

## **Chapter 8**

### **PHOTOGRAPHIC PROCEDURES**

#### **8.1 INTRODUCTION**

Photography is the principal method used in the AREDS to document morphologic status of the retina and the lens at entry into the study and during follow-up. Thus, obtaining photographs of uniformly good quality is a very high priority. Protocols for taking the photographs and evaluating their quality are set forth in this chapter, as are procedures for certification of photographers and for communication between photographers and the Reading Center.

During the initial part of Phase I, fundus and red reflex photographs taken with the Zeiss fundus camera were required for all participants at the screening visit. On the basis of the experience gained, procedures were modified following the 4/18/91 Clinic Directors' meeting. This chapter describes these modified procedures, which are being used during Phase II for all participants.

Procedures for lens photographs with the Neitz retro-illumination and Topcon slit lamp cameras are also included in this chapter. These photographs are to be taken of all participants (except for pseudo- or aphakic eyes) whenever they undergo fundus photography during Phase II.

#### **8.2 FUNDUS AND RED REFLEX PHOTOGRAPHS**

Fundus and red reflex photographs are taken with the Zeiss FF-series fundus camera, using a transparency film type approved by the Reading Center. Currently approved film types are Kodachrome (ASA 25 and ASA 64) and Ektachrome (ASA 64 and ASA 100). Other film types may be used only with explicit approval by the Reading Center, based upon a review of samples of photographs taken with both the proposed film and Kodachrome or Ektachrome of subjects with at least some drusen. Fujichrome is an acceptable film only if the Professional varieties (ISO 100 or less) are used. The amateur Fuji films are not acceptable for AREDS photography due to its pronounced reddish cast, which tends to mask subtle drusen. Once a Clinical Center has established its choice of film type for Phase II of the AREDS, to maintain consistency further changes are strongly discouraged and should be discussed with the Reading Center in advance.

As soon as the photographs have been processed, they should be reviewed briefly for quality by the photographer (see Section 8.2.4). Photographs are labeled, dated, and assembled in the plastic sheets as outlined in Section 8.2.5. The photographs and the completed shipping list are sent to the Reading Center.

The Qualifying Visit photographs are graded at the Reading Center for eligibility group, photographic quality, and overall severity of media opacities. If the Reading Center judges photographic quality to be inadequate in either or both eyes, the Clinical Center will be given the

option of submitting new sets of photographs of those eyes, if the photographer believes that better quality photographs are not precluded by media opacities or poor pupillary dilation.

### 8.2.1 Fundus Photographs, Standard Fields

Stereo pairs of modified Field 1 (Field 1M) and Field 2 are required, as well as a single photograph of modified Field 3 (Field 3M). Exhibit 8-1 illustrates the field locations. Field 1M is centered on the temporal edge of optic disc. Its slight temporal decentration is designed to include the center of the macula near the edge of the field, where illumination is less direct, allowing better recognition of pigmentary abnormalities. Field 2 is centered 1/8-1/4 disc diameter above the center of the macula so that the central camera artifact does not obscure the center. Field 3M (a single non-stereo photograph) is centered 3/4 to 1 disc diameter temporal to the center of the macula. This field provides another perspective of the macula, which is taken through the clearest available optical pathway with the aim of obtaining maximum image sharpness uncompromised by the need for stereo separation required between the two members of the stereo pair of Field 2.

### 8.2.2 Fundus Photographic Technique

In taking stereo photographs, careful attention should be paid to several principles. First, the pupil should be well dilated, preferably to 6 mm or more (for the Qualifying Visit, dilation to at least 5 mm is required), and the cornea should be undisturbed by prior examination with diagnostic contact lens. The participant should be rested and not exhausted by too many other examinations or annoyed by long waiting. The photographer should have adequate time to do careful work.

Constant attention must be paid to keeping the cross hairs in the camera ocular in focus, otherwise the photos will be out of focus. Proper camera-to-eye distance should be maintained to avoid haziness and artifacts.

An Allen stereo separator or manual lateral movement of the camera may be used to obtain the required, nonsimultaneous stereo pairs. If the manual method is used, the camera should not be rotated; instead, it should be moved from left to right with the joystick (or by sliding the camera base on its table, if preferred). It is customary to take the left member of the pair first, but this is optional depending upon local clinical practice. The first member of the pair is taken as far to one side of the pupil as possible, while maintaining good illumination and a clear image. If the separator is used, it is then flipped to the other side and the second photograph is taken if its quality is good. If the quality is not good, refocusing with spherical or astigmatic correction and/or slight vertical movement of the camera (to avoid lens opacity) may be needed. Such vertical movement will not impair the stereoscopic effect. Somewhat less than optimal focus and clarity is acceptable, if necessary, in the second member of the pair in order to maintain the stereoscopic effect. The same principles apply when the manual technique is used. If the stereo separator is used, it should be set between 2.25 and 2.75 mm. About 2 mm is the minimum separation between members of the stereo pair to be aimed for when moving the joystick or sliding the camera.

Frequent inspection and cleaning of the front surface of the objective lens is essential to remove dust and debris, to avoid photographic artifacts.

### 8.2.3 Red Reflex Photographs

There are three reasons for obtaining red reflex photographs. First, they allow the grader to estimate whether lens opacities or poor pupillary dilation are likely to impair the quality of the retinal photographs. Second, they may be used as an aid to interpreting the slit lamp and Neitz photographs, much as color photographs are useful adjuncts to fluorescein angiograms. Finally, they are used to grade iris pigmentation (color).

8.2.3.1 Red reflex photographs. To best document lens opacities, the red reflex photograph should be magnified until the diameter of the cornea measures approximately 13 mm measured on the film. This degree of magnification is high enough to show lens opacities in sufficient detail, but not so high that depth of field is reduced inordinately. The photograph should be focused on any lens opacities present, or in their absence upon the pupillary margin of the iris. It should also have sufficient stereo effect to allow the grader to determine the location of any opacities in the anterior - posterior dimension.

Described below is the procedure for taking the red reflex photograph using a Zeiss fundus camera. Different models of the camera might require a somewhat altered procedure. The photographer is asked to use his/her discretion to achieve a result similar to the example photograph.

8.2.3.2 Magnification and focus. To obtain suitable magnification, the auxiliary "plus" lens system (+16/+33) of the camera is put in place. The focus knob is positioned near the end of its travel, increasing the distance between the camera lens and the film plane, and the joystick placed in the straight vertical position. Then the headrest is pushed away from the camera until the lens opacities (or iris margin if there are no opacities) are approximately in focus. The joystick may then be used to refine the focus before the picture is taken (use of the focusing knob will change magnification). The participant is asked to open both eyes very widely. The lids may should be gently retracted if necessary so that the entire cornea is visible.

8.2.3.3 Stereo effect. Only limited stereo effect can be obtained in the Zeiss red reflex photographs, and this effect is usually limited to the area in and near the lens. It appears that the best effect is obtained by moving the camera laterally about 3 mm between exposures. At the magnification recommended, this can usually be done without any undesirable camera rotation. The first photograph should be taken about 1.5 mm to the left of the center of the pupil. The second photograph is taken at approximately the same distance to the right of the center of the pupil. This can usually be done without excessive image disparity in the area covered by the left and right members of the stereo pair. The lateral shift can be obtained by moving the joystick, sliding the camera, or using the Allen stereo separator.

8.2.3.4 Position of the optic nervehead. Some photographers follow the practice of placing the optic nervehead behind the lens to obtain greater retro-illumination. For red reflex photographs taken with the fundus camera this is undesirable, because the major vessels on or near the optic nervehead are often visible enough to interfere with the assessment of lens opacities. The fixation target may be used to direct the subject's gaze in the primary (straight ahead) position, so that the disc does not appear.

## 8.2.4 Photographic Quality

Without good photographic quality, the maculopathy status of participants cannot be evaluated reliably. AREDS maintains two procedures to promote and ensure satisfactory quality: a mandatory certification program for fundus photographers and an ongoing quality review program at the Reading Center to provide feedback to photographers and to issue quality reports to the study.

8.2.4.1 Certification for fundus photography. Photographers joining the study during Phase II must receive provisional certification before they can take photographs of AREDS participants. To become provisionally certified, photographers must submit photographs of four eyes of non-study participants and will be provisionally certified if all of these are of at least fair quality. The eyes selected for fundus certification should allow reasonably clear visualization of retinal features. (Photographers nominated by their principal investigators to perform fundus photography during Phase I are considered to be at least provisionally certified for Phase II, unless they have not taken any photographs during Phase I.) Photographers whose photographs are consistently of good quality (overall grade of good or fair in at least 75% of a series of at least 20 eyes of AREDS participants) will become "fully certified." If photographic quality for a fully certified photographer falls below this criterion, certification will revert to provisional status, and special attention will be paid to interacting with the photographer to improve quality (see Section 8.4).

8.2.4.2 Fundus photographic quality grading. Each set of photographs should be assessed briefly for quality by the photographer before being sent to the Reading Center. All photographs are assessed for quality at the Reading Center, and feedback is given to the photographers as needed to help with resolution of any problems.

The Reading Center assessment of fundus photographic quality is recorded on the form shown as Exhibit 15-1. An initial grading of overall quality, including need for retakes, is carried out on all photo sets submitted. (At the same time the grader also makes a preliminary determination of maculopathy status, and for qualifying visit photographs, of study eligibility.)

Specific criteria for the evaluation of fundus photographic quality are presented in Appendix 8A.

8.2.4.3 Retake policy for fundus photographs. Because the need for retakes of Qualifying Visit photographs is connected to AMD Category, the latter will be assessed on the Preliminary Grading Form, as well as the need for retakes. Below are the photographic quality requirements for each AMD Category. If photograph quality of either eye is found to be less than the required grade and media opacities are not considered sufficient to preclude better quality photographs, the Reading Center will request retakes of that eye. These retakes must be reviewed at the Reading Center before eligibility can be determined and the participant entered into the study. However, if lens opacities are considered sufficient to explain the reduced quality, the patient will be considered ineligible.

AMD Category 1 or 2 (maculopathy milder than large or extensive intermediate drusen, noncentral geographic atrophy, or end-stage AMD)

Retinal photograph sets of each eye must be of at least fair quality.

AMD Category 3 (large or extensive intermediate drusen or noncentral geographic atrophy in either eye)

Retinal photograph sets of each eye must be of at least borderline quality.

AMD Category 4 (advanced AMD or a visual acuity score of 73 or less attributable to AMD in one eye, fellow eye eligible for AMD Category 1, 2 or 3)

Photograph quality of eye(s) without advanced AMD must be at least borderline. The photograph quality of the eye with advanced AMD may be inadequate to grade other features of maculopathy, as long as it can be determined that advanced AMD is present.

During follow-up, retakes will be requested when photographs are evaluated as less than borderline, and explanatory factors such as media opacity are not noted. These may be obtained at a specially scheduled photography session if convenient, otherwise at the next scheduled visit. If retakes are requested, Clinical Center staff should use their discretion as to whether a request to the participant for repeat photographs will jeopardize that participant's cooperation with the study. If the participant returns for retakes and he or she experiences a 10-letter drop in vision, document the event but do not take extra photographs to fulfill the prior retake request. Notify the Reading Center to grade what they can and notify the Coordinating Center so an exception for the retakes can be granted.

#### 8.2.5 Duplication and Shipment of Photographs

Duplication of the fundus photographs required by the protocol and their retention at the Clinical Center are optional. The original fundus photographs, properly labeled, dated, and assembled in plastic sheets for each participant examination (see Exhibits 8-2 and 8-3), are mailed to the Reading Center with the shipping list.

Plastic sheets should be clear and stiff so as not to interfere with grading. Not allowed are sheets with a translucent (rather than transparent) back or "archival" polyethylene sheets.

### 8.3 LENS PHOTOGRAPHS

The Neitz retro-illumination and Topcon slit lamp cameras have been modified to increase the reproducibility of lens photographs among Clinical Centers, among participants at each Center, and between visits of the same participant. The Neitz camera modifications reduce variation in illumination by controlling fixation and provide a mechanism for focusing the photographs at standardized depths within the lens. The Topcon camera modifications provide a slit beam of standard dimensions and orientation, and, by controlling fixation, produce comparable slit lamp photographs for right and left eyes.

### 8.3.1 Camera Modifications

#### 8.3.1.1 Topcon SL-6E Photo Slit Lamp Camera.

a) The slit width and height are fixed at 0.3 and 9.0 millimeters, respectively. The binocular assembly, with the magnification changer, is fixed perpendicular to the cross-slide base. The slit beam is locked at an angle of 45 degrees (Exhibit 8-4) to the assembly, and remains always at the photographer's left. The magnification changer is fixed at 16X magnification and the fill-in illuminator is disconnected.

b) Fixation for each eye is controlled by a separate light emitting diode (LED). The two LEDs are suspended through a ring mounted around the camera objective lens (Exhibit 8-5). The LEDs, 1 mm in diameter and of approximately equal brightness, fall on an imaginary horizontal line bisecting the front objective lens. The LED for fixation of the right eye is positioned directly between the two viewing lenses. The LED for the left eye is mounted approximately 11 mm to the right of the first LED, so that the left eye is turned inward by twice angle alpha, the angle between the optical and visual axes of an average emmetropic eye (Exhibit 8-6). This rotation is necessary so that the path of the slit beam through the lens is symmetrical in the two eyes, although it comes from the temporal side of the right eye and from the nasal side of the left eye, as shown in Exhibit 8-6 (a scaled diagram based on Gullstrand's schematic eye, with a diameter of 24.3 mm and a nodal point 17 mm from the posterior focal point). The LED viewed by the participant's left eye is in the optical pathway of the observers left eye (Exhibit 8-6), but this has little effect on stereo viewing and no effect on the photograph, which is taken through the right side of the biomicroscope. Test slit lamp photographs using these fixation targets have confirmed that the sections of lens illuminated in right and left eyes are similar.

c) A small switch box, mounted above the magnification lens changer assembly, allows the photographer to switch on the appropriate fixation LED for the eye being photographed. The switch is pointed to the participant's right for photography of the right eye and to the participant's left for photography of the left eye.

#### 8.3.1.2 Neitz CT-R Cataract Camera.

a) A linear potentiometer (in effect, an electronic ruler) capable of measuring anterior - posterior movement to an accuracy of .01 millimeters is attached to the wheel cover on the right hand side of the camera platform. The measuring arm rides over the cross-slide base axle and is positioned so that the operator experiences no restriction in camera movement. A digital display unit is mounted on top of the CT-R camera body in place of the Polaroid camera back. The initial (anterior) photograph is focused on the edge of the pupillary margin with the digital display set at zero. As the camera is moved forward, to focus deeper into the lens, the distance traveled is displayed in the window of the potentiometer. The second photograph is taken between 3 and 5 mm posterior to the first, focusing clearly on any posterior subcapsular lens opacities or favoring the middle of this range if no posterior subcapsular lens opacities are observed. If posterior subcapsular opacities are present beyond the 3-5 mm range, a third Neitz photograph should be taken, clearly focused on the opacity.

b) Two blinking red fixation targets, 1 mm in diameter, one for each eye, are added to the face of the camera. These targets are positioned so that, for most eyes, the optic nerve is directly behind the lens (Exhibit 8-7), thus providing the brightest retro-illuminated image possible. Use of the fixation lights helps to standardize illumination from visit to visit and provides similar illumination for both right and left eyes. The lights are positioned on an imaginary horizontal line bisecting the center of the camera lens and are spaced 12 mm from the center of the camera lens. The camera body pivot lock is fixed with the camera perpendicular to the cross-slide base axle. With this orientation, when the visual axis is directed toward the fixation light the optic nerve is positioned directly behind the lens in the great majority of eyes. With the Neitz camera (unlike the Zeiss), this position is desirable because the increased reflectance of the optic nerve is needed to provide adequate illumination of the lens for proper exposure. Because of the shallow depth of field of the Neitz camera, the retinal vessels on the disc are sufficiently out of focus that they do not impair the view of the lens.

The target on the participant's left is illuminated when photographing the right eye, and vice versa, and the target is viewed with the eye being photographed. To prevent the gaze from shifting, the fellow eye is occluded. The occluder is affixed to the headrest and may be moved to occlude either eye. A noticeable decrease in retro-illumination is apparent if the wrong light is used.

c) The fixation lamps operate independently of the viewing lamp. This allows them to remain on when the viewing lamp is turned down or off. The photographer initially confirms fixation with the viewing lamp off. The lamp is then turned on, adjusted for adequate viewing, focus is confirmed, and the photograph taken.

### 8.3.2 Camera Maintenance

#### 8.3.2.1 Topcon SL-6E Photo Slit Lamp Camera.

##### a) Daily

The front objective lens should be inspected and, when necessary, cleaned before each participant is photographed. This is done by removing the small set screw that holds the fixation light ring to the front of the lens barrel. This ring must be carefully repositioned after the objective lens is cleaned to insure that the LEDs remain in the same horizontal plane. Orientation marks have been placed on the ring, fixation lamp control box and microscope body to aid with the alignment.

The mirror involved in the delivery of the slit beam should be kept free of dust, dirt, and finger prints. Since this is a front surface mirror, it should be wiped with a wet cloth only. It is important to remove loose dirt with compressed air or an air bulb before wiping it so that scratches are kept to a minimum. A spare mirror is provided with the microscope. The headrest and chin assembly should be kept clean with alcohol (need for this can be minimized by the use of paper chin rest pads).

The camera back should be inspected each time film is changed to remove any loose film particles, dust or dirt. Care should be taken not to damage the shutter when blowing the dirt from the camera back. Camera cables and shutter release connections should be kept tight and inspected for damage. The mounting screw between the motor drive and the camera body needs periodic tightening. A daily check of the integrity of the LED lamps should be made. The lamps were selected because of their long life and should last for the duration of the study. Should one burn out, the Reading Center will replace the LED ring. The defective ring will need to be sent to the Reading Center for repair.

The microscope is equipped with a dust cover which should be used whenever the microscope is not in use to keep dust and dirt collection to a minimum.

b) Weekly

The camera table top should be cleaned weekly with a conventional kitchen cleaner. The plastic pad under the joystick should be kept very clean to prevent sticking. This can be done with an alcohol pad followed by a tissue sprayed with a little WD-40 (or similar light lubricant). This creates a very slick surface and allows the microscope to travel freely.

c) Annually

The Topcon flash lamp should be changed annually, even if it has not burned out. This is because the aging Topcon flash lamp may produce under-exposed slitlamp images.

d) As Needed

The tracks for the microscope should be inspected and cleaned to remove loose dirt and dust that accumulate on them. This can be done by removing the protective covers and wiping a damp cloth across the teeth on the camera platform. The wheels should also be kept clean with WD-40 spray. Spare viewing and flash lamps should be stocked in each clinic for easy replacement as they burn out.

Image quality needs to be monitored throughout the life of the study. The flash lamp may discolor over time producing darker images, requiring it to be changed more frequently than annually. The Photography Protocol Monitor will alert the clinic if the flash lamp needs more frequent changing. The optical surfaces involved in the slit production need to be kept clean. The viewing lamp housing and condensing lens system (with the flash lamp attached) can be removed, cleaned and reassembled without affecting the slit width or height.

### 8.3.2.2 Neitz CT-R Cataract Camera.

a) Daily

The front objective lens is less vulnerable to dirt and dust than the Topcon SL-6E lens because it is recessed behind a front plate, giving it somewhat greater protection. However, it should be inspected and cleaned as necessary.

The observation ocular should be kept clean to provide the clearest view possible. The 35 mm camera body should be inspected and cleaned internally each time the film is changed. This is done in the same manner as for the Topcon back.

A daily check of the fixation lamps should be made. These lamps have been selected because of their long life and are expected to last the duration of the study. Should one fail, a replacement assembly will be provided by the Reading Center. The defective fixation lamp assembly will have to be sent to the Reading Center for repair.

b) Weekly

The camera table should be wiped with a damp cloth to keep it clean and free of dust and the plastic pad under the joystick should also be cleaned and treated with WD-40 spray to keep it operating smoothly. Any cleaning of the camera tracks which involves removal of the wheel cover requires disconnection of the potentiometer. The power cable is easily removed from the potentiometer. The wheel cover, with potentiometer attached, can be removed and set aside. A routine inspection for loose or frayed cables or connections should be made.

c) Monthly

The metal edges of the linear potentiometer rail should be wiped with light oil or WD-40 to keep the potentiometer moving freely. Otherwise, as the tracks become dry the camera becomes difficult to move.

d) As Needed

Routine flash and view lamp replacements should be made as these lamps deteriorate and burn out. Image quality needs to be monitored throughout the life of the study and the flash lamp changed or the optics cleaned if the images become unacceptably dark.

The Neitz seems to be particularly prone to loose screws and attachments. Periodically, any loose components should be tightened with a screw driver or Allen wrench.

Motor drive batteries should be replaced as they wear down, unless rechargeable batteries such as nickel cadmium are used. The potentiometer is powered by a battery which should last one year. The potentiometer should be turned off after each participant is photographed to prolong battery life. The liquid crystal display on the face of the potentiometer will not light if the battery is weak. A weak battery will also cause the display on the black box to fail. If the wrong mode is selected, i.e. inches rather than millimeters, the black box display will brighten and freeze to show all 8's.

The view lamp fuse is located on the bottom of the camera base and requires the removal of the potentiometer to access.

### 8.3.3 Photographic Techniques

The examiner should describe the photographic procedures to the participant prior to taking photographs. Participants are often anxious about this part of the examination, being frightened that the bright lights may cause a problem or that x-rays are used. The examiner should stress how important photography is for evaluating the lenses, that the bright lights are not harmful and that any afterimage (often associated with color changes) will fade within a short time.

High quality photographs should be obtained for every participant in the study. The presence or absence of specific lens changes will be determined based on the grading of the photographs. No part of the lens images should be lost because of interference from lids or lashes. Help should be summoned, if needed, to hold eyelids or eye lashes.

Concentration on alignment and focus is essential. When aligning the slit beam be sure that the beam is centered from 12:00 to 6:00 in order to illuminate all of the lens visible through the dilated pupil. Remember that the goal for slit lamp photographs is to illuminate the lens sulcus from 12:00 to 6:00. That means that the slit beam will strike the anterior lens surface a few millimeters to the left of center.

Log sheets for each camera should be carefully maintained. Information in the log should include date, photographer's initials, participant's name, eye photographed and any comments to be passed on to the Reading Center to explain problems encountered. It is strongly recommended that an ID frame be photographed before the lens photos are taken of each participant and that very careful records be made to prevent any mix-up between pictures taken of the right and left eyes. A routine should be established so that the right eye is always photographed first. It may be advisable to take several exposures of each lens to assure proper beam placement and focus on the sulcus.

#### 8.3.3.1 Topcon SL-6E Slit Lamp Photography.

##### a) Film, Illumination and Magnification

The following parameters are specified:

Ektachrome 200 slide film (Professional, not Elite)

Slit angle 45°

Beam width 0.3mm

Beam height 9mm

Flash intensity 5

Magnification 16X

##### b) Initial Preparation

The photograph is taken through a maximally dilated pupil. It is recommended that 2 sets each of 2.5% Neo-Synephrine and 1% Mydriacyl be instilled 2 - 5 minutes apart. The flash intensity is set to position 5 and Ektachrome 200 Professional color slide film loaded into the camera.

The photographer positions the ocular with the focusing hairs in the right ocular and adjusts it to the sharpest focus possible. The chin rest is adjusted so that the lateral canthus is in line with the black mark on the headrest support. An ID frame is taken with the participant's name or ID number. This is essential because, unlike fundus photographs, no clear landmarks exist to differentiate the right eye from the left eye. If no ID frames are taken to separate them, it becomes difficult to sort the photographs and they may be incorrectly identified.

c) Participant Fixation

The participant is asked to fixate on the red target light with the fellow eye occluded to avoid diplopia and confusion. The photographer must be certain that the correct fixation light is illuminated. The fixation light switch is set to the participant's right for photography of the right eye and to the participant's left for photography of the left eye. When the fixation lights are correctly plugged in, the center fixation light is illuminated for the right eye.

d) Slit Beam Placement and Focus

The slit beam should completely fill the pupil, vertically bisecting the central lens from 12:00 to 6:00. In the proper position, the slit beam falls on the anterior lens surface 1-2 mm to the left of center. Focus should be on the sulcus of the lens, if visible, so that the presence and extent of a central optically-clear zone can be graded. For the right eye, the red fixation target reflection will appear near the center of the sulcus. For the left eye, this reflection may appear up to 3 "fixation dot widths" further left of the anterior edge of the sulcus. The red fixation target reflection should appear out of focus (because it is reflected from the anterior lens surface). The photographer should imagine that the clearly focused sulcus, if extended superiorly and inferiorly, would contact the iris at 12 and 6 o'clock respectively. If the sulcus is not clearly visible, then the photographer must use his/her best judgement to estimate the proper position so that the degree of lens opalescence can be accurately graded.

The reflection of the mirror from the anterior lens surface (appearing at or near the posterior lens surface) should fall directly behind the lens, where it may help delineate posterior subcapsular opacities and will aid in estimating lens color.

A single, good quality slit lamp photograph is required of each lens to document nuclear sclerosis. Extra photographs should be taken if the first photograph is of questionable quality.

If an eye is aphakic or pseudophakic, no slit lamp photograph is obtained.

8.3.3.2 Neitz CT-R Retro-illumination Photography.

a) Film and Illumination

The following parameters are specified:

Ektachrome 200 slide film (Professional, not Elite)

Aperture setting 1  
Pupil size setting 8  
Flash intensity 4  
Orange contrast filter on

b) Initial Preparation

The pupil is widely dilated. Flash intensity, aperture, and pupil diameter settings are checked. Ektachrome 200 Professional color slide film is used. Precise aperture or flash settings may be adjusted at each Clinical Center to provide uniform exposures.

The photographer adjusts the ocular to focus the cross hairs to the sharpest image possible. One ID photograph is taken of the participant's name or ID number prior to photography.

The participant is seated comfortably behind the camera with chin firmly on the chin rest and forehead snugly against the headrest. The chin rest is adjusted so that the participant's lateral canthus is in line with the black mark on the headrest support.

c) Participant Fixation

The occluder is adjusted in front of the participant's left eye. The photographer selects the appropriate fixation light and instructs the participant to fixate on the flashing red light. At this point it is helpful to keep the viewing lamp intensity low or off to enable the participant to locate the target. Once fixation is confirmed (evidenced by a brighter, steady retro-illuminated image) the viewing lamp intensity can be increased to achieve clear focus.

d) Focus

The camera is focused on the iris at the pupillary margin, at 12:00 and 6:00, and the first photograph is taken with the potentiometer at zero. The circular illumination lamp should be centered in the pupil to maximize entry of light into the eye so as to produce the brightest retro-illumination. When the participant is fixating on the correct target, the entire iris edge will not be in sharp focus because the plane of the iris is not parallel to the film plane. The photographer pushes the button to initialize the potentiometer, advances the camera to scan the 3-5 mm range for opacities, and then takes the picture, focusing on posterior subcapsular opacities, if present, or using the potentiometer to focus about 4 mm posterior to the plane of the anterior photograph. If any posterior subcapsular opacities are present beyond the 3-5 mm range, a third posterior Neitz photograph is taken focused clearly on the opacity. The potentiometer readings for posterior Neitz photographs are recorded in the log book and on the slide mounts.

This procedure is repeated with the left eye, being certain to use the appropriate fixation light.

If an eye is aphakic or pseudophakic, no Neitz photographs are taken.

### 8.3.4 Lens Photographic Quality

Each set of photographs should be assessed briefly for quality by the photographer before being sent to the Reading Center. All photographs are graded for quality at the Reading Center, and feedback is given to the photographers as needed to help with resolution of any problems.

8.3.4.1 Certification for lens photography. Photographers joining the Study during Phase II must receive provisional certification before they can take photographs of AREDS participants. To become provisionally certified, photographers must submit photographs of four eyes of non-Study participants and will be provisionally certified if all of these are of at least fair quality. The eyes selected for lens certification should have lens opacities ranging from mild to extensive, with at least one eye having posterior subcapsular opacities and at least one having moderate to severe nuclear cataract. (Photographers nominated by their principal investigators to perform lens photography during Phase I are considered to be at least provisionally certified for Phase II, unless they have not taken any photographs during Phase I.) Photographers whose photographs are consistently of good quality (overall grade of good or fair in at least 75% of a series of at least 20 eyes of AREDS participants) will become "fully certified." If photographic quality for a fully certified photographer falls below this criterion, certification will revert to provisional, and special attention will be paid to interacting with the photographer to improve quality (see Section 8.4).

8.3.4.2 Photographic quality grading. Each set of photographs should be assessed briefly for quality by the photographer before being sent to the Reading Center. All photographs are assessed for quality at the Reading Center, and feedback is given to the photographers as needed to help with resolution of any problems.

Based upon assessment of photographic characteristics, the Reading Center grader assigns overall quality grades to the slit lamp and Neitz photographs. Specific criteria for the evaluation of lens photographic quality are presented in Appendix 8A.

8.3.4.3 Retake policy for lens photographs. At the Qualifying Visit, slit lamp and Neitz photographs of both eyes must be of acceptable quality upon review at the Reading Center. If any are found ungradable, retakes will be requested for that type of photograph for that eye. The photographs may be retaken at the Randomization Visit, but if they are also unsatisfactory, a special retake visit must be scheduled as soon as possible.

During follow-up, retakes will be requested when photographs are evaluated as less than borderline, and explanatory factors are not noted. These may be obtained at a specially scheduled photography session if convenient, otherwise at the next scheduled visit. If retakes are requested, Clinical Center staff should use their discretion as to whether a request to the participant for repeat photographs will jeopardize that person's cooperation with the study. If the participant returns for retakes and he or she experiences a 10-letter drop in vision, document the event but do not take extra photographs to fulfill the prior retake request. Notify the Reading Center to grade what they can and notify the Coordinating Center so an exception for the retakes can be granted.

### 8.3.5 Duplication and Shipment of Photographs

Duplication of the lens photographs required by the protocol and their retention at the Clinical Center are optional. The original lens photographs, properly labeled, dated, and assembled in plastic sheets for each participant examination (see Exhibits 8-2 and 8-3), are mailed to the Reading Center with the shipping list.

Plastic sheets should be clear and stiff so as not to interfere with grading. Not allowed are sheets with a translucent (rather than transparent) back or "archival" polyethylene sheets.

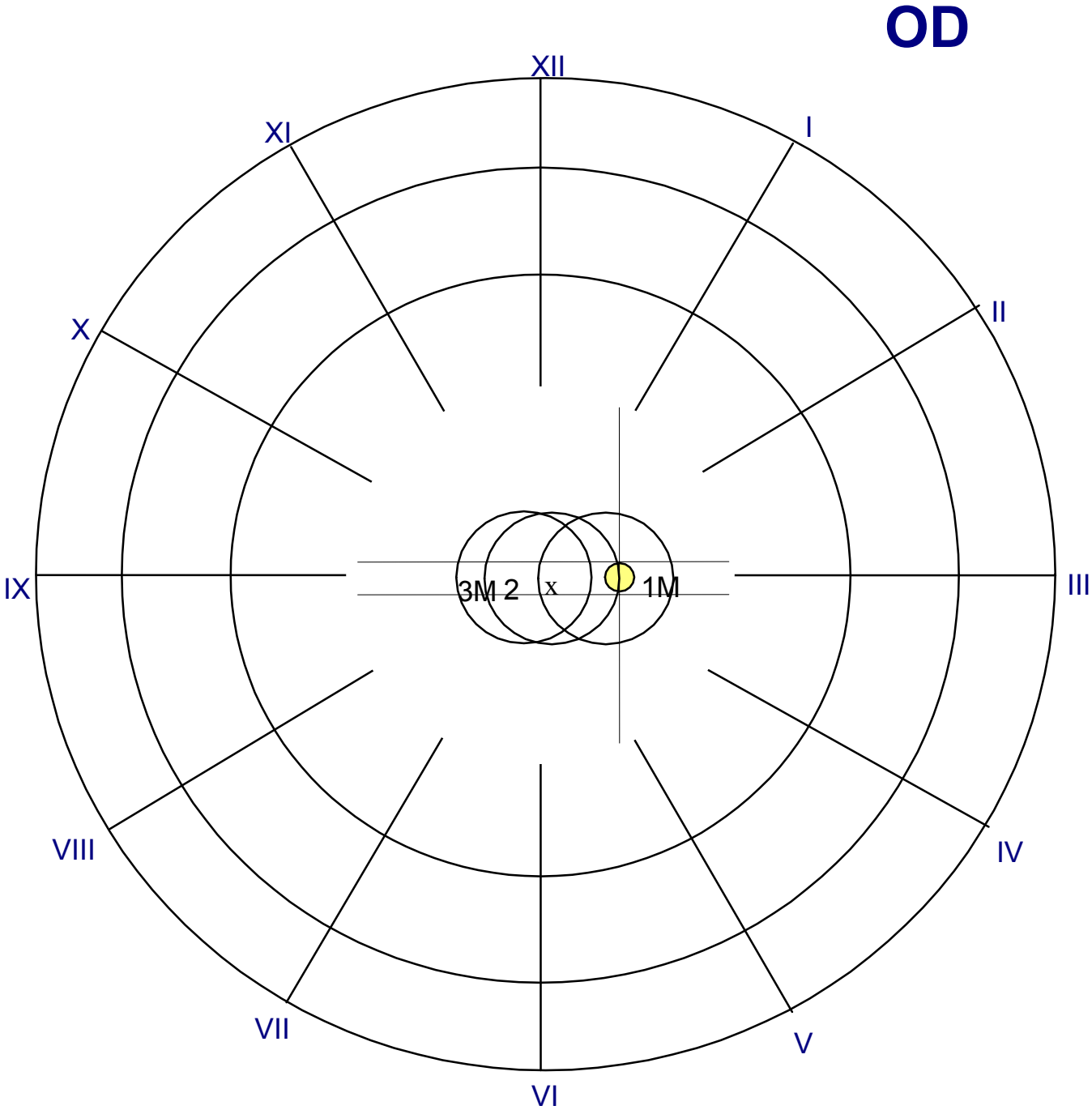
## 8.4 READING CENTER - PHOTOGRAPHER COMMUNICATION

As photographs are received at the Reading Center, they are graded for photographic quality. Quarterly, the grading staff review the quality of each photographer's work with the Reading Center photographic protocol monitor, a photographer with extensive experience of study photography. The monitor then calls the photographers by telephone to discuss any significant problems observed. This contact also allows the photographers an opportunity to ask questions or make comments. The monitor represents the viewpoints of photographers to the study as a whole.

When substantial problems are observed (particularly if a photographer has reverted from full to provisional certification), the photographic protocol monitor phones the photographer more frequently. If the problems cannot be adequately addressed by telephone, the monitor may arrange to conduct a special photographic site visit for the purpose of observing the photographer at work and demonstrating the desired technique.

Occasionally, the Reading Center issues a newsletter for study photographers, regarding issues of particular interest to them and discussing methods for obtaining optimum results.

Exhibit 8-1. Standard Fields for Fundus Photography, Right Eye

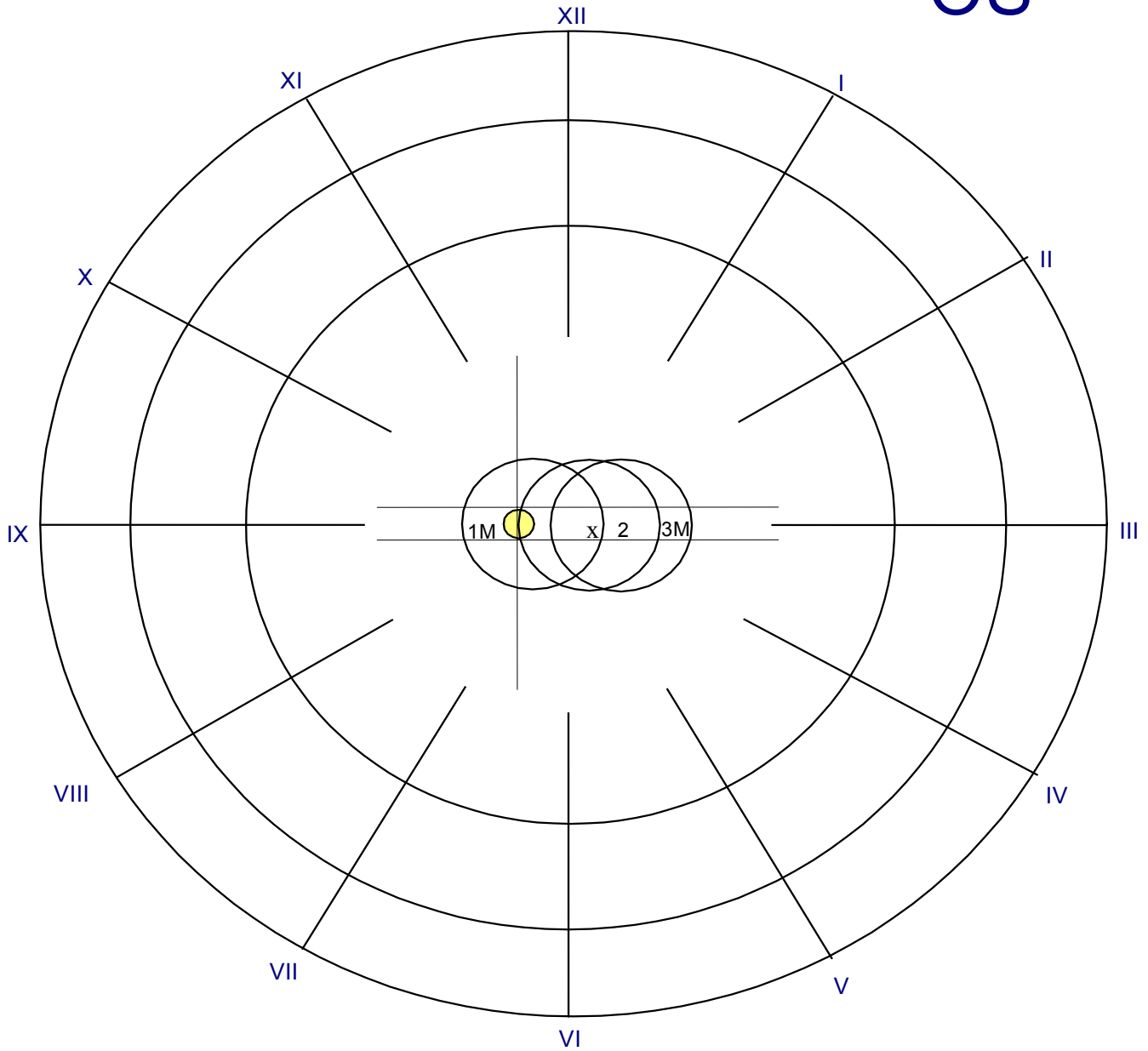


Field 1 - centered on temporal edge of disc of macula  
Field 2- centered 1/8-1/4 DD superior to center of macula  
Field 3M - centered 3/4-1DD temporal to center of macula

x - indicates center of macula  
● - optic disc

**EXHIBIT 8-1. (continued) Standard Fields for Fundus Photography, Left Eye**

OS













Field 1M - centered on temporal edge of disc  
Field 2 - centered 1/8-1/4 DD superior to center of macula  
Field 3M - centered 3/4-1 DD temporal to center of macula

X - indicates center of macula  
O - optic disc



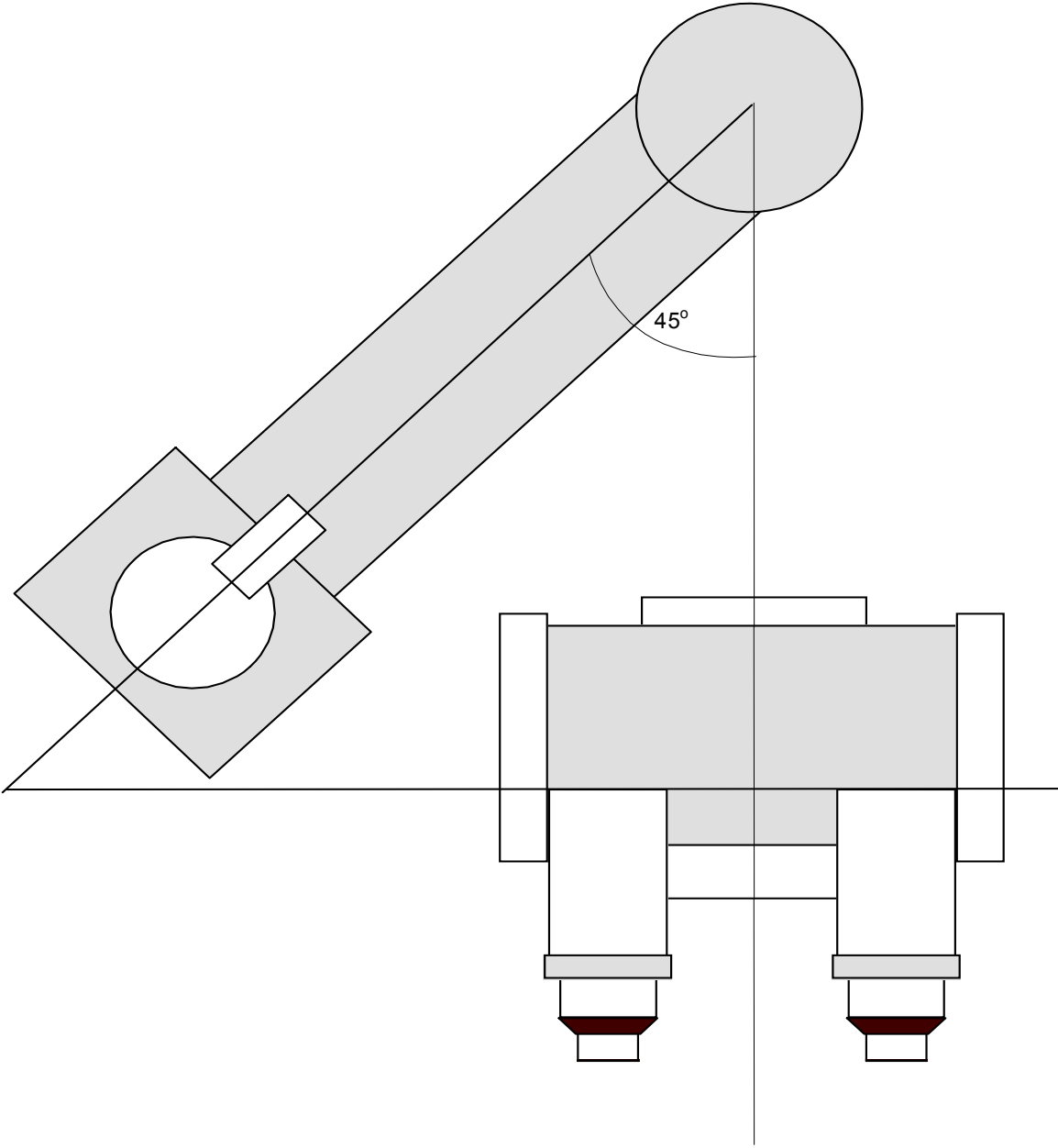
**Exhibit 8-3. Arrangement of Photographs in Plastic Sheet, Right Eye**

		 AREDS 06 99 _____ RE FLD1M _____ LS	 AREDS 06 99 _____ RE FLD1M _____ RS
	 AREDS 06 99 _____ RE FLD3M _____	 AREDS 06 99 _____ RE FLD2 _____ LS	 AREDS 06 99 _____ RE FLD2 _____ RS
 AREDS 06 99 _____ RE REFLEX _____ LS	 AREDS 06 99 _____ RE REFLEX _____ RS		
 AREDS 06 99 _____ RE ANT. NEITZ _____	DISTANCE FROM ZERO _____  AREDS 06 99 _____ RE POST. NEITZ _____		 AREDS 06 99 _____ RE SLIT LAMP _____
		AREDS CLINIC: 99 _____ TEST SITE ID: 99 _____ NAMECODE: _____ PHOTO DATE: _____/_____/_____ VISIT NUMBER: _____ PHOTOGRAPHER: _____ CERT. NUMBER: _____	

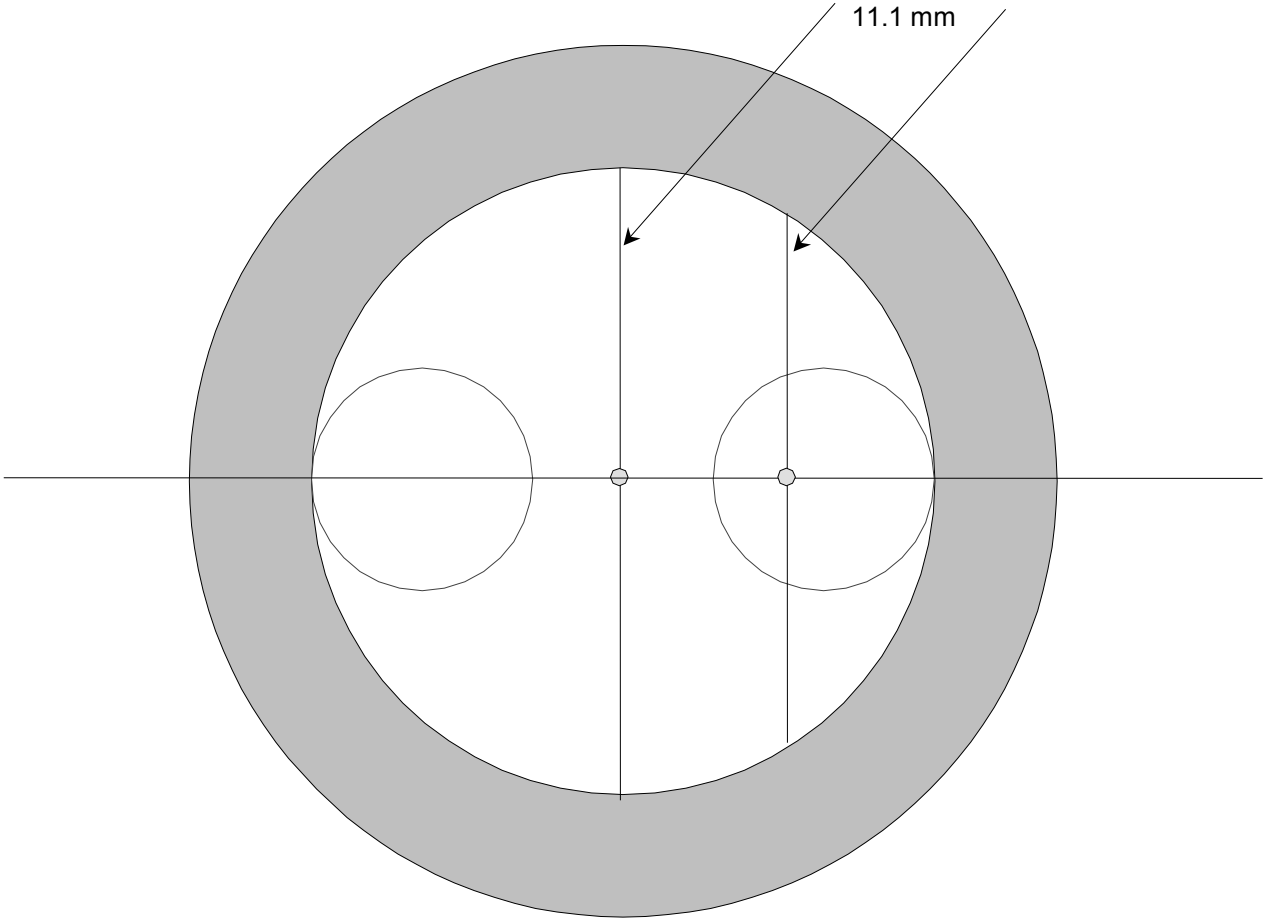
**Exhibit 8-3. (Continued) Arrangement of Photographs in Plastic Sheet, Left Eye**

<div style="border: 1px solid black; width: 100%; height: 100%; display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 80%; height: 80%; margin: 0 auto;"></div> </div> <p>AREDS 06 99 _____ LE FLD1M _____ LS</p>	<div style="border: 1px solid black; width: 100%; height: 100%; display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 80%; height: 80%; margin: 0 auto;"></div> </div> <p>AREDS 06 99 _____ LE FLD1M _____ RS</p>		
<div style="border: 1px solid black; width: 100%; height: 100%; display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 80%; height: 80%; margin: 0 auto;"></div> </div> <p>AREDS 06 99 _____ LE FLD2 _____ LS</p>	<div style="border: 1px solid black; width: 100%; height: 100%; display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 80%; height: 80%; margin: 0 auto;"></div> </div> <p>AREDS 06 99 _____ LE FLD2 _____ RS</p>	<div style="border: 1px solid black; width: 100%; height: 100%; display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 80%; height: 80%; margin: 0 auto;"></div> </div> <p>AREDS 06 99 _____ LE FLD3M _____</p>	
<div style="border: 1px solid black; width: 100%; height: 100%; display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 80%; height: 80%; margin: 0 auto;"></div> </div> <p>AREDS 06 99 _____ LE REFLEX _____ LS</p>	<div style="border: 1px solid black; width: 100%; height: 100%; display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 80%; height: 80%; margin: 0 auto;"></div> </div> <p>AREDS 06 99 _____ LE REFLEX _____ RS</p>		
<div style="border: 1px solid black; width: 100%; height: 100%; display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 80%; height: 80%; margin: 0 auto;"></div> </div> <p>AREDS 06 99 _____ LE ANT. NEITZ _____</p>	<p>DISTANCE FROM ZERO _____</p> <div style="border: 1px solid black; width: 100%; height: 100%; display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 80%; height: 80%; margin: 0 auto;"></div> </div> <p>AREDS 06 99 _____ LE POST. NEITZ _____</p>	<div style="border: 1px solid black; width: 100%; height: 100%; display: flex; align-items: center; justify-content: center;"> <div style="border: 1px solid black; width: 80%; height: 80%; margin: 0 auto;"></div> </div> <p>AREDS 06 99 _____ LE SLIT LAMP _____</p>	
		<p>AREDS CLINIC: 99 _____ TEST SITE          ID: 99 _____ NAMECODE: _____          PHOTO DATE: ____/____/____          VISIT NUMBER: _____          PHOTOGRAPHER: _____          CERT. NUMBER: _____</p>	

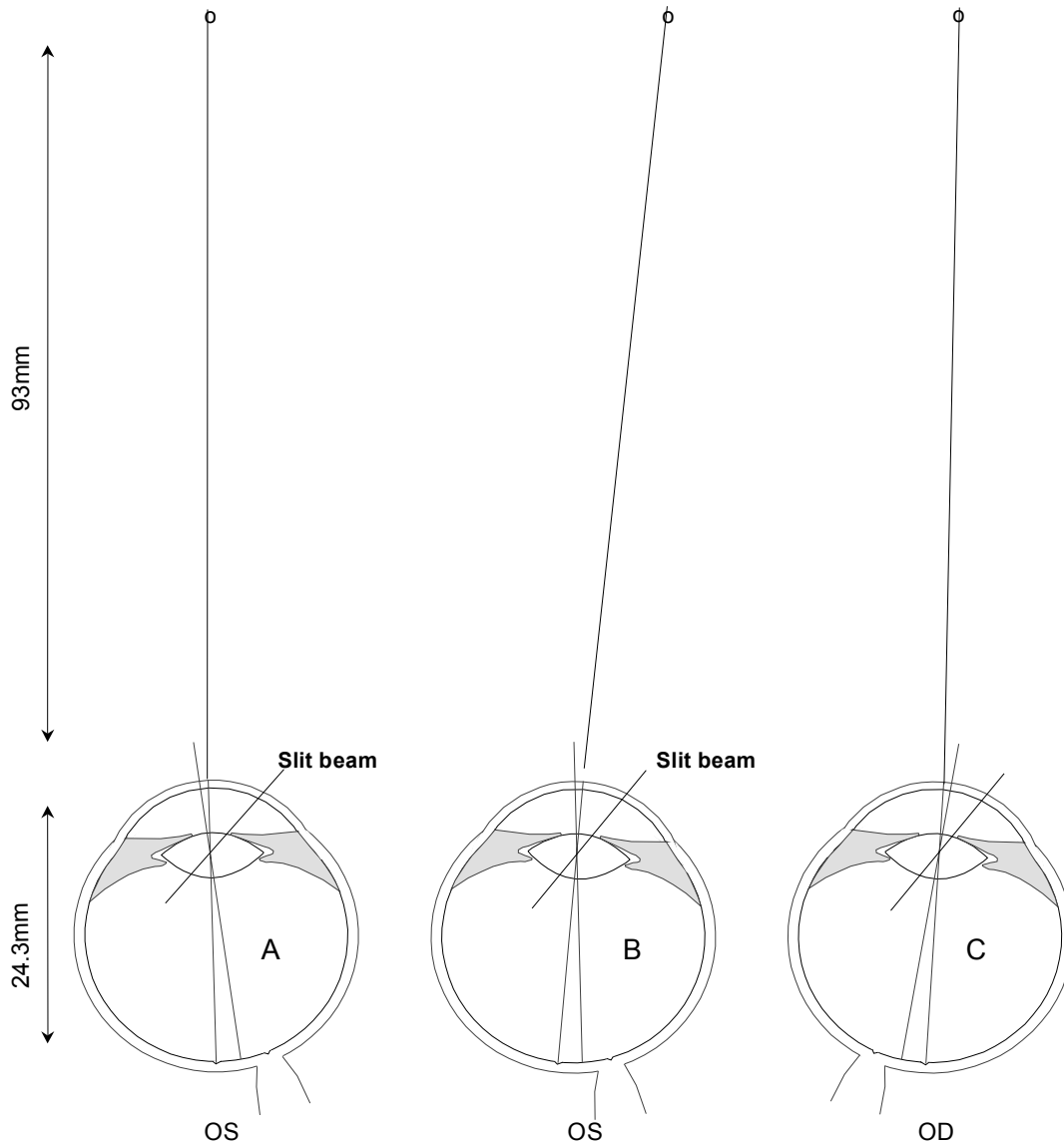
**Exhibit 8-4. Slit-lamp camera beam locked at a standard 45° angle.**



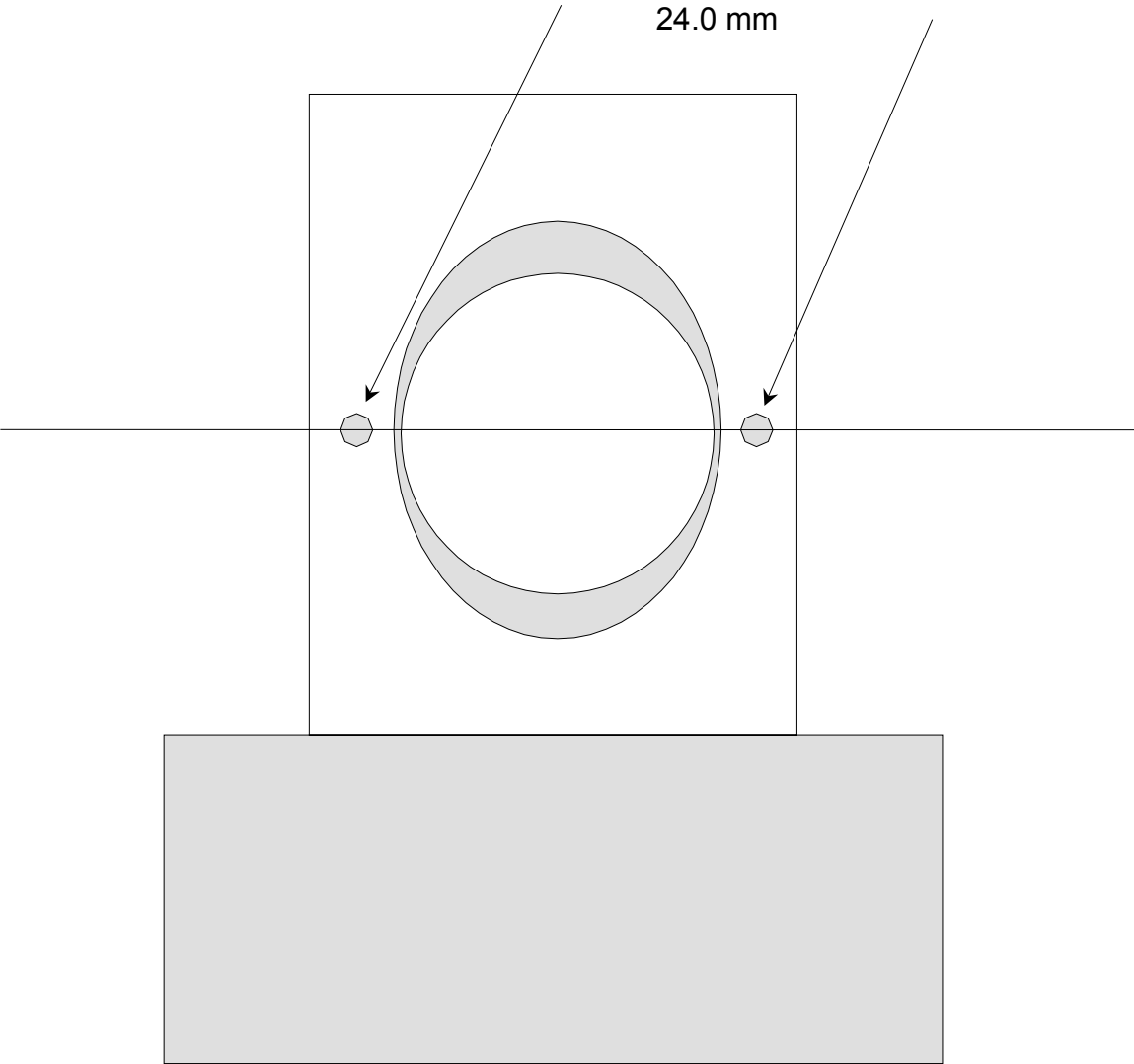
**Exhibit 8-5. Slit-lamp camera fixation targets suspended from a ring mounted around the objective lenses**



**Exhibit 8-6. Schematic diagram based upon Gullstrand's showing the paths of the slit-lamp beam and the fixation of the eye upon the target (dashed lines). The second and third diagrams show correct fixation resulting in symmetrical sections of the lenses of the left and right eyes. The first diagram shows incorrect fixation of a left eye resulting in a nonstandard section of lens.**



**Exhibit 8-7. Neitz camera lens assembly showing modified position of the fixation targets**



**Appendix 8A**

**CRITERIA FOR EVALUATION  
OF PHOTOGRAPHIC QUALITY**

## Appendix 8A

### CRITERIA FOR EVALUATION OF PHOTOGRAPHIC QUALITY

#### 1.0 EVALUATION OF FUNDUS PHOTOGRAPH QUALITY

##### 1.1 Introduction

The detailed grading of retinal photographs is a field-by-field assessment of three characteristics: focus/clarity, stereoscopic effect, and location (field definition). Grades for each of these features are combined to yield an overall grade for the eye.

##### 1.2 Focus/clarity

When fundus details are not sharp, the cause may be technical (incorrect focus or camera position) or ocular (media opacities or small pupil), and it may be difficult to differentiate between these categories. Thus focus/clarity is graded as a single characteristic. The focus/clarity in each field is evaluated as good, fair, borderline, or poor, as defined below.

*Good:* Retinal details are defined sharply and crisply when viewed binocularly.

*Fair:* Retinal details are slightly fuzzy but lesions <63 microns in diameter can still be graded.

*Borderline:* Clarity is decreased so that retinal lesions <63 microns in diameter might be missed, but is sufficient for assessment of characteristics of larger drusen and recognition of subtle abnormalities of advanced AMD in their early stages (see Section 3.1.3.1, criterion 2).

*Inadequate:* Does not meet above requirements for borderline.

##### 1.3 Field definition

Definitions for each of the required fields are as follows:

Field 1M      The temporal edge of the optic disc (at the horizontal meridian) should be in the center of the field.

Field 2        The center should be about 1/8 to 1/4 disc diameter above the center of the macula.

Field 3M      A single (non-stereoscopic) photograph is centered 3/4 to 1 disc diameter temporal to the center of the macula.

Field definition is evaluated as follows:

*Good:*            <1/4 disc diameter from definition.

*Fair:*              $\geq$ 1/4 disc diameter but <1/2 disc diameter from definition.

*Borderline:*     $\geq$ 1/2 disc diameter but <1 disc diameter from definition.

*Inadequate:*     $\geq$  1 disc diameter from definition.

#### **1.4 Stereoscopic effect**

Depth should be clearly discernible between the retinal vessels and the retinal pigment epithelium in Field 2, and between the floor of the cup and the remainder of the disc in Field 1M. Stereoscopic effect in each field is evaluated as follows:

*Good:*            Substantial stereoscopic effect (comparable to slit lamp and contact lens biomicroscopy), so that retinal vessels are perceived to be anterior to the RPE background by at least the diameter of an average large retinal vein at the disc margin.

*Fair:*             Stereoscopic effect definitely present, but less than specified above.

*Borderline:*    Stereoscopic effect barely discernible.

*Inadequate:*    No stereoscopic effect. When right and left sides of a stereo pair are reversed, little or no difference can be discerned.

#### **1.5 Quality of an individual photographic field**

An individual field is classified by the grade of the worst characteristic. Thus "good" is assigned if all characteristics are graded good, "fair" if one or more characteristics are fair and none worse than fair, "borderline" if one or more characteristics are borderline and none is worse than borderline, and "inadequate" if any characteristic is graded inadequate.

#### **1.6 Quality of a set of fundus photographs**

A set of fundus photographs (documenting one eye) will be graded "excellent," "good," "fair," "borderline," or "ungradable" according to the following hierarchy.

*Excellent (E):* All three fields are "good."

*Good (G):* Field 2 is "good" and the other two fields are both "fair" or better.

*Fair (F):* Field 2 is "good" or "fair," and the other two fields are both "borderline" or better.

*Borderline*

*(B1 or B2):* The set does not meet the requirements for "good" or "fair," but quality is sufficient for assessing characteristics of larger drusen and recognizing subtle abnormalities of advanced AMD in their early stages (see 3.1.3.1, criterion 2). Grade B1 is assigned if factors are apparent to explain reduced quality (such as media opacity or a comment by the photographer indicating difficulty with participant cooperation), whereas Grade B2 is assigned if no such explanatory factors are observed.

*Ungradable*

*(U1 or U2):* The set does not meet the requirements for borderline. Grade U1 is assigned if explanatory factors are apparent (as described for "borderline" above), whereas Grade U2 is assigned if no such factors are observed.

## **2.0 RED REFLEX PHOTOGRAPH**

The red reflex photographs will be graded for quality as follows:

*Good:* All of the pupil is visible and in good focus, some stereoscopic effect is present, and corneal diameter on the film is between 11 and 15 mm.

*Fair:* All of the pupil is visible and in good focus but no stereoscopic effect is present and/or corneal diameter is < 11 or > 15 mm.

*Borderline:* The quality does not meet the definition of "good" or "fair," but the photograph is gradable.

*Ungradable:* Photograph is not gradable.

## **3.0 EVALUATION OF LENS PHOTOGRAPH QUALITY**

Both types of lens photographs, slit lamp and Neitz retro-illuminated, are evaluated for several characteristics: focus, placement, and artifacts. The results of this assessment are combined into an overall grade for each type of photograph.

### 3.1 Slit lamp photograph quality

The slit lamp photographs receive an overall quality grade based on focus, beam placement and the presence or absence of illumination problems, artifacts such as lids/lashes, or small (< 5mm) pupil size. The quality grades for the photograph overall are defined as follows:

*Good (G):* Both focus and beam placement meet the definition of "good" for both parameters as described below and problematic artifacts are absent.

*Fair (F):* Focus and beam placement receive a score no poorer than "fair" and any artifacts present do not preclude grading.

*Borderline (B1 or B2):* The photograph is less than "fair" but in the opinion of the grader allows reliable assessment of cataract status. B1 is assigned if explanatory factors (such as inadequate dilation or a comment from the photographer indicating poor participant cooperation) are observed, while B2 is assigned if no such factors are noted.

*Ungradable (U1 or U2):* Either focus or beam placement is "inadequate," or artifacts or small pupil size preclude grading. Grade U1 is assigned if explanatory factors are apparent (as described for "borderline" above), whereas Grade U2 is assigned if no such factors are observed.

#### 3.1.1 Focus of slit lamp photographs

Nuclear opalescence is more accurately graded when the sulcus of the lens nucleus is in sharp focus. The slit lamp camera has a shallow depth of field, so that there is a narrow band (1-2 mm) of clarity extending anterior and posterior to the precise plane of focus. Five zones into which the plane of focus may fall are identified below.

Zone 1 - The focus is on the anterior lens surface in the optic axis or anterior to it. Plane of focus within this zone will mandate a request for retakes.

Zone 2 - The focus is in the lens anterior to the sulcus.

Zone 3 - The focus is in the sulcus.

Zone 4 - The focus is in the lens posterior to the sulcus.

Zone 5 - The focus is on the posterior lens capsule in the optic axis or posterior to it. Plane of focus within this zone will mandate a request for retakes.

Focus is considered good, fair or inadequate as defined below.

- Good:* The plane of focus is in Zone 3.
- Fair:* The plane of focus is in Zones 2 or 4.
- Inadequate:* The plane of focus is in Zones 1 or 5.

### 3.1.2 Beam placement of slit lamp photographs

For the opalescence of the nucleus to be graded accurately, the slit beam should pass through the center of the nucleus, or very nearly through the center. When properly positioned, the out-of-focus slit beam crosses the iris at 11 and 7 o'clock. The vertical meridian of the lens within the pupil should be illuminated so that the sulcus is clearly visible in the beam and an imaginary vertical line drawn through the sulcus would intersect the iris at 12 and 6 o'clock.

Beam placement is considered good, fair, or inadequate as defined below.

- Good:* The vertical meridian of the lens within the pupil is illuminated so that the sulcus is clearly visible in the beam and an imaginary vertical line drawn through the sulcus would intersect the iris at 12 and 6 o'clock. All of the nucleus is visible. The out-of-focus slit beam is visible on the pupillary margin of the iris at approximately 11 and 7 o'clock.
- Fair:* The vertical meridian of the lens within the pupil is illuminated so that the sulcus is clearly visible in the beam and an imaginary line drawn through the sulcus would intersect the iris between 10:30-12 o'clock or 12-1:30 o'clock. At least 2/3 of the nucleus is clearly visible.
- Inadequate:* An imaginary line drawn through the sulcus would intersect the iris to the left of 10:30-7:30 or to the right of 1:30-4:30 o'clock, or less than 2/3 of the nucleus is visible.

If the slit lamp photograph receives an overall quality grade less than "good," wholly or in part because of improper beam placement, the position of the beam will be indicated according to the categories defined below.

Beam 10:30-1:30. The sulcus is not illuminated exactly between 12-6 o'clock but is illuminated between 10:30 to 7:30 and 1:30 to 4:30 o'clock with respect to the pupillary margin.

Beam Left. The sulcus is illuminated left of the 10:30 to 7:30 o'clock position with respect to the pupillary margin.

Beam Right. The sulcus is illuminated right of the 1:30 to 4:30 o'clock position with respect to the pupillary margin.

Beam High/Low. The vertical position of the slit beam fails to completely fill the pupil, resulting in some portion of the top or bottom of the lens being unilluminated. This problem is usually due to improper camera alignment. This category will not be used to report the normal loss of some portion of the top or bottom of the lens that may result from the slit beam making contact with the iris.

### 3.2 Neitz photograph quality

The Neitz lens photographic pair will receive an overall quality grade based on focus, the presence or absence of illumination problems or artifacts such as lids/lashes, or small (< 5mm) pupil size. The quality grades for the photograph pair overall are defined as follows:

*Good (G):* The focus of both photographs meets the definition of "good" as described below and problematic artifacts are absent.

*Fair (F):* The focus of both photographs receives a score no poorer than "fair" and any artifacts present do not preclude grading.

*Borderline (B1 or B2):* Either or both photographs are less than "fair" but in the opinion of the grader allow reliable assessment of cataract status. B1 is assigned if explanatory factors (such as inadequate dilation or a comment from the photographer indicating poor participant cooperation) are observed, while B2 is assigned if no such factors are noted.

*Ungradable (U1 or U2):* Focus is "inadequate" in either or both photographs, or artifacts or small pupil size preclude grading. Grade U1 is assigned if explanatory factors are apparent (as described for "borderline" above), whereas Grade U2 is assigned if no such factors are observed.

#### 3.2.1 Focus of Neitz photographs

The presence and extent of opaque anterior and posterior subcapsular lens opacities are best seen and graded in retro illumination photographs. The anterior opacities are seen when the plane of focus is coincident with the iris and the pupillary margin is sharp at 12 and 6 o'clock. In this position, at least 180 degrees of pupillary margin will usually appear in sharp focus. Posterior subcapsular opacities (if present) should be in clear focus 3-5mm behind the pupillary margin. Because of the very shallow depth-of-field of the camera, the pupillary margin will be out-of-focus in this position. The circular illumination lamp should be centered in the pupil for both photographs, with little or no light illuminating the iris. The retro-illuminated lens will be bright because of the heightened light reflection from the optic nerve head.

Focus of the **anterior Neitz** photograph is considered good, fair, or inadequate as defined below.

- Good:* The pupillary margin is in sharp focus at 12 and 6 o'clock. At least 180 degrees of the pupillary margin is in focus. Illumination is bright and no problematic artifacts exist.
- Fair:* Part of the pupillary margin is in focus. Illumination is bright and the lid (or other artifact) obscures no more than 50% of the superior quadrant of the lens, defined as the part of the lens extending horizontally from 10 to 2 o'clock and vertically from the center of the lens (a central circle of 2 mm diameter) to the pupillary margin.
- Inadequate:* No part of the pupillary margin is in acceptable focus. Illumination is too dim to allow grading. More than 50% of the superior quadrant is obscured.

**Posterior Neitz** photograph focus definitions for the three levels of quality are as follows.

- Good:* The plane of focus is between 3-5mm and any visible posterior subcapsular cataract is in good focus. No problematic artifacts exist.
- Fair:* Focus is questionably too anterior or too posterior. Illumination is bright and no more than 50% of the superior quadrant is obscured by the lid (or artifacts).
- Inadequate:* Focus is unquestionably too anterior or too posterior for grading, illumination is too dim to allow grading, or more than 50% of the superior quadrant is obscured.

When a Neitz lens photograph receives an overall quality grade less than "good", wholly or in part because of incorrect focus, one of the following categories defined below will be checked.

Anterior Focus Incorrect: Less than 180 degrees of the pupillary margin are in focus.

Posterior Focus too Deep: The focus of the posterior photograph appears to have been too deep or appears inconsistent with the distance recorded on the slide mount.

Posterior Focus too Anterior: The focus of the posterior photograph appears to have been too anterior or appears inconsistent with the distance recorded on the slide mount.