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### 3. Selection of Angiograms for Review

The **angiograms** were selected from among a group of **530** randomly selected patients from the total of **2,792** patients in the **EPILOG** trial. Patients from the **EPILOG** trial were stratified by risk status at **time of randomization** and at time of CRF completion. Patients who had had an MI within **7 days** were excluded from the selection process, as these would be classified as high risk by that criterion regardless of lesion characteristics.

**Patients** who had been assigned low risk **status** at randomization accounted for **two** thirds of the **angiograms** in the study. The main group of concern for the re-review was those who had changed from **low risk** at randomization to high risk by CRF. One hundred **forty angiograms** were randomly selected from that group (139 actually selected). One hundred angiograms were selected from the group that were low risk at randomization and low risk by CRF. Of those that were designated high risk at randomization, 50 were selected from those that were also designated high risk by CRF, and **70** (actually 71) were selected from those that were changed to low risk by CRF. See Table 2 below. The proportion sampled from each subgroup was determined prospectively with concurrence of the CBER review staff.

**Table 2 Angiogram Sampling for Re-Review**

Risk Status at Randomization	Risk Status by CRF Data	Number of Patients Films Re-Reviewed n = 360
Low	Low	100
Low	High	139
High	Low	50
High	High	71

### 4. Preparation of Films

**Angiograms** were forwarded by the study sites to the Cleveland Clinic **Angiography** Core Lab. The angiograms reviewed were not the actual pre-procedure angiograms, on which the randomization assessment had been based. In many cases, videotape was used in the **cath** lab for the baseline **determination**, and videotapes were no longer available. The films to be reviewed in this study were taken **from** the angiograms done during the index procedure. **The** Core Laboratory staff reviewed **the** films and spliced the films so that only the pre-intervention portion of the angiogram was available for review. The portion of the film showing the balloon and/or **STENT**, the procedure and the **post**-procedure images was edited out. The films were then **pre-reviewed** by the Cleveland Clinic Foundation (CCF) staff to confirm the identity of the **lesion** (\$) being **scored**.

### 5. Logistics of Review

The re-review was conducted **at** the Cleveland Clinic Foundation. **Ten reviewers** reviewed films on the first day; 8 reviewers on the second day. Each reviewer was given a box of **20** films and directed to an individual **review** station. **When** review of the **20** films was completed, a new **box** was **obtained**. Each reviewer reviewed 60 films. They were allowed "as much time as necessary" to **complete** the task.

Each reviewer had his/her own review station. Reviewers were advised not to talk to one another about any review. Monitors were present to ensure that no discussions occurred between reviewers.

Each reviewer was given a packet of **CRFs** that matched the films. They recorded their responses, and returned these to the monitor. Each film was read by three (3) reviewers. A total of 1,080 reviews took place on the 360 films.

#### Data Collection and Management

A copy of the data collection **form** appears in Attachment 1. The forms were preprinted with patient identification numbers (EPILOG ID number), age, gender, and diabetes history (these were taken **from** the **CRFs** by Centocor), and the location of the lesion to be reviewed. The forms list brief descriptions **of** each lesion attribute category and checkboxes for completion by reviewers. A **CCF** staff member reviewed each form for completeness and to ensure that only one classification was checked for each attribute. Data-forms were then forwarded to Centocor for data entry and analysis.

#### 6. Data Evaluation / Statistical Methods

No formal hypothesis testing was involved. The kappa statistic was used as a measure of correlation of the agreement between reviewers' readings. **Kappas** were **calculated for** the re-review itself, and for the re-review compared to the CRF review, and for the **re-review compared to the** randomization review. Agreement was judged to be good if the kappa was  $\geq 0.7$  for each of the comparisons. For the re-review statistics, an average kappa value was derived by simulations (approximately 1200) making a random selection of one re-review for each patient and computing the kappa for this set of readings and the corresponding CRF or randomization classifications. The number of simulations were planned to ensure 99% confidence that the kappa value was accurate to within 0.01. The number of reviewers classifying patients as high risk was compared between subgroups using **Cochran-Mantel-Haenszel** statistics. Again, the Agency reviewers were in concurrence **with the planned** statistical methods, including the absence of formal hypothesis testing and the establishment of **the 0.7** criterion denoting good agreement.

#### 7. Definitions Used

Lesions were classified by the most severe lesion characteristic, and patients then classified as high or low risk by the **ACC/AHA** guidelines used in the main EPILOG study (see Attachment 2). High risk patients were defined as those with any of the **following** characteristics:

- Stenosis with 2 1 type C characteristic in the **artery** to be treated, or
- Stenosis with 2 2 type B characteristics in the artery to be treated, or
- Age  $\geq 65$  years and female gender with 2 1 type B characteristic, or
- Diabetes **mellitus** and stenosis with 2 1 **type B** characteristic.

### D. Study Results

#### 1. Study Population

Demographics of the patients in the entire study, those eligible for re-review, and those in the **re-review are** listed in Table 3 on the next page. (All patients in the study except those with **MI occurring** within 7 days prior to enrollment were eligible). **The average weight, height, and age** are comparable between the re-review group and the overall group. The percentage of women was lower in the re-review group (21 % vs 28 % in the overall study), due to the over-sampling of low risk patients, because in women over age 65 only one type B lesion was **required** to classify a patient as high risk, thus a higher percentage of women were classified as high risk in the study overall.

The number, location, TIMI Grade and percent stenosis of the lesions reviewed are listed in Table 4 on the second page following. The table compares the n-review sample to the overall study population and to those eligible for re-review. The re-review group was similar to the larger groups on all parameters. Most patients had one native vessel with lesions attempted. A small percentage had grafts attempted. The location of lesions attempted was divided almost evenly among LAD, RCA, and LCX. Most patients (74 %) had one segment attempted. The minimum pre-intervention TIMI grade was 3 for 76 to 82 % of patients, and the maximum stenosis was 90% for all groups,

Table 3 Patient demographics: comparison Of total EPILOG population and patients eligible for re-review in the angiographic n-review study

	Total (n = 2792)	Pts Eligible for Re-review (n = 2203)	Pts with Re-review of Baseline Angiograms (n = 360)
<b>Gender</b>			
Male	2012 (72.1%)	1576 (71.5%)	284 (78.9%)
Female	780 (27.9%)	627 (28.5%)	76 (21.1%)
<b>Age (years)</b>			
n	2792	2103	360
Mean $\pm$ SD	59.7 $\pm$ 11.0	60.3 $\pm$ 10.9	58.5 $\pm$ 10.5
Median	60.0	61.0	59.0
Range	(29.0, 89.0)	(32.0, 89.0)	(32.0, 82.0)
<b>Weight (kg)</b>			
n	2790	2201	360
Mean $\pm$ SD	85.1 $\pm$ 16.7	85.0 $\pm$ 16.6	84.9 $\pm$ 15.3
Median	84.0	84.0	84.0
Range	(44.0, 164.0)	(44.0, 164.0)	(44.0, 130.9)
<b>Height (cm)</b>			
n	2748	2168	357
Mean $\pm$ SD	172.3 $\pm$ 9.9	172.1 $\pm$ 10.0	172.6 $\pm$ 10.1
Median	172.7	172.7	173.0
Range	(126.0, 205.7)	(126.0, 205.7)	(137.0, 193.0)
<b>Race (n, %)</b>			
Caucasian	2513 (90.0%)	1981 (89.9%)	327 (90.8%)
Black	167 (6.0%)	131 (5.9%)	14 (3.9%)
Oriental	7 (0.3%)	6 (0.3%)	2 (0.6%)
Hispanic	63 (2.3%)	51 (2.3%)	9 (2.5%)
American Indian	10 (0.4%)	7 (0.3%)	3 (0.8%)
Other	31 (1.1%)	26 (1.2%)	5 (1.4%)
unknown	1 (0.0%)	1 (0.0%)	0 (0.0%)

**Table 4** Number of patients by number, location, minimum TIMI grade and maximum stenosis of lesions attempted during index intervention: comparison of total EPILOG population, patients eligible for re-review and patients in the angiographic re-review study.

	<b>Total (n = 2792 )</b>	<b>Pts Eligible for Re-review (n = 2203 )</b>	<b>P t s w i t h Re-review of Baseline Angiograms (n = 360 )</b>
<b>Pts with intervention attempted</b>	2752	2203	360
<b>Number of native vessels with lesions attempted</b>			
0	84 (3.1%)	77 (3.5%)	6 (1.7%)
1	2439 (88.6%)	1935 (87.8%)	329 (91.4%)
2	227 (8.2%)	189 (8.6%)	25 (6.9%)
≥3	2 (0.1%)	2 (0.1%)	0 (0.0%)
<b>Vessels with lesions attempted<sup>a</sup></b>			
Left main	6 (0.2%)	6 (0.3%)	0 (0.0%)
LAD	1034 (37.6%)	857 (38.9%)	132 (36.7%)
LCX	832 (30.2%)	660 (30.0%)	115 (31.9%)
RCA	1027 (37.3%)	796 (36.1%)	132 (36.7%)
<b>Pts with grafts attempted</b>	100 (3.6%)	93 (4.2%)	9 (2.5%)
<b>Number of segments attempted<sup>b</sup></b>			
1	2050 (74.5%)	1635 (74.2%)	268 (74.4%)
2	573 (20.8%)	463 (21.0%)	78 (21.7%)
≥3	129 (4.7%)	105 (4.8%)	14 (3.9%)
<b>Minimum pre-intervention TIMI grade in any target lesion</b>			
0	205 (7.4%)	138 (6.3%)	21 (5.8%)
1	132 (4.8%)	99 (4.5%)	15 (4.2%)
2	251 (9.1%)	192 (8.7%)	24 (6.7%)
3	2105 (76.5%)	1732 (78.6%)	296 (82.2%)
Unknown	59 (2.1%)	42 (1.9%)	4 (1.1%)
<b>Maximum pre-intervention stenosis in any target lesion (%)</b>			
n	2751	2203	360
Median	90.0	90.0	90.0
Interquartile range	(80.0, 95.0)	(80.0, 95.0)	(80.0, 95.0)
Range	(47.0, 100.0)	(47.0, 100.0)	(50.0, 100.0)

<sup>a</sup> Some patients had more than one vessel with lesions attempted.

<sup>b</sup> Includes grafts

**E. Inter-Reviewer Agreement Findings**

The kappa statistic for the re-review was 0.29. The kappa for the re-review compared to the CRF assessment was 0.22. The kappa for the re-review compared to the randomization assessment was 0.09. These values indicate poor agreement among reviewers within the re-review, and among the re-review and each of the assessments conducted in the overall study (see Table 5 below).

Agreement among the reviewers in the n-review was modest, but similar to the agreement of the re-reviewers with the CRF assessments. There was substantially less agreement of the n-reviewers with the randomization assessment.

**Table 5 Overall Agreement by Kappa Values**

Agreement Between	Kappa Value
Re-Review Alone (Inter-Rater)	.29
Re-Review and CRF	.22
Re-Review and Randomization	.09

Table 6 shows the number of reviewers (0, 1, 2 or 3) who classified a given patient as high risk. The table shows there was agreement among all 3 reviewers in 227 out of the 360 cases (63.1 %). One reviewer disagreed with the other two in evaluation of the other 133, or 36.9 %.

**Table 6 Number of Re-Reviewers Classifying Angiogram as High Risk**

	0	1	2	3
Number of patients	23 (6.4)	41 (11.4)	92 (25.6)	204 (56.7)

Table 7 shows the percent of lesions classified as high or low risk by the re-reviewers in each subgroup of risk status as categorized by randomization and CRF status. Sixty percent of the re-reviews indicated a high-risk classification for the group thought to be low risk by both randomization and CRF. Over eighty percent of the re-reviews indicated a high risk status for the group classified as low risk at randomization and reclassified as high risk at CRF. Over ninety percent or re-reviews indicated a high risk status for those categorized as high risk both at randomization and CRF.

**Table 7 Number of reviews indicating low or high risk by risk status at randomization and risk based on CRF data**

	Number of Pts Reviewed	Total Number of Patient Reviews	% of Reviews Indicating High Risk	% of Review Indicating Low Risk
<b>Pts randomized as low risk</b>				
Low risk based on CRF	100	300	60.3%	39.7%
High risk based on CRF	139	417	83.2%	16.8%
<b>Pts randomized as high risk</b>				
Low risk based on CRF	50	150	76.0%	24.0%
High risk based on CRF	71	213	91.6%	8.5%

Tables 8 and 9 compare the overall agreement between the re-review and the CRF and the re-review and the randomization assessments regarding high or low risk status. Overall, 65 % (697 of 1080) re-reviews were in agreement with the CRF reading. The Re-review readings agreed with the as-randomized readings in only 46 % of cases (498 of 1080).

Eighty-six percent of those read as high risk by CRF were read as high risk by the n-reviewers. However, 65 % of those read as low risk by the CRF reviewers were also read as high risk by the re-reviewers (only 34 % agreement). A similar proportion of agreement regarding high risk status is seen in the comparison with the randomization assessment (85.1 %). There was a greater level of disagreement with the low risk assessments made at randomization (73.6 % of those assessed as low risk at randomization were assessed as high risk by the E-review).

Table 8 Risk classification based on CRF data and re-review<sup>a</sup>

		Re-review		Total	
		High	Low		
CRF	High	542 (86.0%)	88 (14.0%)	630	(2.10)
	Low	295 (65.6%)	155 (34.4%)	450	(1.73)
	Total	837	243	1080	

<sup>a</sup> Results are presented as number and % of patients by risk classification by CRF evaluation (i.e. "row %")

Table 9 Risk classification based on randomization data and re-review<sup>a</sup>

		Re-review		Total
		High	Low	
Randomization	High	309 (85.1%)	54 (14.9%)	363
	Low	528 (73.6%)	189 (26.4%)	717
	Total	837	243	1080

<sup>a</sup> Results are presented as number and % of patients by risk classification at time of randomization (i.e. "row %")

The most severe lesion characteristic, classed as A, B1, B2 or C, for the re-review and for the CRF determinations are compared in Table 10. **The overall agreement between the Re-review and the CRF readings is only 41 %**, (448 of 1080 reviews). The **Re-review** reading was **more** severe in 42 % (455 of **1080**), and the CRF reading was more severe in **only 12 %** (177 of 1080). From this table, it can also be seen that the majority of reviews were read as B2 by both the n-reviewers (587) and the CRF (459). However, more of the re-reviewers found lesions with C characteristics (**212**) than did the **CRF** (129). More of the CRF reviews found A or **B1** as the most severe characteristic than did the re-reviews. **The** percentage agreement between the re-reviewers and the CRF reviews was highest among those classified as B2 (61.9 %) and lowest among those classified as A (15.2 %). The table shows also that when the re-review assessment differed, the n-review more **often** indicated a higher risk category, while then were also a substantial number of re-reviews indicating lower risk categories than the CRF.

**Table 10 Most severe lesion characteristic based on CRF data and re-review<sup>a</sup>**

	<u>Re-review</u>				<u>Total</u>
	<u>A</u>	<u>B1</u>	<u>B2</u>	<u>C</u>	
<u>A</u>	30 (15.2%)	57 (28.8%)	94 (47.5%)	17 (8.6%)	198
<u>B1</u>	25 (8.5%)	74 (25.2%)	152 (51.7%)	43 (14.6%)	294
<u>B2</u>	24 (5.2%)	59 (12.8%)	284 (61.9%)	92 (20.0%)	459
<u>C</u>	3 (2.3%)	9 (7.0%)	57 (44.2%)	60 (46.5%)	129
<u>Total</u>	82	199	587	212	1080

<sup>a</sup> Results are presented as number of lesion characteristics and % of lesion characteristics by CRF evaluation (i. e. "row &#3

**Table 11 Most severe lesion characteristic based on randomization data and re-review<sup>a</sup>**

	<u>Re-review</u>				<u>Total</u>
	<u>A</u>	<u>B1</u>	<u>B2</u>	<u>C</u>	
<u>A</u>	34 (12.2%)	56 (20.1%)	130 (46.6%)	59 (21.2%)	279
<u>B1</u>	34 (6.7%)	101 (19.9%)	293 (57.8%)	79 (15.6%)	507
<u>B2</u>	11 (4.5%)	39 (15.8%)	138 (56.1%)	58 (23.6%)	246
<u>C</u>	3 (6.2%)	3 (6.2%)	26 (54.2%)	16 (33.3%)	48
<u>Total</u>	82	199	587	212	1080

<sup>a</sup> Results are presented as number of lesion characteristics and % of lesion characteristics by lesion assessment at the time of randomization (i. e. "row %")

Table 11 (previous page) shows the same comparison for the re-review and the randomization assessments. The overall agreement between the **Re-review** and the as-randomized readings is only 28 % (289 of 1080). The Re-review readings were more severe in 675, or 62 %. The Randomization readings were more severe in **only** 116, or 10%. Three-quarters of the randomization assessments indicated A or **B1** as the most severe lesion characteristic, while a similar proportion of **the** re-review assessments indicated B2 or **C**.

The individual lesion characteristics were assessed at **both** the CRF review and the re-review. The re-review revealed significant disagreement on which patients had Type A, **B1** and C lesions. Most ratings fell into the A category on each of the individual characteristics. Comparison shows substantial disagreements in both directions **on** several important characteristics; the re-review **consistently** assessed lesions as more severe than did the CRF assessment (Table 12).

**Table 12 Agreement Between Re-Review and CRF on Selected Lesion Characteristics<sup>1</sup>**

Characteristic	Percent Agreement	% Assessed by CRF as More Severe	% Assessed by Re-Review as More Severe
Length	60 %	16 %	23 %
Accessibility	73 %	11 %	16 %
Contour	59 %	13 %	27 %
Eccentricity	58 %	13 %	28 %

Excludes a **small** number who were assessed as unknown by CRF or re-review

There was substantial agreement on assessment of other lesion characteristics, including **angulation**, calcification, **ostial location**, presence of **thrombus**, and occlusion.

*Reviewer's Note: Individual lesion characteristics were not assessed at randomization, thus no comparison between the re-review and **randomization data** on lesion **characteristics** was possible.*

#### **F. Sponsor's Conclusions**

The sponsor concludes that the low agreement among n-reviewers and among the re-reviewers and the as randomized and CRF classifications, indicates that risk status determined by the **ACC/AHA** angiographic risk criteria cannot be reliably reproduced by a group of experienced, practicing cardiologists. They state these results suggest that there is no reproducible way to identify, using these criteria, a low **risk** subgroup of the **all-comers PTCA** population enrolled in **the** EPILOG trial that will not benefit **from** Abciximab treatment.

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#### **G. Reviewer's C o -**

There is a striking level of disagreement seen among the n-reviewers in this study. Responsible factors are likely to include differences in how the individual reviewers apply the criteria, biases acquired through practice experience, and perhaps less tangible effects of the review situation (travel time, **fatigue**, etc.) on individual performance.

There was a shift in risk level assessment towards a higher proportion of high risk assessments in both the CRF review and the re-review compared to the randomization review. It is possible that the formalized process of review requiring ranking specific lesion characteristics results in a bias toward higher risk assessments.

It is possible that the process of re-review outside the acute patient care setting lends to a closer examination of the films, and an inherent bias toward assessments of even higher risk status. The re-reviewers were told the purpose of the re-review was to establish the utility of the ACC/AHA lesion morphology rating system for high risk characteristics. The re-reviewers could have assumed most of the lesions reviewed would have high-risk characteristics, and had a bias toward favoring high risk readings. It is possible, though also less likely, that the group of reviewers selected was unusually diverse.

The fact that the films to be reviewed were taken from the actual intra-procedural angiograms, and the image quality was expected to be enhanced over that of the video images viewed at randomization, could have contributed to the readings differing more significantly from those made at randomization. The CRF assessments may have been affected by the bias of post-procedural knowledge of outcomes in some cases, but this does not appear to have been a major factor contributing to the different assessments.

It is likely that most or all of the above factors were operative in producing the level of disagreements seen among reviewers and among reviews. Therefore the criteria for lesion assessment, as applied in the EPILOG study, do not appear sufficiently reliable to have enabled adequate assessment of risk status.

#### **H. Conclusions Regarding BLA # 97-0200**

One of the two main objectives of the EPILOG trial was to evaluate the performance of Abciximab in a broader population of patients than the high risk patients enrolled in the EPIC trial. The sponsor has presented data indicating the patients enrolled in the EPILOG study were not at as high a risk for abrupt vessel closure, or for acute ischemic syndromes and their consequences, as were the patients in the EPIC trial. The highest risk patients in the EPIC trial, those presenting with acute MI and acute unstable angina, were excluded from the EPILOG trial. Thus the EPILOG population was distinct from the EPIC population. Efficacy has been established for the EPILOG population as a whole, and for patients in the trial who were regarded as at high risk for ischemic events. Efficacy has not as clearly been established for patients regarded as at lower risk for events.

The CRF risk assessments differed substantially from those made at randomization in the EPILOG study. The risk status subsets identified during the study were not reproduced in the independent angiogram re-review; those assessments differed significantly from the CRF assessments. Thus, the lesion classification system employed to identify patients in the EPILOG trial by risk status does not appear sufficiently reliable to recommend its use in stratifying patients by risk in advance of treatment. Therefore, the efficacy seen in the risk subsets in the EPILOG study may not be confidently generalized to the larger population.

By the randomization classification, the sponsor claims benefit is shown on the low risk subgroup. When the placebo event rates for patients randomized as low and those randomized as high risk in the EPILOG trial are compared, the patients identified as low risk do show a lower placebo event rate. However, it is uncertain that the randomization method of risk assessment would provide a reproducible result; thus the efficacy data for the subgroups should not be relied upon.

*Comment: The as-randomized assessment employed an overall assessment of whether A, **B1**, B2 or C characteristics were present. **That** method has not been reproduced and has not been formally assessed in the re-review. Perhaps the randomization **risk** assessment is more reliable than the **CRF** assessment, but there **is** not adequate evidence to show **this**. It would require an independent angiogram re-review employing the **films** and the **methods** used at randomization to **validate** those assessments.*

By **the** CRF determination, a subgroup of patients is identified who were thought to be low risk and demonstrated low placebo event rates; these patients do not appear to demonstrate significant benefit **from** the **administration** of Abciximab. By the re-review determinations, even fewer patients were identified as low risk, and event rates do not **correlate** as clearly **with** the assessments. Thus the efficacy data based on these subset analyses may not be relied upon either.

**There** are no data **contradicting the** sponsor's statement that the EPILOG trial enrolled "all comers", that is, all patients referred for coronary **angioplasty**, regardless of anticipated risk status. **The** sponsor has also submitted literature indicating that there are **factors** arising during **coronary** interventions which may change a patient from a lower risk to a **higher** risk category (dissection, thrombus formation, etc.). While it may be possible to discern risk status with greater certainty post-procedure, (once the procedural outcome and the clinical **course** of the patient is known), it is not possible to make that distinction prospectively.

The bleeding risk profile of Abciximab **from** the **EPILOG** study appears considerably improved over that which was seen in the EPIC trial when the lower dose, **weight-adjusted** and shorter duration **heparin** regimen is used concomitantly. "The patients at greatest risk for significant bleeding complications do not appear to be the patients with lower cardiac risk profiles as identified at randomization. **Thus** they do not appear to be risks associated with treatment that would outweigh the potential for benefit in a broad population of patients.

For these reasons, it would not be appropriate to **specifically** state in product literature, **labelling** or advertising that low risk patients have been demonstrated to benefit (or not to benefit) from Abciximab treatment. It would be preferable to state in the product literature and **labelling** that it is not reliably possible to discern a patient's risk **for** ischemic cardiac complications prior to the performance of the procedure. There are not appreciable risks outweighing the potential for benefit for most patients referred for **coronary** angioplasty, and the product

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Attachment 1

## ANGIOGRAPHY REVIEW

The Cleveland Clinic Foundation, Cleveland, Ohio

August 2nd and 4th, 1997

Patient Identification		Demographics	
patient Number: 12345	Age and Sex: <b>52 yrs Female</b>		
Patient Initials: DLD	Diabetes: Unknown		
Date of Intervention: <b>26-Feb-1995</b>	Date of most recent MI: Nov-94		
Lesion Identification			
Lesion Location: SVG to <b>Unknown</b>			
Number of Lesions: <b>2 of 4</b>			
CASS Lesion Number: 29			
Check <u>one</u> column (lesion type) for <b>each</b> characteristic listed below, Do not leave a characteristic blank. In case of error, put a slash through the incorrect mark and date and Initial. Mark and <b>circle</b> the correct entry.			
Characteristic	Type A	Type B	Type C
Length	<input type="radio"/> <sub>1</sub> < 10 mm	<input type="radio"/> <sub>2</sub> 10 to 20 mm	<input type="radio"/> <sub>3</sub> > 20 mm
Eccentricity	<input type="radio"/> <sub>1</sub> Concentric	<input type="radio"/> <sub>2</sub> Eccentric	
Accessibility	<input type="radio"/> <sub>1</sub> Readily accessible	<input type="radio"/> <sub>2</sub> Moderate tortuosity of proximal segment	<input type="radio"/> <sub>3</sub> Excessive tortuosity of proximal segment
Lesion Angulation	<input type="radio"/> <sub>1</sub> < 45 degrees	<input type="radio"/> <sub>2</sub> > 45 and < 90 degrees	<input type="radio"/> <sub>3</sub> > 90 degrees
Lesion Contour	<input type="radio"/> <sub>1</sub> Smooth	<input type="radio"/> <sub>2</sub> Irregular	
Ostial Location	<input type="radio"/> <sub>1</sub> Not ostial	<input type="radio"/> <sub>2</sub> Ostial	
Calcification	<input type="radio"/> <sub>1</sub> Little or none	<input type="radio"/> <sub>2</sub> Moderate to heavy	
Thrombus	<input type="radio"/> <sub>1</sub> Absent	<input type="radio"/> <sub>2</sub> Present	
Occlusion	<input type="radio"/> <sub>1</sub> Less than total	<input type="radio"/> <sub>2</sub> Total < 3 months old	<input type="radio"/> <sub>3</sub> Total > 3 months old
Bifurcation	<input type="radio"/> <sub>1</sub> No major involvement	<input type="radio"/> <sub>2</sub> Bifurcation lesions requiring double guide wires	<input type="radio"/> <sub>3</sub> Inability to protect major side branches
Grafts	<input type="radio"/> <sub>1</sub> NA		<input type="radio"/> <sub>2</sub> Degenerated vein grafts with friable lesions
Reader #: _____			
Reader's Signature: _____		Date: _____ -19____ (D-M-Y)	

## Attachment 2

### CHARACTERISTICS OF TYPE A, B, AND C LESIONS

#### Type A lesions (minimally complex)

- Discrete (length  $\leq 10$  mm)
- Concentric
- Readily accessible
- Nonangulated segment ( $< 45^\circ$ )
- Smooth contour
- Little or no calcification
- Less than totally occlusive
- Not ostial in location
- No major side branch involvement
- Absence of thrombus

#### Type B lesions (moderately complex)

- Tubular (length 10 to 20 mm)
- Eccentric
- Moderate tortuosity of proximal segment
- Moderately angulated segment ( $> 45^\circ, < 90^\circ$ )
- Irregular contour
- Moderate or heavy calcification
- Total occlusions  $< 3$  mo old
- Ostial in location
- Bifurcation lesions requiring double guidewires
- Some thrombus present

#### Type C lesions (severely complex)

- Diffuse (length  $> 2$  cm)
- Excessive tortuosity of proximal segment
- Extremely angulated segments  $> 90^\circ$
- Total occlusions  $> 3$  mo old and/or bridging collaterals
- Inability to protect major side branches
- Degenerated vein grafts with friable lesions

(From: Ryan et al. Guidelines for Percutaneous Transluminal Coronary Angioplasty: A Report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Committee on Percutaneous Transluminal Coronary Angioplasty). J Am Coll Cardiol 1993; 20:33-54.