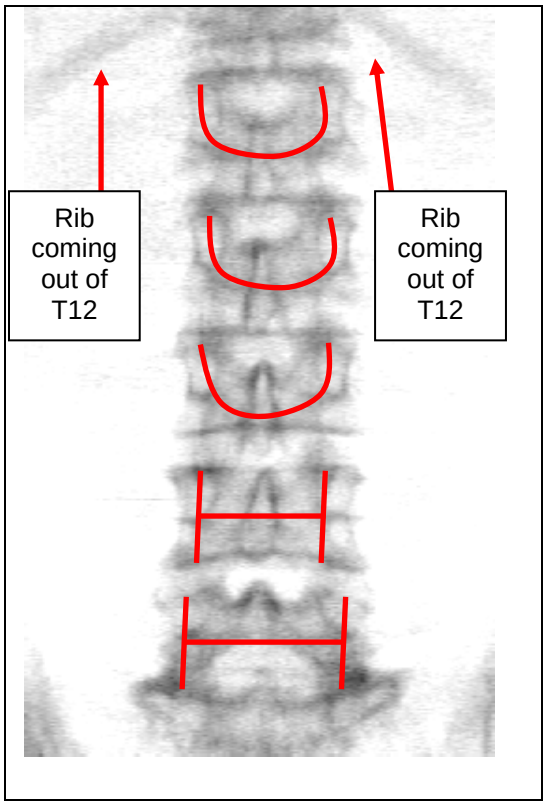
- Center the subject on the scanner table.
  - Use the centerline as a reference to align the subject
- Ensure the subject is straight.
- Place arms alongside the subject's body with their hands flat and palms down on the scanner table.
- Place a pillow under the subject's head.
- Position the block under the subject's lower legs to reduce lordosis.
- Ensure that the subject is comfortable and remains still.
- If duplicate scans are being acquired in a study, ensure that the subject gets up from the scanner and is repositioned between scans by getting off the table or, if getting off the table is difficult, at least sitting up and swinging their legs off the table before lying back down.

3.2 Vertebral Identification

Use anatomical markers and vertebral shape to ensure complete acquisition. Every person's anatomy will vary, and may not match all of these shapes and markers.

- L5 is at the level of the iliac crest if visible, is generally wider than L4 and often looks like the letter **I** on its side.
- L4 is typically the largest vertebra; it tends to be narrower than L5 but consists of more scan lines. L4 generally looks like the letter **H** and lies at the top of the iliac crest.
- L1, L2 and L3 are generally similar in shape to each other; they may be square or circular and have a **U** or **V** shape. L1 is the smallest and L3 is the largest.
- T12 has the ribs coming out on both sides.

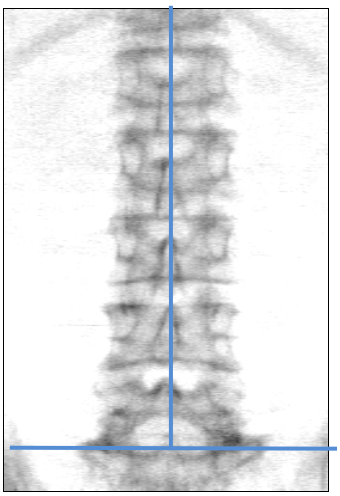
Figure 10-3: Vertebral identification



3.3 Baseline Scan Acquisition

- Always ensure the Auto-Analysis feature is disabled (see Appendix D on page X-9).
- Use the correct scan mode (see Appendix A: Scan Modes on page X-2) and positioning method.
- Ensure the spine is reasonably straight.
  - Reposition the subject if necessary.
- Use the repositioning tool to center the spine in the scan field and ensure that adequate soft tissue is acquired on both sides of the spine.

Figure 10-4: Lumbar Spine—Image of repositioning tool to center spine



- This image shows proper placement of the image using the Hologic repositioning tool.
- Refer to the instructions in the Hologic manual for instructions on using the repositioning tool.

- Begin the scan below L5 to include some pelvis and end at mid T12.
  - Use the repositioning tool to begin at the correct level.
  - If scoliosis exists, ensure that the L1-L4 region is centered from side to side within the scan field; this may require starting the scan with L5 off center

Figure 10-5: Lumbar Spine—Scan acquisition when scoliosis is present

Not well-centered, unacceptable scan	Well-centered, corrected acceptable scan
	

- Ensure landmarks (ribs and pelvis) are visible.
- If the ribs are not apparent at the expected T12 level, continue acquisition to the middle of vertebra with visible ribs.
- Document variations to normal procedure and presence of internal artifacts in the comment section of the DXA Transmittal Form.

3.4 Baseline Spine Image Quality Checklist

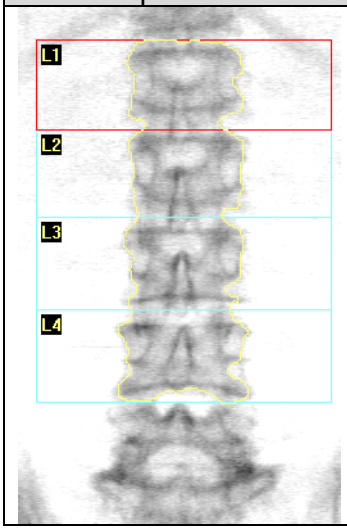
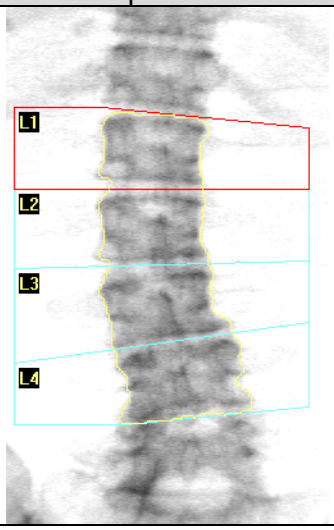
- Correct scan mode is used.
- There are no external artifacts in the scan field.
- There is no evidence of subject motion in the scan.
- The spine is as straight as possible and is centered in the scan field.
- The entire L1-L4 region is visible including part of L5 and T12.
- The pelvis and ribs are visible as anatomical landmarks.
- The image is of good quality.
- **Reposition and rescan if necessary.**

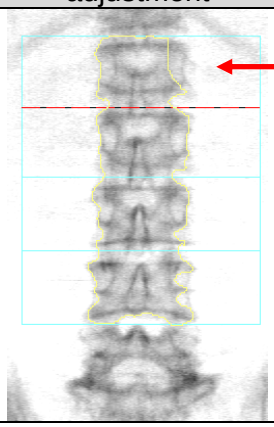
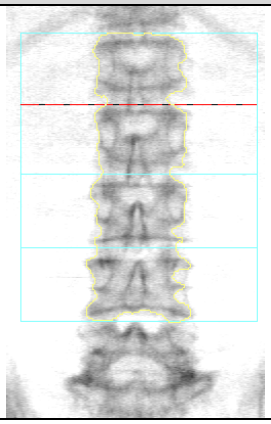
3.5 Baseline Scan Analysis

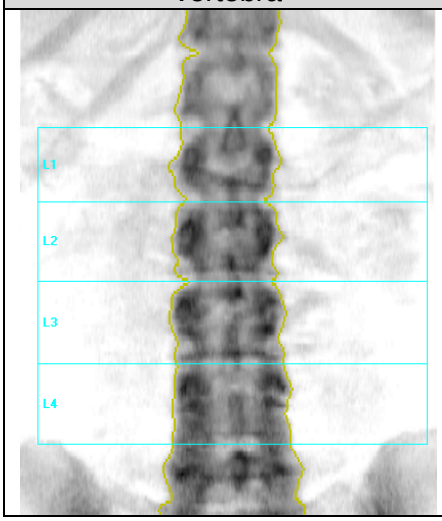
- Do not analyze baseline images unless instructed to do so in study-specific materials.
- Instructions on disabling the auto-analysis feature can be found in Appendix D on page X-9.
- For subjects with scoliosis, if the scan is too short, the ROI boxes may not fit on the image and the patient will need to be rescanned.

- Use the default global ROI width.
- Center the spine within the global ROI.
  - Include equal amounts of soft tissue on each side.
- Use the scoliosis (point) mode only when necessary.
  - Use if a horizontal line intersects a vertebra.
  - Ensure a portion of the top and bottom global ROI remains horizontal.
- Review the scan to ensure the bone mapping appears correct.
- Only alter the bone map if it is obviously incorrect.
- Determine the vertebral labels by counting from the bottom up.
- Include L1-L4 in the analysis.

Figure 10-6: Lumbar Spine—Scan analysis

Standard spine Well-placed ROI	Scoliosis present Well-placed ROI
	

Bone mapping needs adjustment	Corrected
	

Subject has an extra lumbar vertebra	Notes
	When a subject has an extra vertebra, ensure that L5 is connected to the pelvis. When analyzing baseline count vertebral bodies from the bottom up.

4 Follow-up Scans

4.1 Follow-up Subject Positioning

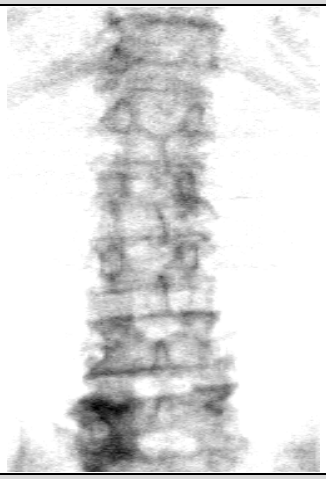
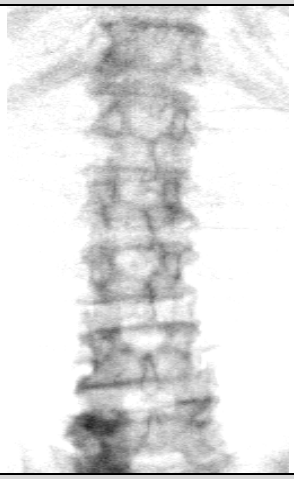
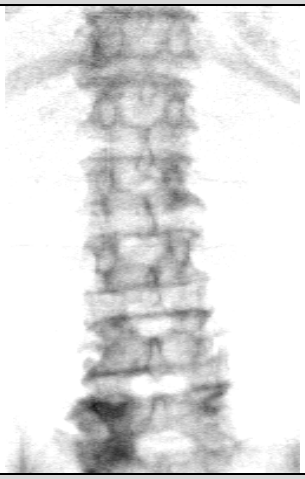
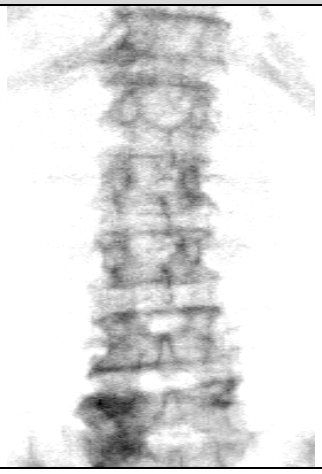
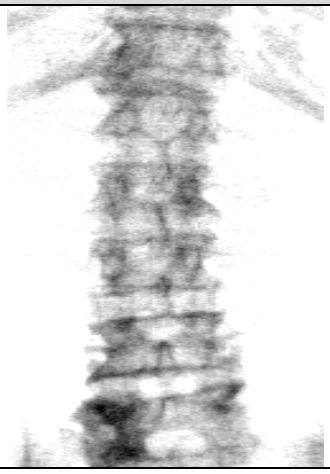
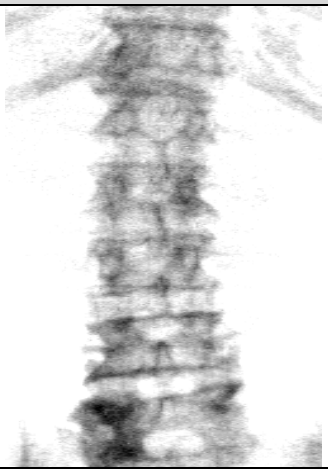
- Refer to a printout of the baseline DXA image taken to ensure that the follow-up positioning is the same. **If more than one image was taken at the baseline visit, be sure that the correct one is chosen for comparison of subject positioning and scan acquisition modes. If it is not clear what image should be used, contact Bioclinica.**
  - **Always** match the baseline positioning of subjects at follow-up; this is crucial to reliable measurement of changes in BMD.
  - Use the positioning block in the same manner as at baseline (same height, same leg angle).

- If duplicate scans are being acquired in a study, ensure the subject is repositioned between scans by at least sitting up and swinging their legs off the table before lying back down.

4.2 Follow-up Scan Acquisition

- Always ensure the Auto-Analysis feature is disabled (see Appendix D page X-9).
- **Always** use the same scan mode used at baseline.
- Verify that the L4-L5 intervertebral space appears the same as in the baseline scan.
- Ensure that L1-L4 are located in the same position within the scan field as in the baseline scan.
- Ensure that the L1-L4 orientation and angle in the baseline scan are reproduced in the follow-up scan.
- Use the repositioning tool to ensure accurate acquisition; see Figure 10-4 on page S-6.
- Document variations to normal procedure and presence of internal artifacts in the comment section of the DXA Transmittal Form.

Figure 10-7: Lumbar Spine—Examples of acceptable follow-up scans

Baseline Scan	1st Follow-up Scan	2nd Follow-up Scan
		
3rd Follow-up Scan	**4th Follow-up Scan**	**5th Follow-up Scan**
		

4.3 Follow-up Spine Image Quality Checklist

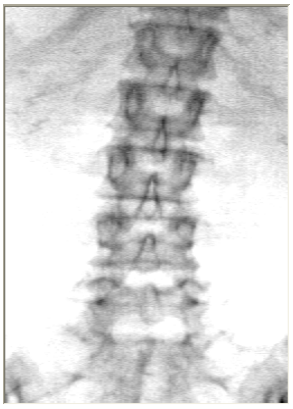
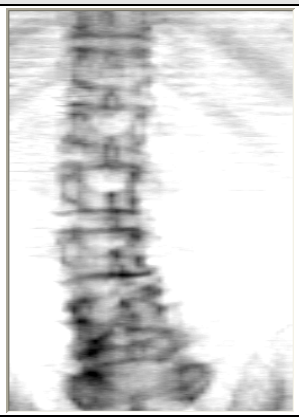
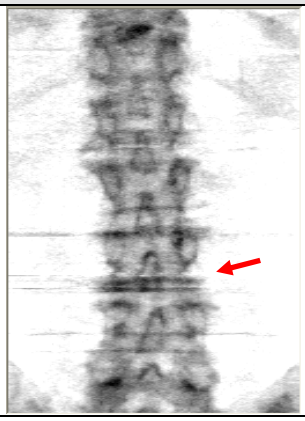
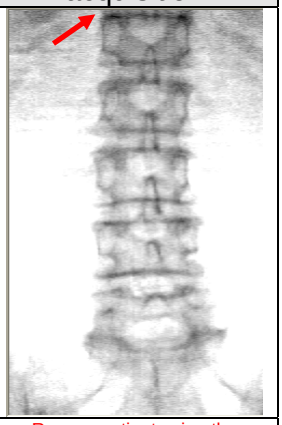
- The scan mode used at follow-up matches the scan mode used at baseline.
- The follow-up positioning matches the positioning at baseline.
- There are no external artifacts in the scan field.
- There is no evidence of subject motion in the scan.
- The image is of good quality.
- **Reposition and rescan if necessary.**

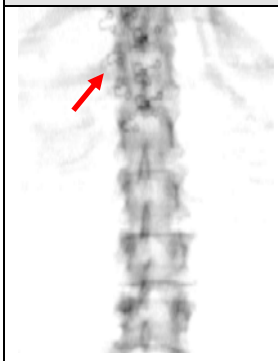
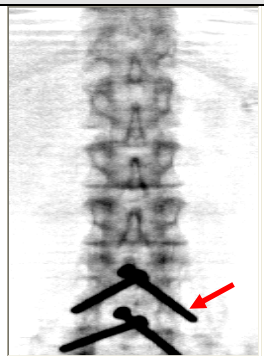
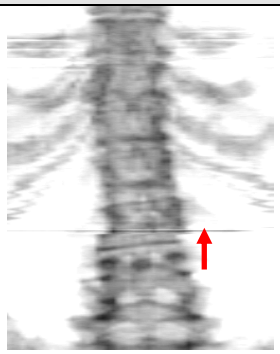
4.4 Follow-up Scan Analysis

- Do not analyze follow-up images unless instructed to do so in study-specific materials; it is not a common practice.

5 Common Problems with Lumbar Spine Scans

Figure 10-8: Common problems with Lumbar Spine scans

Spine rotated/ not straight	Poor centering	Subject motion	Incomplete acquisition
			
Reposition patient using the respositioning tool and block positioner to reduce lordosis, and ensure spine is straight and centered.	Rescan patient using the the repositioning tool to ensure the spine is straight and centered withtin the scan field and there is an equal amount of tissue on either side.	Rescan patient; ask patient to remain still during scanning procedures.	Rescan patient using the repositioning tool; begin the scan at the level of mid L5 and end at mid T12 to ensure entire region has been acquired.

External artifact	Internal artifact	Software Error
		
Remove external artifact and reacquire the spine scan; send only the good image to Bioclinica.	Make a note of the internal artifact(s) in the comment section of the DXA Transmittal Form.	Reposition patient and reacquire the spine scan; review scan to ensure the software error no longer exists and send only the good scan to Bioclinica.

FEMUR

SECTION F

TABLE OF CONTENTS

LIST OF FIGURES

FEMUR

1 Example of a good quality Femur scan

Figure 10-9: Example of a good quality Femur scan

- The image is of good quality.
- The greater trochanter is fully acquired.
- The femoral head is fully acquired.
- Enough femoral shaft is acquired.
- The femoral shaft is as straight as possible.
- The femur is optimally rotated.
- There are no internal or external artifacts visible.
- There is no evidence of subject motion.

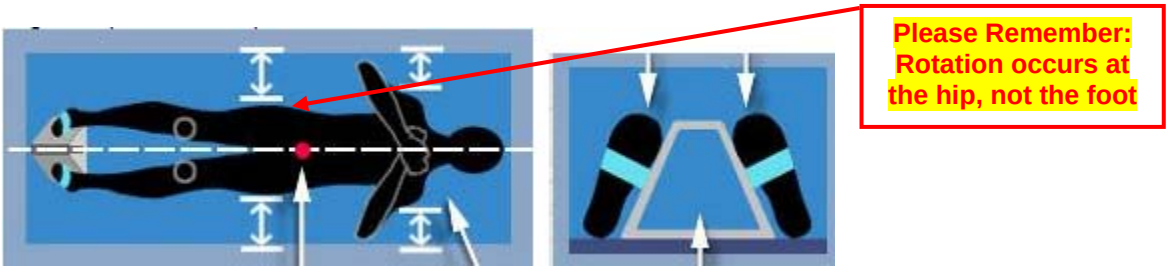
2 Subject Preparation

- Describe the procedure to the subject.
- Remove all external artifacts from the scan field
  - Examples: pocket items (wallet, coins, keys, cell phone, etc.), zipper, buttons, snaps, belt, thick elastic waistband, hands.
- Remove the subject's shoes.

3 Baseline Scan

3.1 Baseline Subject Positioning

Figure 10-10: A well-positioned subject for a Femur scan



- Scan the left or right femur as indicated in study-specific materials.
  - In case of hip replacement, prior fracture, arthritic condition or other difficulty, the opposite femur may be scanned (include the reason why in the comment section of the DXA Transmittal Form).
- Center the subject on the scanner table.
  - Use the centerline as a reference to align the subject
- Place a pillow under the subject's head.
- Rotate the entire leg to the positioning device.
  - Ensure that the entire inner edge of the subject's foot rests against the angled portion of the positioning device. Take the subject's thigh and gently lift and rotate the subject's entire leg toward the midline.
  - Ensure that the foot is secured to the positioner.
  - **NOTE:** Do not strap both feet to the positioner as may be instructed in your DXA Operator's manual. Strap only the foot of the femur side being scanned.
- Adjust the angle of the leg to obtain a straight femoral shaft
  - **NOTE:** It may be necessary to move the positioning device off-center in order to ensure the leg is appropriately abducted.
  - Abduct the leg as necessary to obtain a straight femoral shaft.
- Have subjects place their hands on their chest.
- Ensure that the subject is comfortable and remains still.
- If duplicate scans are being acquired in a study, ensure the subject gets up from the scanner and is repositioned between scans by at least sitting up and swinging their legs off the table before lying back down.

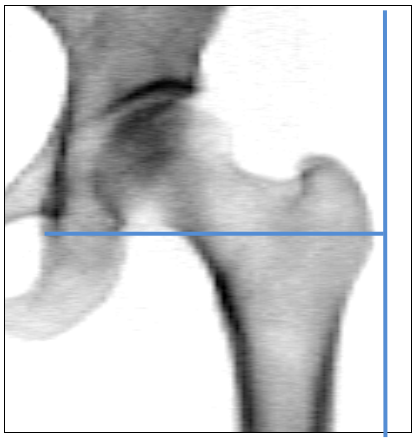
3.2 Baseline Scan Acquisition

- Always ensure the Auto-Analysis feature is disabled (see Appendix D on page X-9).
- Use the correct scan mode (listed in Appendix A on page X-2) and positioning method.
- Ensure the femoral shaft is reasonably straight and properly rotated.

- A minimum amount of the lesser trochanter, or none at all, should be visible.
- Reposition the subject if necessary.

- Ensure that the femur is correctly positioned in the scan field.
  - Use the repositioning tool to ensure adequate acquisition.

Figure 10-11: Femur – Use of repositioning tool



- This image shows proper placement of the image using the Hologic repositioning tool.
- Refer to the instructions in the Hologic manual for instructions on using the repositioning tool.

  - Allow the scan to end by default.

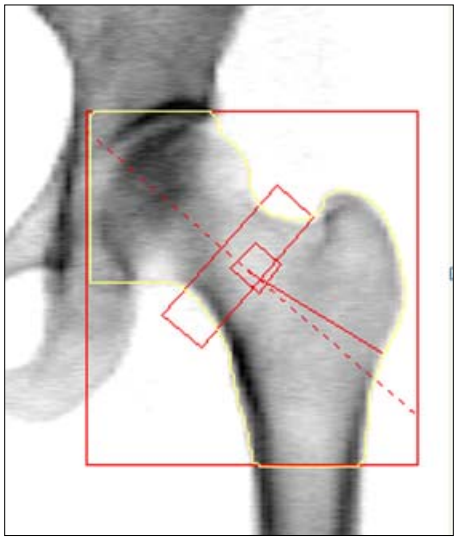
- Document variations to normal procedure and presence of internal artifacts in the comment section of the DXA Transmittal Form.

3.3 Baseline Femur Image Quality Checklist

- Correct scan mode is used.
- There are no external artifacts in the scan field.
- There is no evidence of subject motion in the scan.
- The femur is centered in the scan field.
- The greater trochanter is fully acquired.
- The femoral head is fully acquired.
- Enough femoral shaft is acquired.
- The femoral shaft is as straight as possible.
- The femur is optimally rotated.
- The image is of good quality.
- **Reposition and rescan if necessary.**

3.4 Baseline Scan Analysis

Figure 10-12: Femur baseline scan analysis



- Do not analyze baseline images unless instructed to do so in study-specific materials.
- Instructions on disabling the auto-analysis feature can be found on page X-9.

Global ROI Placement

- Set the lower active dotted line at the bottom of the lesser trochanter.
  - If the lesser trochanter is not visible, estimate the placement.
- Set the upper active dotted line above the femoral head.
- Set the active dotted line at the outer edge of the greater trochanter.
- Set the active dotted line at the medial edge of the femoral head.

Bone Map Adjustment

- Review the scan to ensure the bone mapping appears correct.
- Only alter the bone map if it is obviously incorrect.
- Delete the pelvis if necessary to avoid inclusion within the femoral neck box.

Midline Adjustment

- The midline is centered through the long axis of the femoral neck.
- Alter the midline if the femoral neck box needs to be rotated perpendicular to the femoral neck axis.

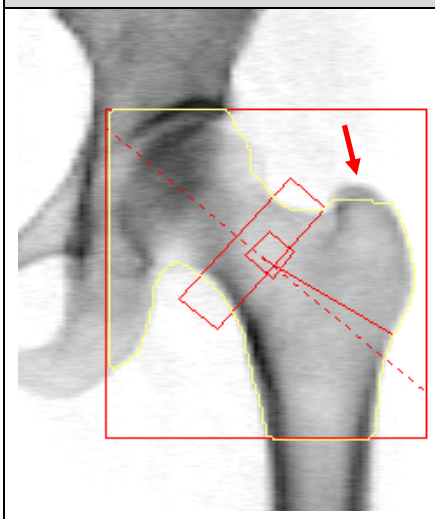
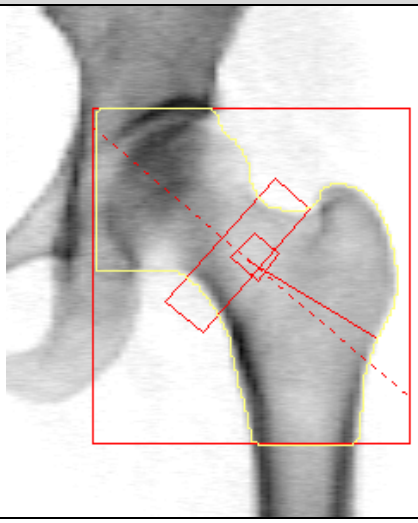
Femoral Neck Box Placement

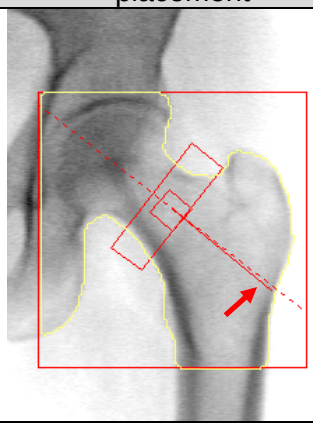
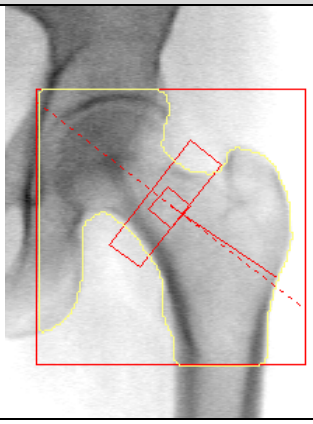
- Use the default size femoral neck ROI if possible; anchor the corner of the ROI at the notch at the base of the femoral neck where the transition to the greater trochanter occurs.
- Narrow the femoral neck ROI width only if necessary to avoid inclusion of the greater trochanter or the femoral head in the femoral neck ROI.

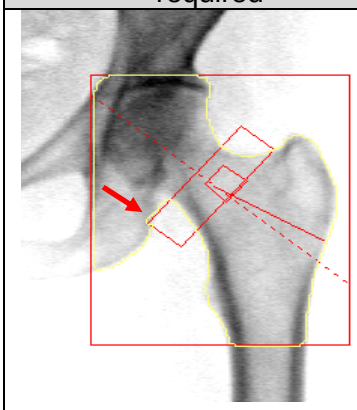
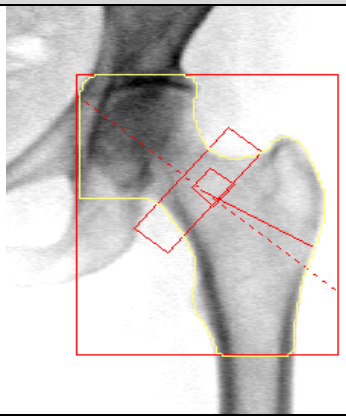
Trochanter Line

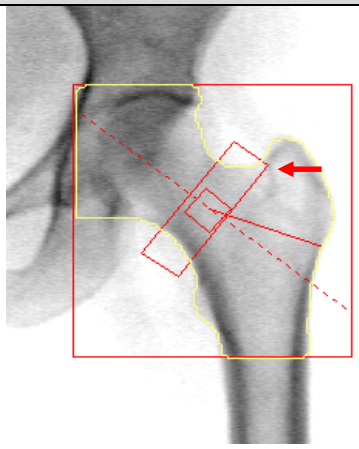
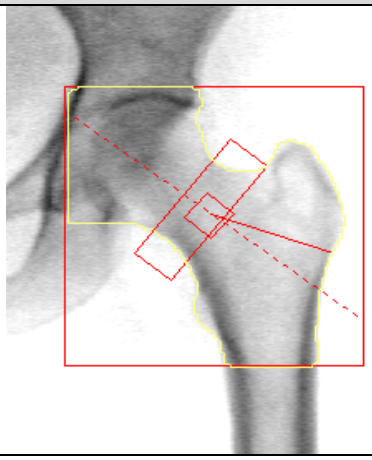
- The trochanter line marks the base of the greater trochanter; it should intersect the outer edge of the femur at the point where the transition to the femoral shaft occurs.
- Only alter the trochanter line if it is incorrect.
- The trochanter line should not fall below the midline; if it does, move it up so that is above the midline.

Figure 10-13: Femur—Common analysis problems

Bone mapping needs adjustment	Corrected	Notes
		The bone mapping was incorrect at the greater trochanter. Adjustment to the mapping made in this region.

Incorrect trochanter line placement	Corrected	Notes
		The trochanter line must not be below the midline. Adjust trochanter line so that it is one pixel above the midline marker.

Deletion of ischium when required	Corrected	Notes
		The neck box must not include the ischium. Delete the ischium bone mapping to ensure none is included in the neck box.

Incorrect placement of neck box	Corrected	Notes
		The neck box must not include any greater trochanter. Move the neck box higher up the neck region to ensure no greater trochanter is included.

5 Follow-up Scans

5.1 Follow-up Subject Positioning

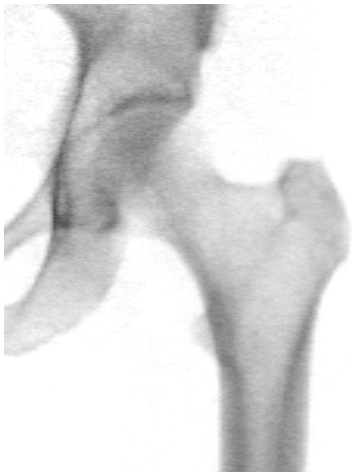
- Refer to a printout of the baseline DXA image taken to ensure that the follow-up positioning is the same. **If more than one image was taken at the baseline visit, be sure that the correct one is chosen for comparison of subject positioning and scan acquisition modes. If it is not clear what image should be used, contact Bioclinica.**
  - **Always** match the baseline positioning of subjects at follow-up; this is crucial to reliable measurement of changes in BMD.
- Always scan the same femur as at baseline.
  - If the side that was acquired at baseline is no longer evaluable, discontinue acquisition of this anatomical region; leave a note in the Comment section of the Transmittal Form with the reason.
- If duplicate scans are being acquired in a study, ensure the subject is repositioned between scans by at least sitting up and swinging their legs off the table before lying back down.

5.2 Follow-up Scan Acquisition

- Always ensure the Auto-Analysis feature is disabled (see Appendix D on page X-9).
- **Always** use the same scan mode as at baseline.
- Use the same degree of rotation as at baseline.
- Make sure that the same amount of lesser trochanter is visible as at baseline.
- Verify that the hip appears the same size as at baseline.
- Ensure the same femoral shaft orientation as at baseline.
- Verify that the hip is located in the same position within the scan field as at baseline.
- Use the repositioning tool to ensure accurate acquisition; see Figure 10-11 on page F-5.
- Document variations to normal procedure and presence of internal artifacts in the comment section of the DXA Transmittal Form.

Figure 10-14: Femur—Examples of acceptable follow-up scans

Baseline Scan	1st Follow-up Scan	2nd Follow-up Scan
		

3rd Follow-up Scan	4th Follow-up Scan	5th Follow-up Scan
		

5.3 Follow-up Femur Image Quality Checklist

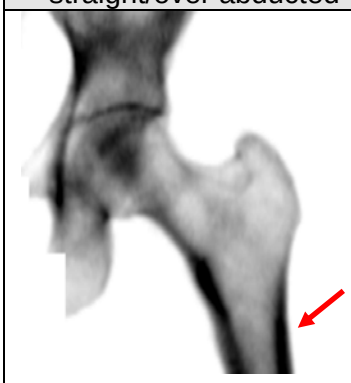
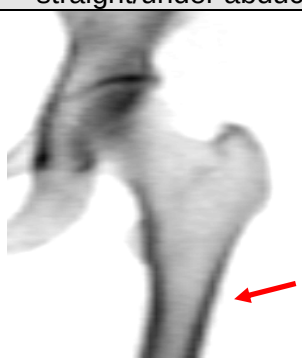
- The scan mode used at follow-up matches the scan mode used at baseline.
- There are no external artifacts in the scan field.
- There is no evidence of subject motion in the scan.
- The follow-up positioning matches the positioning at baseline.
- The image is of good quality.
- **Reposition and rescan if necessary.**

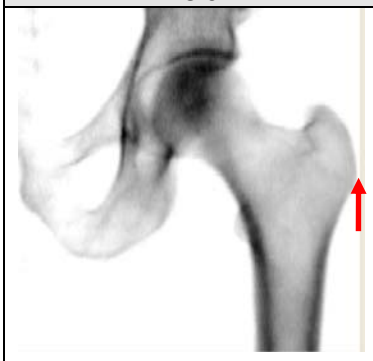
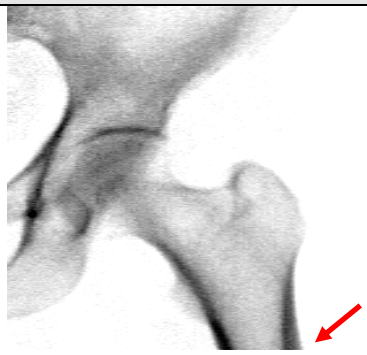
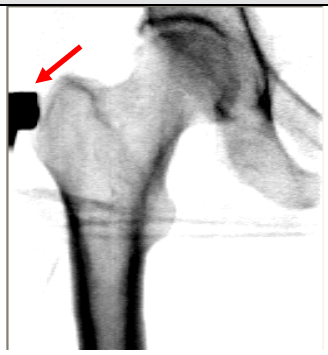
5.4 Follow-up Scan Analysis

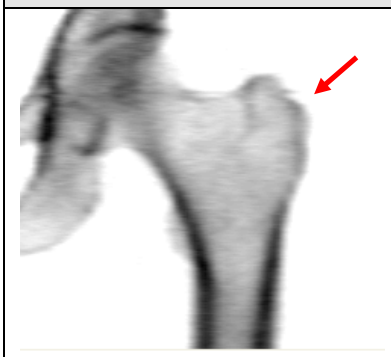
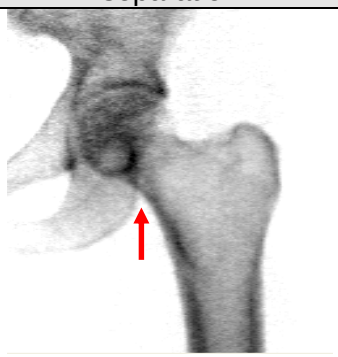
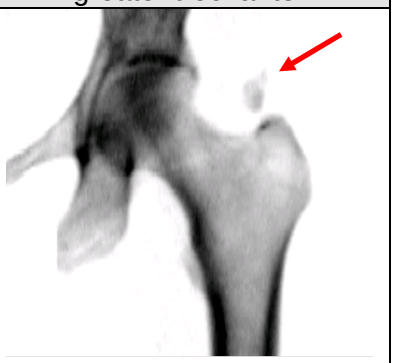
- Do not analyze follow-up images unless instructed to do so in study-specific materials; it is not a common practice.

6 Common Problems with Femur Scans

Figure 10-15: Common problems with Femur scans

Femoral shaft not straight/over abducted	Femoral shaft not straight/under abducted	Femoral shaft not properly rotated
		
Recommended Action		
Reposition the patient bringing the femoral shaft in towards the body so that it is as straight as possible. Rescan the patient.	Reposition the patient bringing the femoral shaft away from the body so that it is as straight as possible. Rescan the patient.	Reposition the patient by rotating the entire femur. When the femur is properly rotated the lesser trochanter will be much less prominent. Rescan the patient.

Poor centering of subject's anatomy within the scan field	Incomplete acquisition and over-abducted	External artifact present in scan field
		
Recommended Action		
Rescan the patient so that the femur is centered within the scan field. In this case the edge of the greater trochanter will not be so close the edge of the scan field.	Rescan the patient so that the femur is centered within the scan field, and the shaft is straight. In this case the femoral head will be closer to the top of the scan field, a greater amount of femoral shaft will have been acquired and the shaft will be closer to the body (straight up and down, not abducted).	Remove the external artifact and rescan the patient. Review the new scan to ensure that all external artifacts have been removed. Please note on the Transmittal Form all non-removable internal artifacts.

Subject motion	Insufficient pelvis separation	Calcification in tissue above greater trochanter
		
Recommended Action		
If after you have acquired a scan, motion is detected, please rescan the patient and ask that they remain as still as possible during the scanning procedures.	It is difficult to analyze scans with poor separation between the ischium and the femoral neck. Reposition the patient by adjusting the rotation and abduction to increase tissue space above and below the femoral neck region.	Please make a note on the Transmittal Form whenever there are non-removable internal artifacts present.

INSTRUMENT QUALITY CONTROL

SECTION I

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF FLOWCHARTS

LIST OF FORMS

LIST OF TABLES

INSTRUMENT QUALITY CONTROL

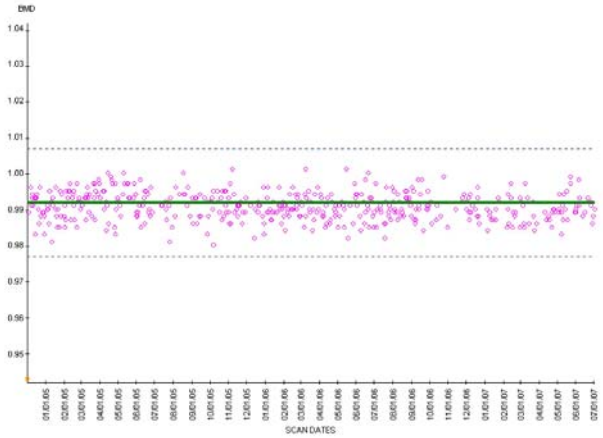
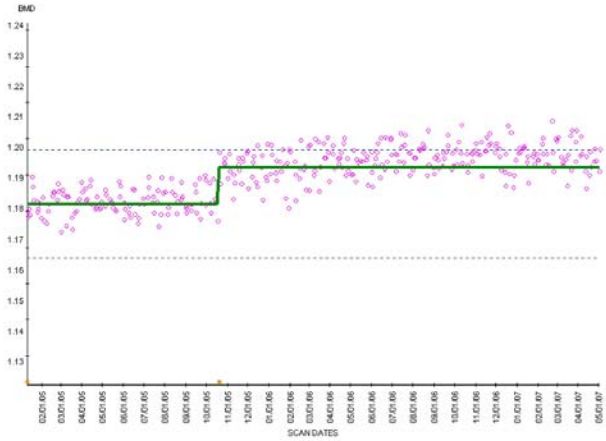
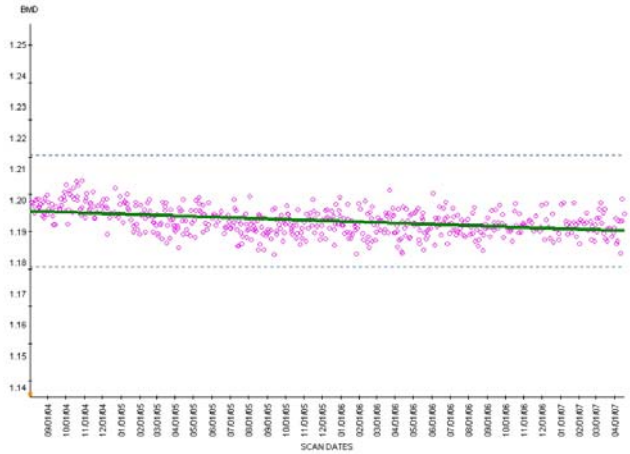
Instrument Quality Control (IQC) procedures are used to monitor DXA machine performance over the course of a clinical trial. This monitoring permits Bioclinica to identify scanners that experience shifts or drift in their BMD readings and to apply correction factors as needed to ensure study data are accurate. Monitoring machine performance and applying appropriate corrections to study data are other components to ensuring that changes in subject BMD over the course of a study are the result of study treatment as opposed to machine performance.

Collecting Baseline IQC data is one step in the DXA Facility authorization process described in the DXA Facility Study Start-Up section beginning on page 10. It is necessary to gather data from your DXA machine using a Spine Phantom, to determine how your machine functions under normal conditions; this is done prior to scanning study subjects.

Once Baseline IQC data has been completed and the site and DXA Technologist are authorized to scan study subjects, the DXA Technologist will complete the ongoing IQC procedures through the end of the study.

Instrument Quality Control Sections:

Figure 12-1: Example longitudinal BMD results of daily spine phantom scans

No change Some scanners will provide consistent BMD results of daily phantom scans throughout the course of a study.	
Shift Shifts in BMD results of daily phantom scans throughout the course of a study may occur following machine maintenance or relocation.	
Drift Drift in BMD results of daily phantom scans throughout the course of a study is most likely the result of aging hardware.	

1. Acceptable Spine Phantoms for Longitudinal IQC

Each DXA Facility must use one of the Acceptable Spine Phantoms listed below for their scanner. The same phantom must be used throughout the course of a clinical trial. The Hologic phantom may be used on GE Lunar scanners, but GE Lunar phantoms may not be used on Hologic scanners.

Table 12-1: Acceptable Spine Phantoms for Longitudinal IQC

Spine Phantom		
Hologic Spine Phantom		

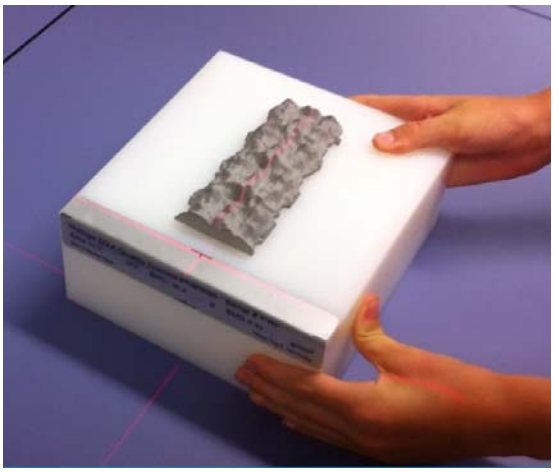
2. Spine Phantom Database and Biography Setup

The Hologic field engineer would have set up your phantom biography at scanner installation. Refer to the DXA Machine Operator's manual on Daily QC process.

3. Spine Phantom Positioning

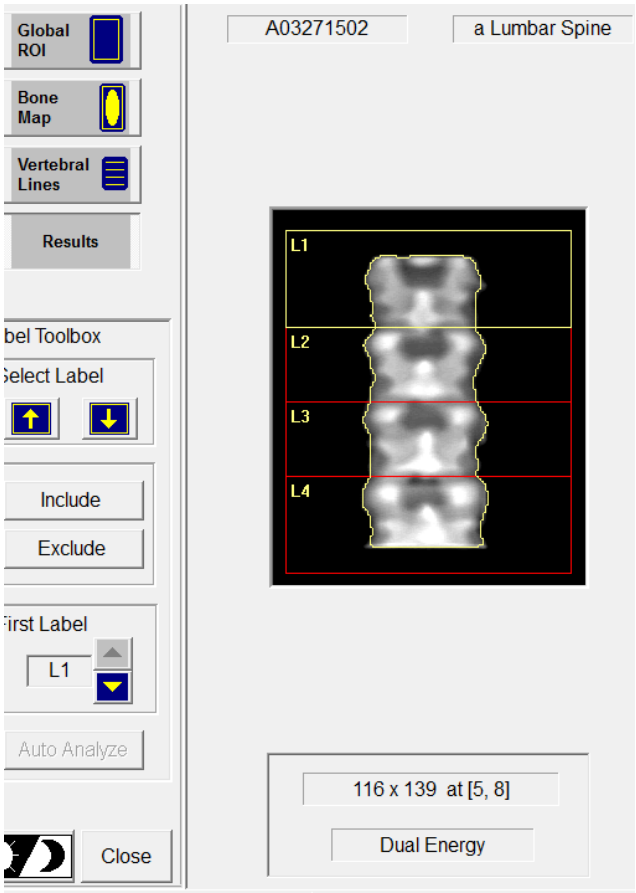
- Center the phantom on the scanner table
- Leave the scanner pad on the table
- Position L4 towards the foot end of the table (a black star or dot indicates the L4 end)
- When centered, position the laser light over the black star or dot on the Spine Phantom, or over the black 'T' (see pictures)

4. Spine Phantom Acquisition



- Refer to the DXA Machine Operator's manual on Daily QC process.

5. Spine Phantom Analysis



Refer to the DXA Machine Operator's manual on Daily QC process. Instructions below may not apply in newer models in which analysis is automated.

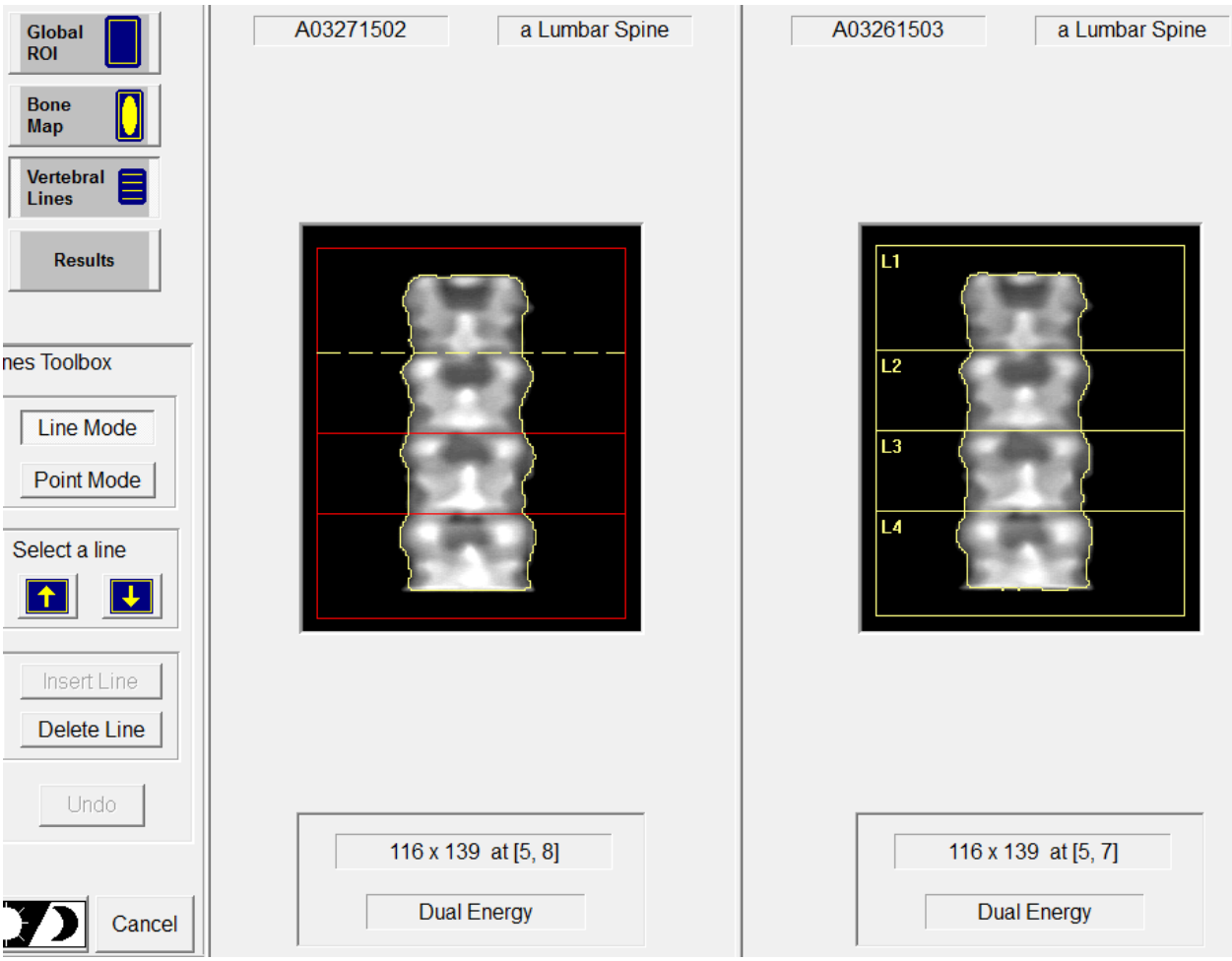
The baseline spine phantom is analyzed using the *Spine* algorithm by default. All subsequent images are compared to the baseline phantom spine scan. Select the Region of Interest (ROI): L1-L4.

To achieve the greatest degree of consistency for measuring BMD, so that machine differences can be accurately measured, set the width of the Global ROI at 116 and the length as close to 139 as possible (length may vary from 138 to 140 depending on spine phantom and site positioning; 139 is ideal).

After all phantom scans have been acquired and analyzed, click on the **[Results]** button in the analysis window, and then **[Close]**. Choose **[Report]** from the Exit Analysis window to print.

Below is a description of how to compare a follow-up scan to the baseline scan:

Double click on the scan you need to analyze. The software offers two choices: *1) Choose Analysis Method* (default) and *2) Compare to Previously Analyzed Scan.* Choose option 2 for follow-up analysis. A list of scans will appear; which defaults to the oldest scan to compare with the new one. Once the scan to be compared against is highlighted, then click on the **[Next]** button toward the bottom of the window.

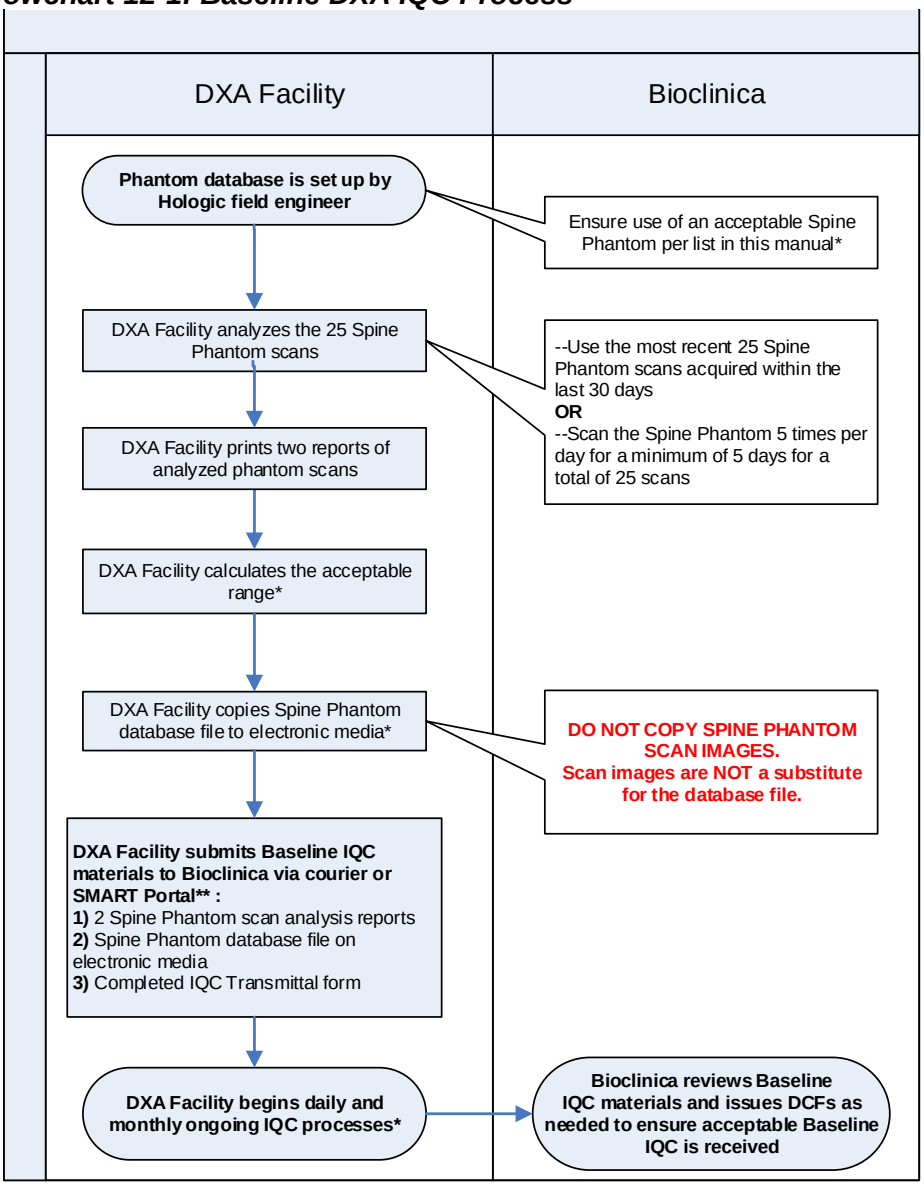


The software will default to the Global ROI analysis step. Click and hold on the Global ROI and match the bone edge overlay to the current scan image as closely as possible. Changes to the ROI height are not necessary when analyzing the spine phantom.

6. Baseline IQC Procedures

If a DXA technologist is using a DXA Machine that is not currently monitored by Bioclinica, acceptable Baseline IQC data must be collected and shipped to Bioclinica prior to that DXA machine being used to collect study data. Submission of acceptable Baseline IQC data is one step in the DXA Facility authorization process described in the DXA Facility Study Start-Up section beginning on page 10.

Flowchart 12-1: Baseline DXA IQC Process



* Acceptable Spine Phantoms are listed on page I-5.
Instructions for calculating the acceptable range are on page I-12.
Instructions for completing the DXA Service Record form are on page I-11.
Instructions for copying the Spine Phantom database to electronic media begin on page X-5.
Daily and monthly IQC processes are outlined on page I-13.

** Please contact your Bioclinica Study Team to acquire your instructions and online password to utilize the SMART Portal. It is not necessary to send any hardcopy materials to Bioclinica when submitting data online. Patient data should be uploaded under the study code and site number, while IQC data should be entered under DXA IQC Submission or IQCS-0003 study and scanner ID (unless alternate study specific procedures have been provided)

7. IQC Transmittal Form

Complete one transmittal form for each scanner. Send the white copy to Bioclinica along with data saved on electronic media in a courier envelope or submit electronically through SMART Portal. The yellow copy is for the DXA Facility's records.

Figure 12-2: Example IQC Transmittal Form

BIOCLINICA®

DXA Instrument Quality Control (IQC) Submission Form

DXA Scanner Information — To be completed at study site or by DXA Technologist

Scanner Number: (submit one form per scanner, or enter replacement scanner number here for Machine Equivalence)

Scanner Manufacturer: ☐ Hologic ☐ Lunar ☐ Norland

Submission Time Point End Date: D D / M M M / 2 0 Y Y

Submission Type: (check one)

- ☐ **Baseline** (include two spine phantom printouts)
- ☐ **Monthly or ongoing submission**
- ☐ **Interim / End of Study** (also submit Interim / EOS Checklist)
- ☐ **Machine Equivalence**
- ☐ **Cross Calibration**
- ☐ Repeat Submission
- ☐ DCF Response

Complete all fields as appropriate.

Submission Contents — To be completed prior to submission to BioClinica

Item	Comments
☐ IQC Phantom Database File (QA.mdb, QC Archive.mdb, Lunar.mdb, filename.txt, scan.dbf/region.dbf, filename.mdf)	
☐ IQC Cross Calibration Scan Files (not printouts)	
☐ Machine Equivalence Scan Files (not printouts) — Original Scanner Number / Replacement Scanner Number	
Form(s): ☐ Cross Calibration ☐ Machine Equivalence ☐ Phantom Scan Printouts ☐ Interim / EOS Checklist ☐ Correspondence ☐ Other _____	

DXA Scanner Service Information — Do not alter the calibration characterisitcs without first contacting BioClinica

Did this DXA scanner have service and/or a software or hardware upgrade since the last submission?

- ☐ N/A (if baseline submission)
- ☐ No
- ☐ Yes -- Please also submit the following: --> ☐ DXA Service Record Form ☐ Manufacturer's Service Report (if available)

Printed Name of person completing form:

Print the name of the DXA Technologist who acquired the scans

Data Shipment MUST include: Completed IQC Submission Form and correctly labeled transfer media containing IQC data listed.

Comments

Use this area for additional comments

---------- *Do not write below this line. For BioClinica use only* ----------

Data Receipt: BioClinica Study Code 0003

(BioClinica Stamp with Date and Initials)

This area is completed by Bioclinica upon receipt

 Final

BioClinica Tracking Number 0 0 0 3 2 0 2 0 1 5 1 0 0 9

S4-FOR-0051-V2.0 CONFIDENTIAL Page 1 of 1

8. IQC DXA Service Record Form

The DXA Service Record Form is required only when there has been service or a relocation as described in Ongoing IQC Processes on page I-13.

Form 12-1: Example DXA Service Record

Scanner ID Number Pre-Printed on Form by Bioclinica

DXA Facility enters the Month and Year here as MMM, YYYY (e.g. JAN, 2015)

BIOCLINICA®

DXA Service Record Form

Scanner ID: Scanner ID **Month, Year:** Enter Month, Year

Hardware Changes*	**If NONE, Check here: ☐**
Date (DD-MMM-YYYY)	Description of Service

DXA Facility enters details of hardware changes here, or if there have been no changes to record for the month, checks the NONE box in the upper right.

***Please refer to the DXA Procedure Manual regarding necessary procedures before and after service, relocation and/or upgrades.**

Software Changes*		**If NONE, Check here: ☐**
Date (DD-MMM-YYYY)	Old Version	New Version

DXA Facility enters details of software changes here, or if there have been no changes to record for the month, checks the NONE box in the upper right

***Bioclinica should be notified 30 days prior to any planned software upgrade.**

Printed name of person completing form	Title
Signature	Date (DD-MMM-YYYY)

PLEASE REVIEW FORM TO ENSURE FORM IS COMPLETE PRIOR TO SENDING TO BIOCLINICA

DXA Facility completes the signature block prior to sending to Bioclinica.

Bioclinica • 11731 NE Glenn Widing Drive • Portland, OR 97220
Fax: +1.503.528.7872
Email: IQC@bioclinica.com

IM-CSM-F003 Bioclinica Confidential Information Page 1 of 1

9. IQC Acceptable Range Calculation

After completing the Baseline IQC Process of scanning the Spine Phantom 25 times, it is strongly recommended to calculate the Acceptable Range of BMD values for ongoing Spine Phantom scans as per ISCD guidelines. Please see the worksheet below for an example on how to determine this range. Make a copy of this page, so that it is available for future use.

Form 12-2: IQC Acceptable Range Calculation Worksheet

Value		
1	Sum of BMD values of 25* scans:	_____
2	Divide **Value 1** by 25* to calculate **BMD mean**:	_____
3	Multiply **Value 2** by **0.015** to calculate **1.5% of mean**:	_____
4	Subtract **Value 3** from **Value 2** to calculate **LOWER LIMIT**:	_____
5	Add **Value 3** to **Value 2** to calculate **UPPER LIMIT**:	_____

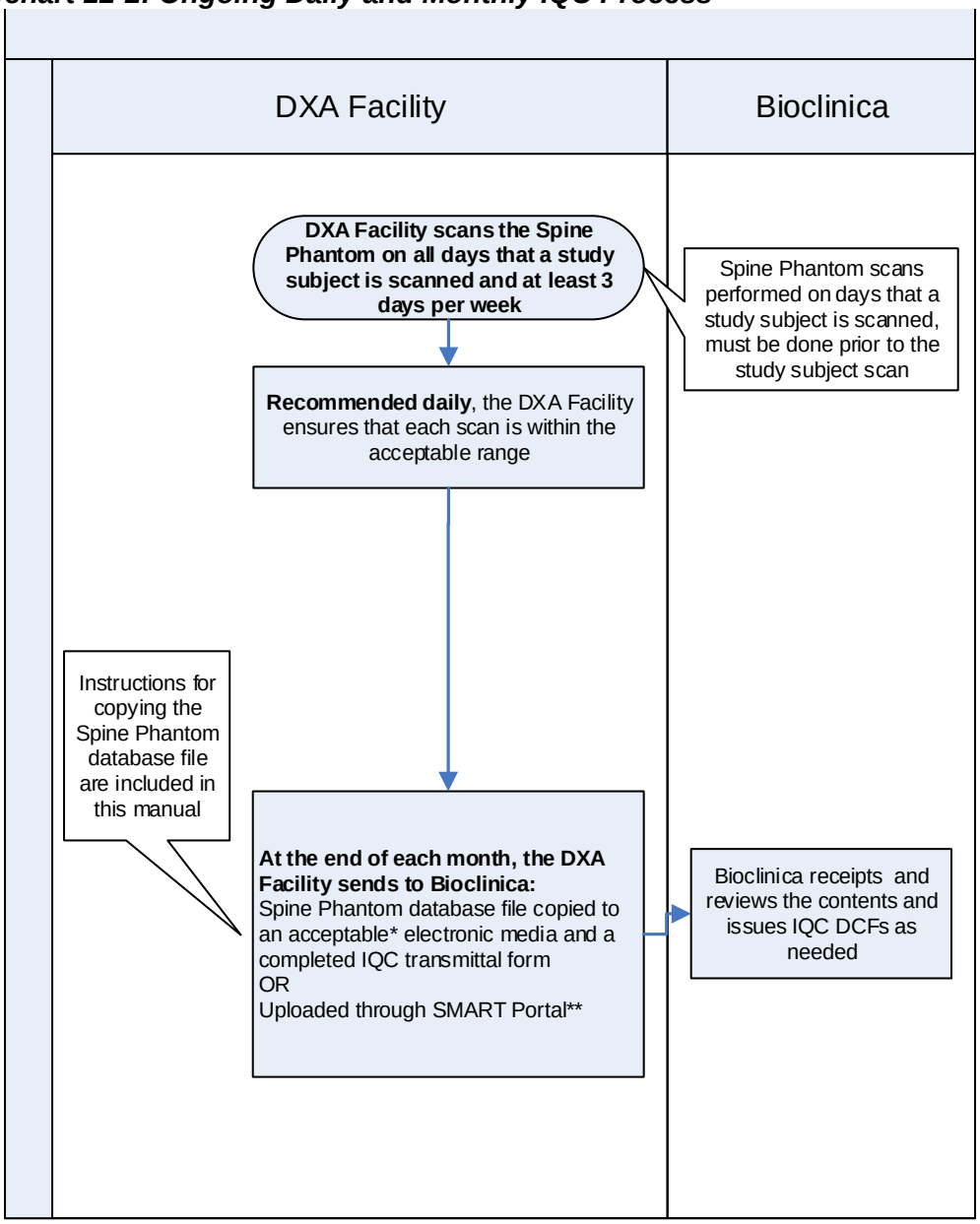
* Worksheet can be adapted for use in recalculating Acceptable Range post service. Substitute “10” for “25” where indicated by *

DO NOT REMOVE OR MARK ON THIS PAGE, MAKE PHOTO COPY.

10. Ongoing IQC Processes

Continuous measurement of the Spine Phantom will be used to monitor DXA Machine performance and to make corrections to subject data if a DXA Machine displays dramatic changes or drifts during the course of a study. **Routine Spine Phantom scans should begin upon completion of Baseline IQC data collection and continue without interruption throughout a study period.**

Flowchart 12-2: Ongoing Daily and Monthly IQC Process



*Acceptable Electronic Media types include: CD, Zip Disk, Super disk, USB thumb drive, etc. Most IQC electronic data files will not fit on a regular floppy disk.

** Please contact your Bioclinica Study Team to acquire your instructions and online password to utilize the SMART Portal. It is not necessary to send any hardcopy materials to Bioclinica when submitting data online. Patient data should be uploaded under the study code and site number, while IQC data should be entered under DXA IQC Submission or IQCS-0003 study and scanner ID (unless alternate study specific procedures have been provided)

11. IQC Notification Form

The IQC Notification Form shown below is used for communication between DXA Facilities and Bioclinica regarding IQC.

Form 12-3: IQC Notification Form

All header information will be completed by Bioclinica

BIOCLINICA® **Instrument Quality Control Notification Form**

Date:	[DD-MMM-YYYY]	DXA Facility Name:	[DXA Facility Name]
Scanner ID:	[Scanner ID]	DXA Technologist:	[DXA Technologist Name]
Scanner Type:	[Scanner Make and Model]	Fax/Email:	[Fax Number or Email Address]

DATA TYPE	NOTICE	REQUESTED ACTION

Details will be completed by Bioclinica

DXA Facility must complete all requested actions listed by Bioclinica in this section of the form

A copy of this form must be filed with the Instrument Quality Control Documents at your site.

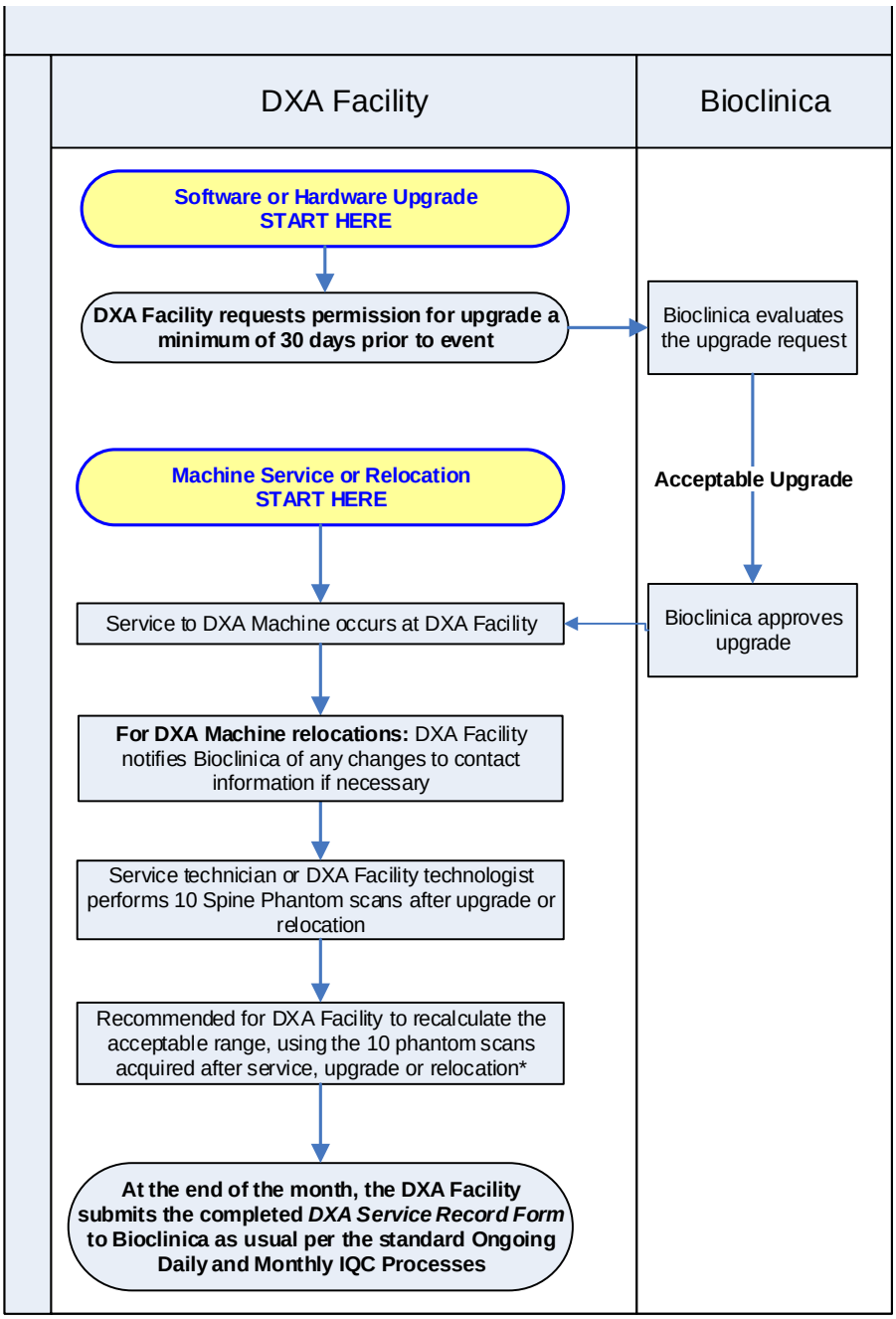
Bioclinica • 11731 NE Glenn Widing Drive • Portland, OR 97220 • Fax: +1.503.528.7872 •
Email: IQC@bioclinica.com

12. DXA Machine Service, Relocations and Upgrades

When a DXA machine requires service (such as preventative maintenance or repair), relocation, or a software or hardware upgrade, DXA Facilities must follow the steps outlined in the flowchart below. Bioclinica evaluates each manufacturer software release to ensure the continuity and compatibility in all related data handling systems and results.

Flowchart 12-3: DXA Machine Service, Relocations and Upgrades

These instructions do **NOT** cover the DXA Machine Change process which is described on page I-16.

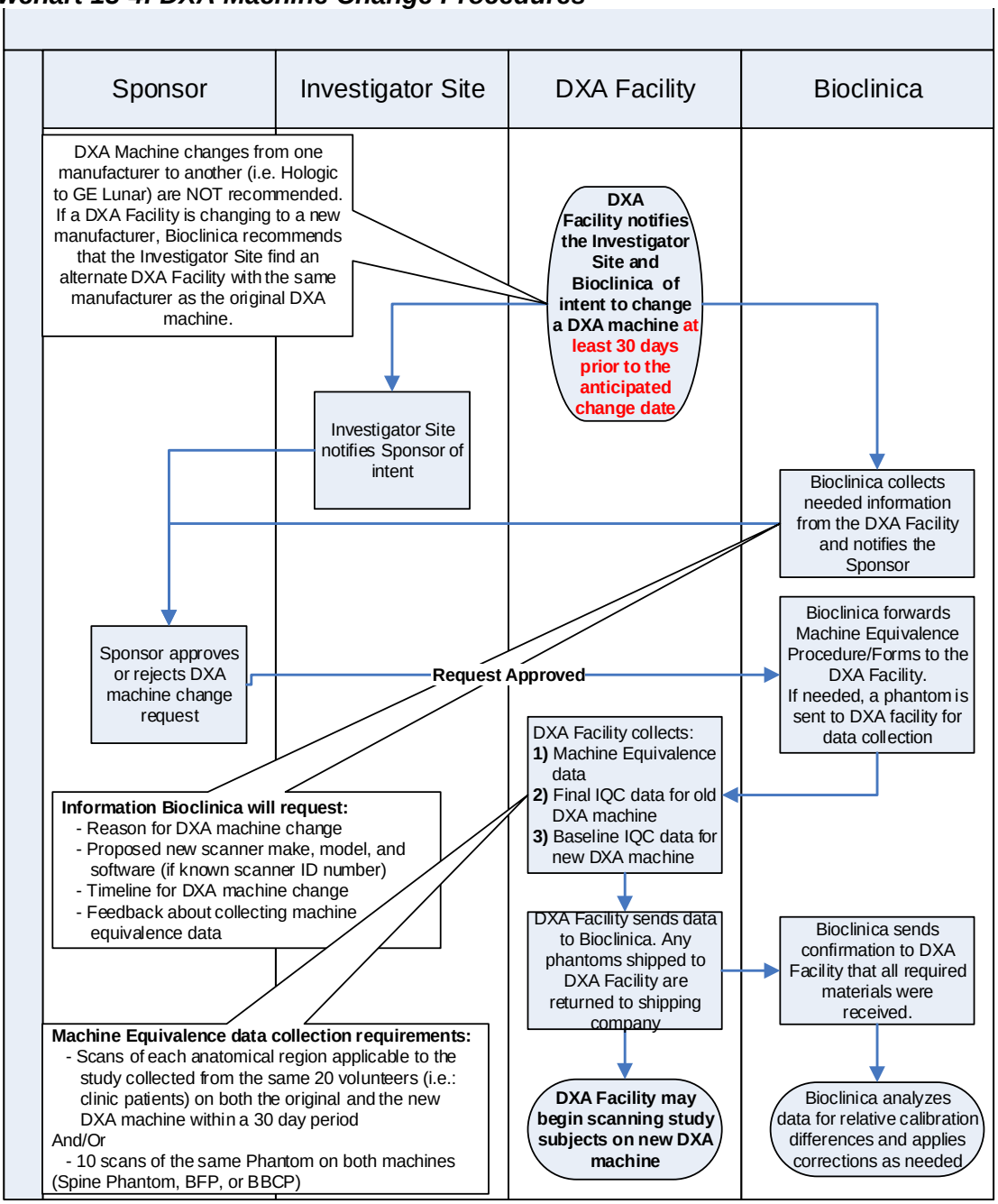


*Instructions for calculating the Acceptable Range can be found on page I-12.

13. DXA Machine Changes

The DXA machine used for collecting baseline DXA measurements should be used for all follow-up visits if at all possible. There are, however, situations which may require installing a new DXA machine. A DXA technologist should contact Bioclinica immediately if their DXA Facility needs or plans to replace a DXA machine that is being used to collect clinical trial data as Sponsor approval is necessary and several machine equivalence processes must be completed to ensure quality study data. Below is a flowchart outlining the required steps:

Flowchart 13-4: DXA Machine Change Procedures



14. INSTRUMENT QUALITY CONTROL—CROSS CALIBRATION

Introduction

In order to accelerate patient recruitment and reduce selection bias, many clinical trials involving DXA are conducted at multiple DXA Facilities simultaneously. The goal of the procedures described in this section is to provide information on system calibration across DXA Facilities.

The following phantom(s) may be used for this purpose:

1. An anthropomorphic spine phantom provides information of system calibration on an anthropomorphic object.
2. A geometric block phantom verifies the linearity of the BMD scale across the clinically useful range.
3. A Bioclinica Bona-Fide Phantom (BFP) provides information of system calibration on an anthropomorphic object and also verifies the linearity of the BMD scale across the clinically useful range.
4. A Bioclinica Body Composition Phantom (BBCP) provides long-term quality assurance for DXA whole body bone mineral and body composition determinations.

Table 14-1: Cross Calibration Phantoms Commonly Used on Bioclinica Studies

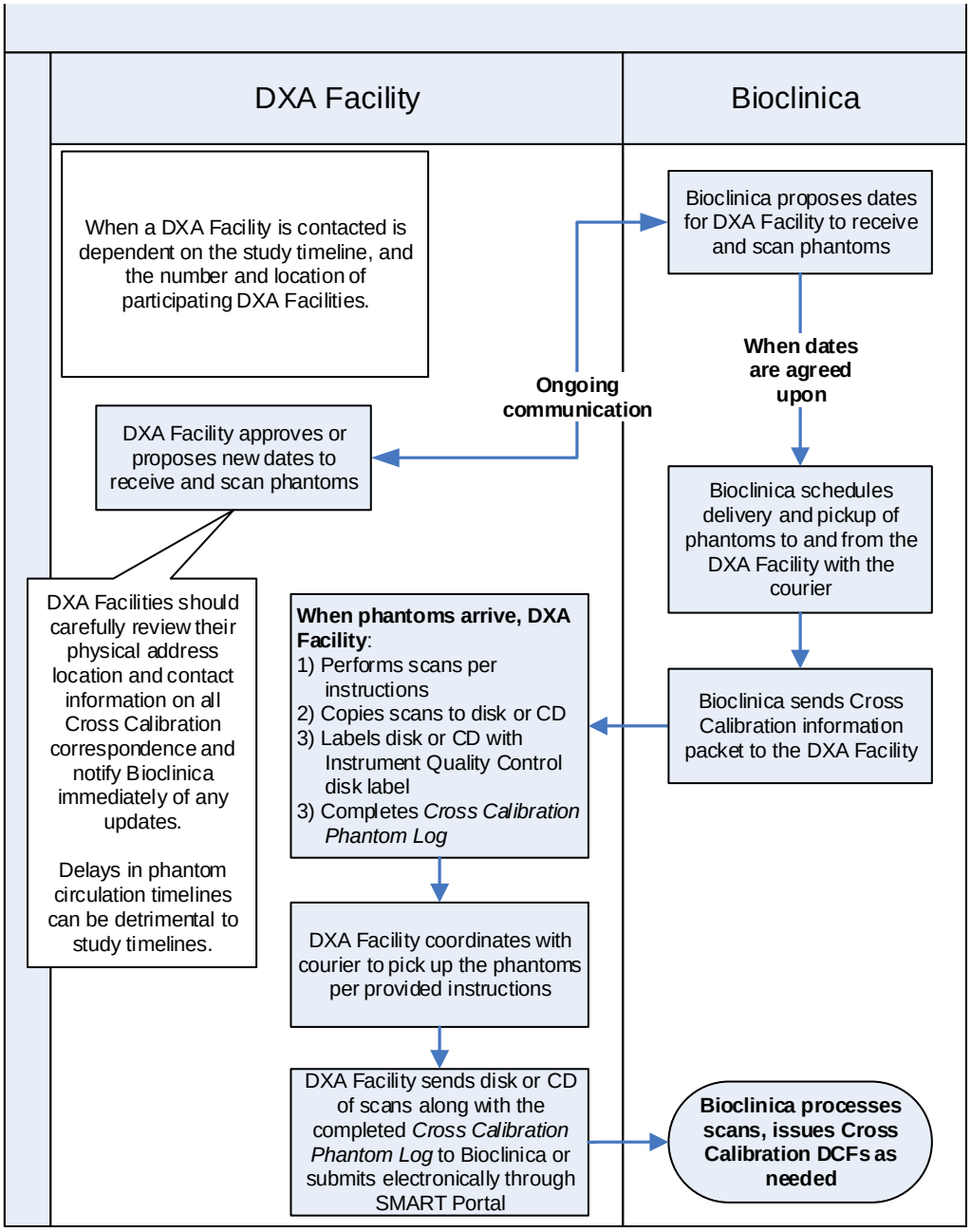
Phantom	Picture
Hologic Spine Phantom (anthropomorphic)	
Hologic Block Phantom	

Phantom	Picture
Bona-Fide Phantom (BFP)	
Body Composition Phantom (BBCP)	

14.1 Cross Calibration Procedures

All DXA Facilities will receive applicable phantom(s) sometime after the study starts. Bioclinica will contact each DXA Facility to determine a time that the phantom(s) will arrive at their site. The phantom set will be on a strict schedule. Instructions will be sent to each DXA Facility prior to the arrival of the phantoms.

Flowchart 14-1: Cross Calibration Procedures



14.2 Patient Biography Entry for Cross Calibration Phantom

Cross Calibration phantom scans should be maintained in a database that is separate from all clinic, spine phantom and study subject scans.

Create a Patient Biography for each phantom received for cross calibration. The Phantom ID number can be found on the manufacturer sticker attached to the phantom. Data must be entered correctly into the fields as follows:

Table 14-2: Cross Calibration Phantom Biography

DOS field name	Windows field name	Enter
Last Name	Last	XXXX_S for Hologic Spine Phantom
		XXXX_B for Hologic Block Phantom
		XXXX_BFP for BFP Phantom
		XXXX_BBCP for BBCP Phantom
		Note: **XXXX** *is the Spine Phantom ID imprinted on the phantom*
		DXA Facility site number
Facility ID	Patient ID	F (Female)
Sex	Gender	White/Caucasian
Ethnic	Ethnicity	01/01/1970
Birth Date	Birth Date	130 lb or 59 kg
Weight	Weight	65 in or 165 cm
Height	Height	Bioclinica XXXX
First Name	Comments	*Note:* **XXXX** *is 4-5-digit Bioclinica study code which is printed on the top right corner of Cross Calibration Phantom Log (see page I-**Error! Bookmark not defined.** for location of this code)*

14.3 Phantom Scanning and Analysis Overview

- Phantoms are to be scanned without repositioning 10 times each.
- Phantom scan analysis is **NOT** required.
- Phantom scans should be recorded on the Cross Calibration Phantom Log shown below.

Form 14-1: Example—Cross Calibration Phantom Log

All header information and Phantom ID numbers will be pre-printed on the form by Bioclinica

BIOCLINICA®

CROSS CALIBRATION PHANTOM LOG

Sponsor:	[Sponsor]	**Study Code:**	[4-digit Study Code]
Protocol Number:	[Protocol Number]	**Site ID:**	[Site Number]
Scanner Type:	[Scanner Make and Model]	**Scanner ID:**	[Scanner ID]

Scan		Filename	Scan Date	Mode
[Spine Phantom or BFP or BBCP] ID [XXXX]	1			
	2			
	3			
	4			
	5			
	6			
	7			
	8			
	9			
	10			
Block Phantom ID [XXXX] if applicable	1			
	2			
	3			
	4			
	5			
	6			
	7			
	8			
	9			
	10			

DXA facility completes this table as each phantom is scanned

DXA Facility completes the signature block prior to sending to Bioclinica.

Printed name of person completing form _____ Title _____

Signature _____ Date (DD-MMM-YYYY) _____

PLEASE REVIEW FORM TO ENSURE FORM IS COMPLETE PRIOR TO SENDING TO BIOCLINICA

Bioclinica • 11731 NE Glenn Widing Drive • Portland, OR 97220 • Fax: +1.503.284.3357 • Email: IQC@bioclinica.com

14.4 Phantom Positioning and Scan Acquisition by Phantom Type

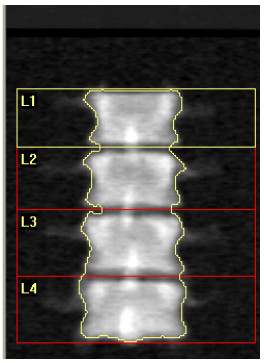
Hologic Spine Phantom

Positioning

- Center the phantom on the scanner table
- Leave the scanner pad on the table
- Position L4 towards the foot end of the table (a black star or dot indicates the L4 end)
- When centered, position the laser light over the black star or dot on the Spine Phantom (see picture)

Scan Acquisition

- Scan the Spine Phantom as Lumbar Spine
- Use a scan mode consistent with study subject scan mode for this study
  - Do not use fast, turbo or express modes
- Set the scan length as follows:
  - 6 inches or 15 cm



- Allow the scan to finish automatically ensuring that no air has been acquired
- Rescan if the phantom is not centered, vertebrae are missing or shortened, and/or there is air in the scan
- **Repeat** the scan 9 additional times without repositioning the Spine Phantom between scans
- Before removing the phantom from the scanner table, check that all 10 scans were properly acquired
- **Note:** Estimated time effort for the entire process is 30 minutes.

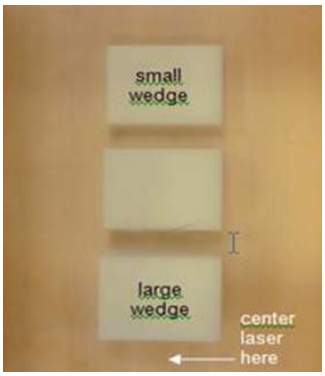
Scan Analysis

- Scan analysis is **NOT** required

Scan Documentation

- Record scans on the Cross Calibration Phantom Log Form 14-1 on page I-21.

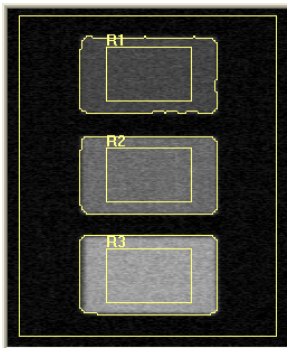
Hologic Block Phantom



Positioning

- Center the phantom on the scanner table
- Leave the scanner pad on the table
- Position the largest wedge towards the foot end of the table (view the block phantom from the side)
- When centered, position the laser light in the same place as for the Hologic Spine Phantom - the black star or dot is not present on Block Phantom (see picture)

Scan Acquisition



- Scan the block phantom as sub-region
- Use a scan mode consistent with study subject scan mode for this study
  - Do not use fast, turbo or express modes
- Set the scan length as follows:
  - 6 inches or 15 cm
- Allow the scan to finish automatically ensuring that no air has been acquired
- Rescan if the phantom is not centered, vertebrae are missing or shortened, and/or there is air in the scan
- **Repeat** the scan 9 additional times without repositioning the block phantom between scans
- Before removing the phantom from the scanner table, check that all 10 scans were properly acquired
- **NOTE:** Estimated time effort for the entire process is 30 minutes.

Scan Analysis

- Scan analysis is **NOT** required

Scan Documentation

- Record scans on the Cross Calibration Phantom Log shown on page I-21

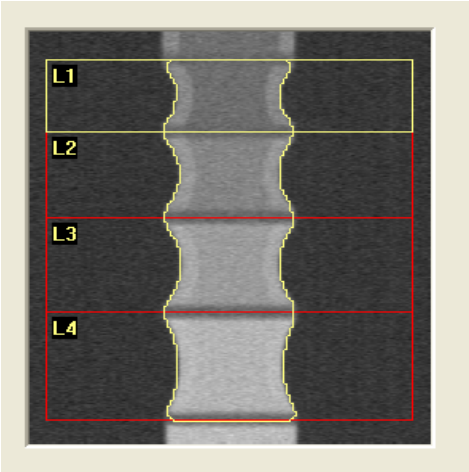
Bona-Fide Phantom (BFP)

Positioning

- Center the phantom on the scanner table with the word “Top” label nearest the head of the scan table. Move the straps of the cloth bag out to the sides of the phantom
- Leave the scanner pad on the table
- When centered, position the laser light just below the bottom of the BFP (near the center of the L5 region)

Scan Acquisition

- Scan the BFP phantom as Lumbar Spine
- Use a scan mode consistent with study subject scan mode for this study
  - Do not use fast, turbo or express modes
- Set the scan length as follows:
  - 6 inches or 15 cm



- Allow the scan to finish automatically ensuring that no air has been acquired
- Rescan if the BFP phantom is not centered, vertebrae are missing or shortened, and/or there is air in the scan
- **Repeat** the scan 9 additional times without repositioning the BFP Phantom between scans
- Before removing the BFP phantom from the scanner table, check that all 10 scans were properly acquired
- **NOTE:** Estimated time effort for the entire process is 30 minutes.

Scan Analysis

- Scan analysis is **NOT** required

Scan Documentation

- Record scans on the Cross Calibration Phantom Log Form 14-1 on page I-21.

Body Composition Phantom (BBCP)

Assembly and Positioning - **BIOCLINICA IS NOT RESPONSIBLE FOR ANY BODILY INJURY OR OTHER DAMAGES RESULTING FROM USE OF THIS DEVICE.**

Remove from case

- Two people are recommended for assembly.
- Do not attempt to lift the phantom when it is assembled.
- The phantom should be removed from its case in pieces prior to assembly. The BBCP will arrive in two components, a top and bottom half.
  - Do not attempt to lift the phantom assembled directly from the case

Assemble on table

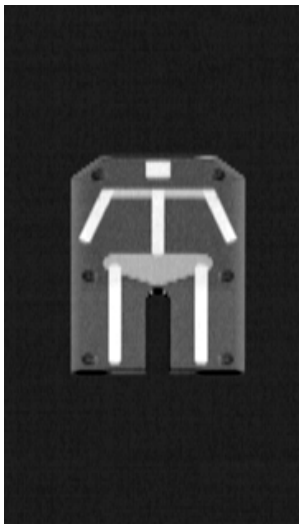
- Place the bottom BBCP half on top of the table pad at the table center. Assemble the BBCP labeled "Top" onto the bottom half, making sure the pegs align so that there is no space between the two components.
- Place the BBCP in the middle of the table. The phantom should be parallel to the long axis of the table and the head located toward the head end of the table.

Scan Acquisition

- Tissue Bar (Step Wedge phantom) Acquisition

  For scanners that have a tissue bar or step wedge phantom:

  - **Older Hologic models**: The tissue bar must be scanned on the table with the phantom; refer to the DXA Machine Operator's Manual for tissue bar scan acquisition instructions.
  - **Newer Hologic models**: The tissue bar must not be scanned with the phantom, but must be scanned separately once a week; refer to the DXA Machine Operator's Manual for tissue bar scan acquisition instructions.



For scanners without a tissue bar, no separate calibration

needs to be done.

- Scan the BBCP phantom as Whole Body
- Use a scan mode consistent with study subject scan mode for this study.
  - Do not use fast, turbo or express modes.
- Accept the default scan length and scan width.
- Allow the scan to finish automatically.
- Inspect the scan image to ensure that the scan is centered, parallel with the long axis of the scanner table, and that the head was completely acquired and is at top of the image.
  - Rescan if the phantom is not centered, the head is missing or shortened, the phantom is upside down, and/or there is air in the scan.
- **Repeat** the scan 9 additional times without repositioning the phantom between scans.
- Before removing the phantom from the scanner table, check that all 10 scans were properly acquired.
- **NOTE:** Estimated time effort for the entire process is 30 minutes.

Scan Analysis

- Scan analysis is **NOT** required

Scan Documentation

- Record scans on the Cross Calibration Phantom Log Form 14-1 on page I-21.

14.5 Sending Phantom to Next DXA Facility

When a DXA Facility has completed scanning the applicable phantoms, the phantoms will need to be collected by the courier for delivery to the next DXA Facility. The DXA Facility should contact the courier and follow any packing instructions. Courier contact information and instructions are included in the cross calibration materials sent by Bioclinica.

14.6 Data Submission and Scan Archiving

Submit the following items to Bioclinica IQC :

1. Individual scan images copied to electronic media labeled with cross calibration disk sticker(s)
2. Completed Cross Calibration Phantom Log form
3. Archive the scans at your facility onto external media or a server.
4. Send the disk(s) and IQC Transmittal Form to the Bioclinica Portland, Oregon, USA office per the instructions provided in study-specific materials.

OR

Submit data electronically through SMART Portal*

*For technical support, please contact our HelpDesk team.
Contact information is located in the study specific Quick Reference Guide.

Note: Contact your Bioclinica Study Team to acquire your instructions and online password to utilize the SMART Portal. It is not necessary to send any hardcopy materials to Bioclinica when submitting data online. Patient data should be uploaded under the study code and site number, while IQC, Machine Equivalence or Cross Calibration data should be upload under the DXA IQC Submission or IQCS-0003 study, and scanner ID (unless alternate study specific procedures have been provided)

Please notify the IQC department with any questions or concerns with submitting Cross Calibration data at IQC@bioclinica.com

(Page intentionally left blank)

APPENDICES

SECTION X

TABLE OF CONTENTS

1 APPENDIX A: SCAN MODES

Scan mode can have an effect on bone density data. For consistency, use the modes listed below for the various scanner models. If the image quality appearing while scanning a subject is not of good quality, stop the scan and check that the scan mode is appropriate; if necessary, try a different scan mode.

- Use the same scan mode used at baseline at all follow-up visits; a change in scan mode will require a follow-up scan to be repeated.

1.1 Hologic—Windows

1.1.1 QDR-4500, Delphi, Discovery and Horizon Series

DO NOT USE the Express, Quick View, Turbo, Fast and Survey modes.

Site	Scan Mode
Lumbar Spine	Array
Femur	Array
Forearm	Left (Right*) Forearm
Whole Body	Whole Body (default)

* Scan forearm indicated in study-specific materials.

1.1.2 Explorer Series

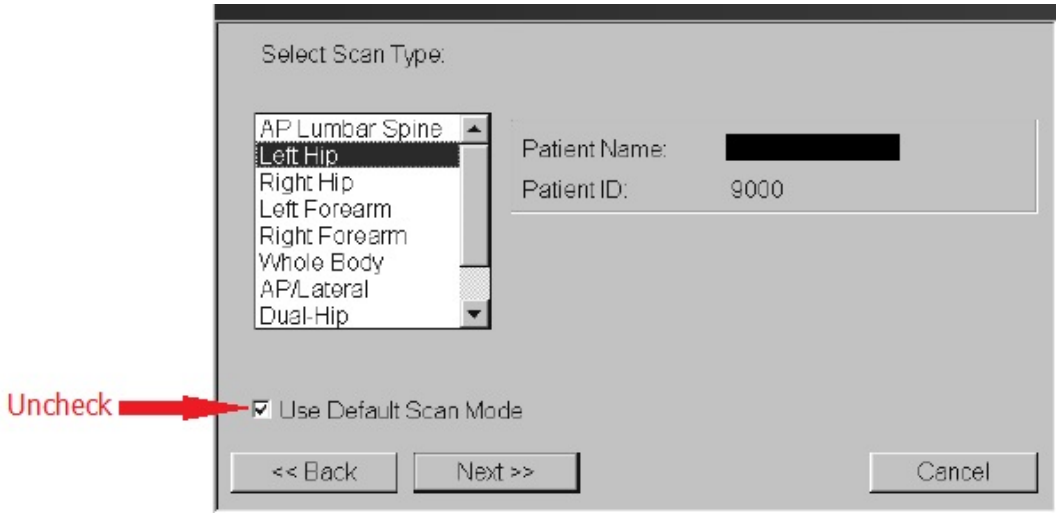
DO NOT USE the Express, Quick View, Turbo, Fast and Survey modes.

Site	Scan Mode
Lumbar Spine	Detail
Femur	Explorer
Forearm	Left (Right*) Forearm
Whole Body	Whole Body (default)

* Scan forearm indicated in study-specific materials.

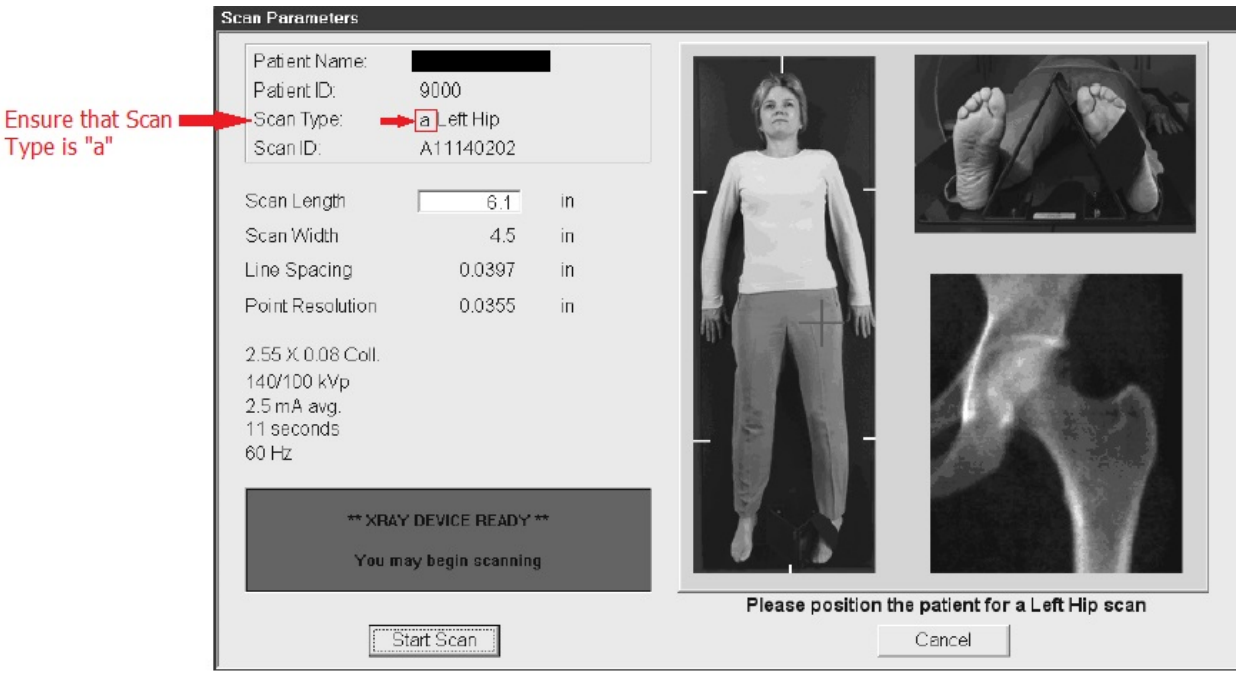
1.2 Changing Scan Mode from Default

1. After selecting a patient and clicking Next, Select Scan Type window will appear. Uncheck “Use Default Scan Mode”



2. Click Next and select the appropriate scan mode as indicated above. Click Next.

3. Confirm the scan mode selected by looking at the “Scan Parameters” screen.



2 APPENDIX B: COPYING SUBJECT IMAGES TO ELECTRONIC MEDIA

Below are step-by-step instructions for copying the electronic scan images to an electronic media or desktop location.

2.1 Hologic—Windows

1. Start from the main screen of the Hologic software.

2. Put the electronic media in the drive, or create a location on your desktop (for writing scans to a CD or submitting data electronically through SMART Portal).

3. From the menu at the top of the screen select the following (cascading menu):

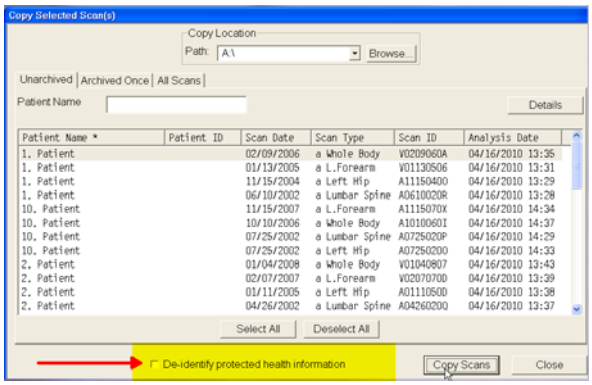
   - Archive

   - Copy Scans

4. At the top of the screen next to **"Copy Location"**, select the disk drive that contains the blank electronic media or select the desktop location.

5. Select the scans to copy; hold the CTRL key to select more than one scan.
   - **Please do not copy more scans per disk than can be clearly entered on the Bioclinica-provided disk labels, if submitting through courier.**

6. Be sure that the check box at the bottom of the screen next to **"De-Identify protected health information" IS NOT checked.**



7. Click “Copy Scans” at the bottom of the screen and follow the prompts.
8. Use the CD writing software installed on the computer to write the files to a CD.

Ensure that you remove the files from your desktop location when complete, to avoid sending the same files in future submissions

3 APPENDIX C: COPYING THE IQC DATABASE FILE TO ELECTRONIC TRANSFER MEDIA

3.1 Hologic—Windows

Below are step-by-step instructions for finding, generating and copying the phantom database file needed for IQC: the QC **Archive.mdb** file.

1. Start from the main screen of the Hologic software.

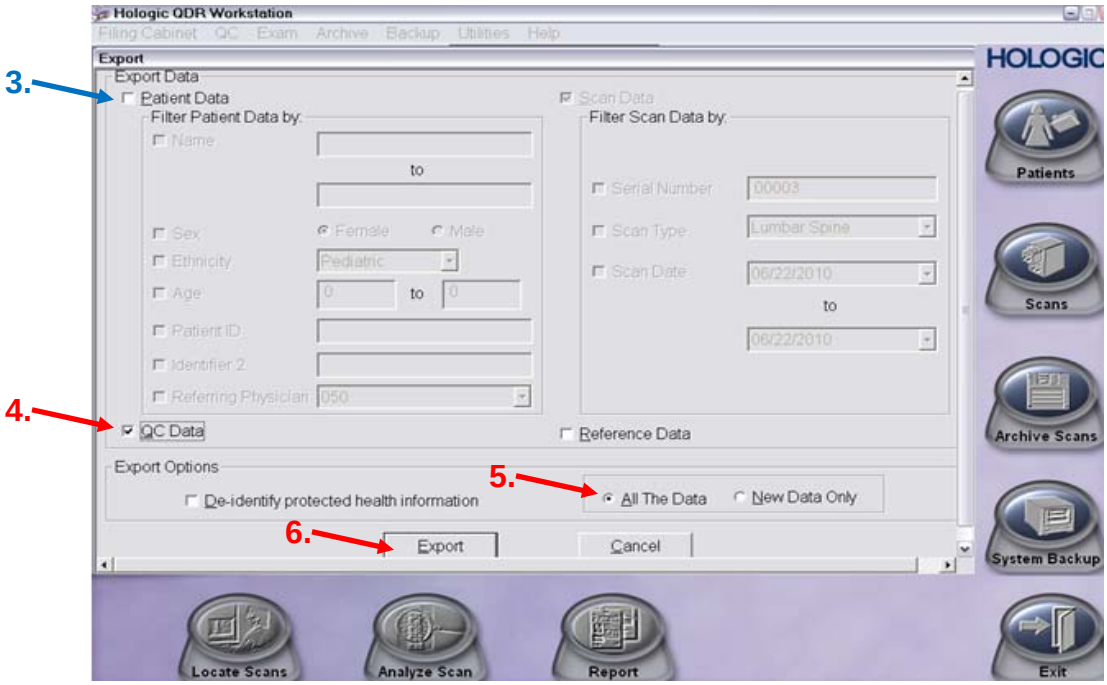
2. From the menu at the top of the screen select the following (cascading menu):
   - Utilities
   - Database Tools
   - Export

3. Remove the check on "**Patient Data**".

4. Place a check next to "**QC Data**".

5. Select "**All the data**" under Export Options.

6. Click on **Export**. It may be necessary to scroll down on the window to locate this button.



7. Create a desktop location (for writing scans onto a CD or submitting data electronically through SMART Portal), OR
   Insert the electronic media into the drive.

8. In the Window that appears, select the desktop location or destination drive under "**Save In**" (e.g. 'A: 3 ½" floppy').

9. Type **QC ARCHIVE** for the filename.

10. Click **Save**. It may take a moment to write the data to the media or location.

11. Check the contents of the desktop location or disk:
    a. Exit to the Windows desktop.
    b. Double-click on the **"My Computer**" icon.
    c. Double-click the drive that contains the media on which the data was saved.
    d. If the file **QC Archive** appears, the export routine was successful. (note: the file may show an extension of .mdb depending on the configuration of the computer's Windows properties.)

12. For copying file to CD:
    a. Locate the file on your desktop location.
    b. Insert the CD.
    c. Open the drive that contains your CD (e.g. D: drive)
    d. Copy the QC ARCHIVE file from desktop to your CD drive.
    e. Use the CD writing software installed on the computer to write the file to the CD.
    f. To verify the file has been copied to the CD, put the CD back in the drive, open the 'View' tab, select 'Refresh', the file should appear in the window, **do not open the file** as this can corrupt the data.

13. Remove the media and label it with the IQC electronic media label included the **Scanner ID number**.

    Ensure that you remove the files from your desktop location when complete, to avoid sending the same files in future submissions

14. Send the disk(s) and IQC Transmittal Form to the Bioclinica Portland, Oregon, USA office per the instructions provided in study-specific materials.

OR

Submit data through SMART Portal*

<u>*For technical support, please contact our HelpDesk team.</u>
<u>Contact information is located in the study specific Quick Reference Guide.</u>

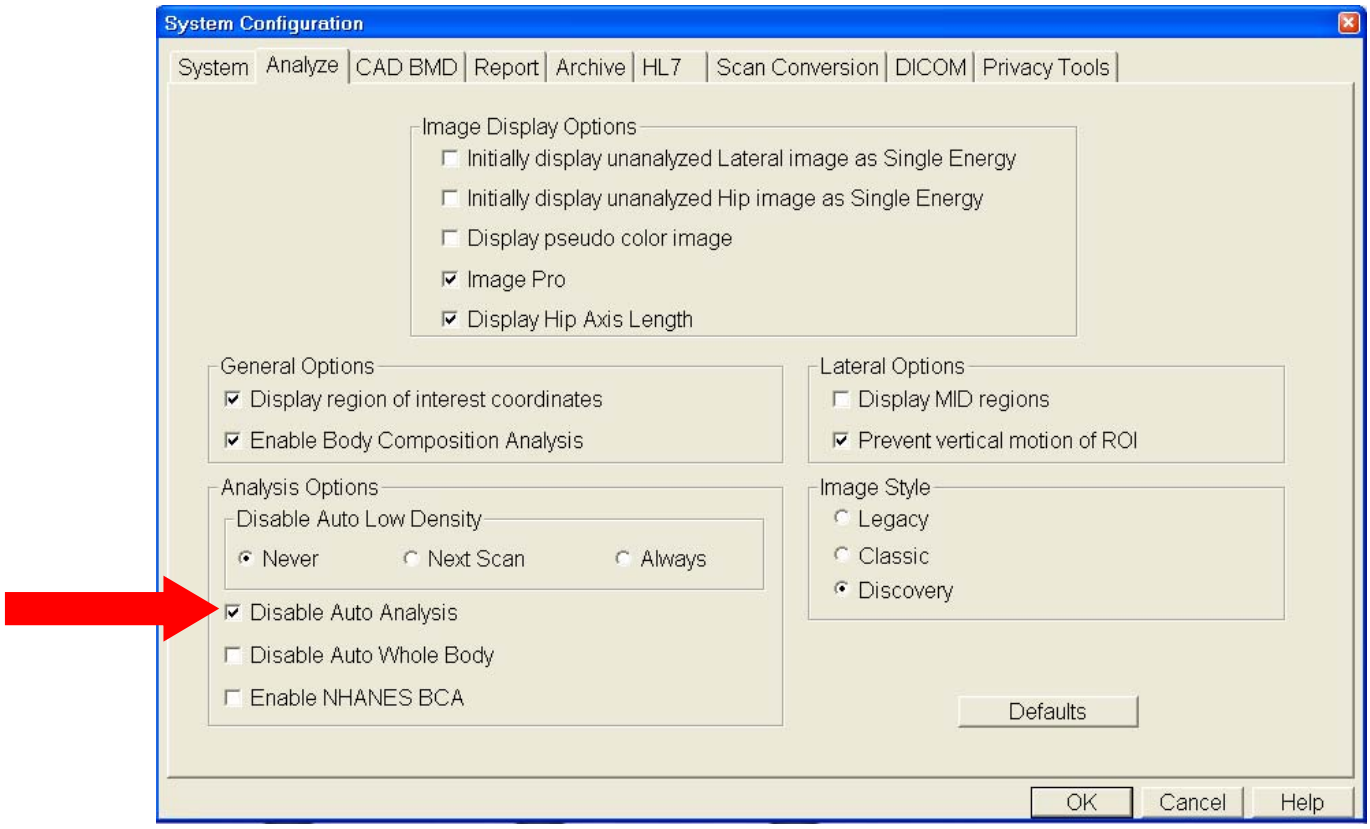
Note: Contact your Bioclinica Study Team to acquire your instructions and online password to utilize the SMART Portal. It is not necessary to send any hardcopy

materials to Bioclinica when submitting data online. Patient data should be uploaded under the study code and site number, while IQC data should be uploaded under the DXA IQC Submission or IQCS-0003 study, and scanner ID (unless alternate study specific procedures have been provided)

Please notify the IQC department with any questions or concerns with copying IQC data at IQC@bioclinica.com

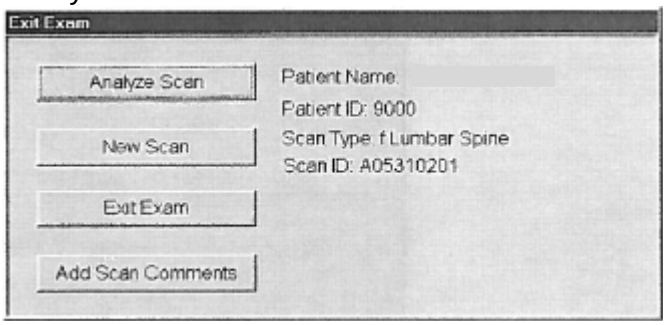
4 APPENDIX D: DISABLING THE AUTO-ANALYSIS FEATURE—HOLOGIC WINDOWS

While in the "System Configuration" window and on the "Analyze" tab, be sure the "Disable Auto-Analysis" box **is checked.**



4.1 Avoiding Analysis after Acquisition of a New DXA Examination

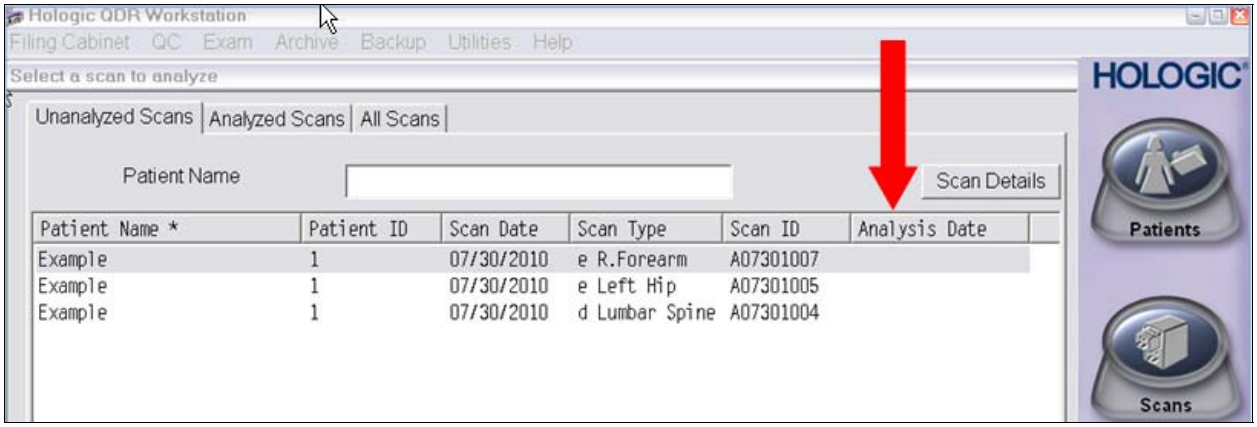
Immediately after the new DXA examination is complete the "Exit Exam" window will display. Be sure to click on the "Exit Exam" button in order to avoid proceeding to the analysis screen.



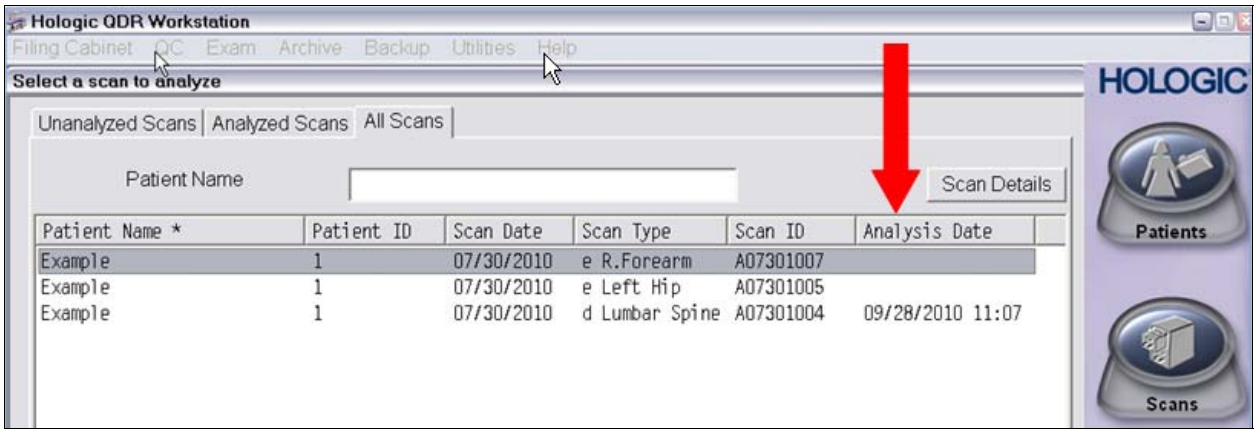
4.2 Verifying the Status of Analysis

The status of analysis can be verified by accessing the “Unanalyzed Scans” tab from the “Analysis” menu. Only scans that are unanalyzed will appear in the “Unanalyzed Scans” tab. It is also possible to view both analyzed and unanalyzed scans from the “All Scans” tab.

The example below demonstrates that all of the scans listed on the “Unanalyzed Scans” tab do not have an analysis date.



The example below demonstrates how both unanalyzed and analyzed scans appear on the “All Scans” tab.



If the DXA scan is inadvertently or intentionally opened the software will perform an Auto-Analysis if the Auto-Analysis feature has not been disabled in the software configuration menu and all steps of the analysis are performed. This analysis may or may not be valid as further review by properly trained staff is needed to ensure the accuracy of an Auto-Analysis.

The user can click on the “Global ROI” button at the top of the screen and then cancel out of the analysis in order to preserve the unanalyzed state.

4.3 Unanalyzing the Analyzed DXA Scan

A DXA scan cannot be unanalyzed in this software. The DXA technologist may contact their Hologic representative for further instruction.