DSRCS REVIEW

NDA#:	21-045
Drug:	Plan B (levonorgestrel) Tablets
Sponsor:	Women's Capital Corporation
Study:	Plan B Over-the-Counter Label Comprehension Study Final Report. Study Number 9728
Study Report Date:	November 5, 2001 (Submission Date April 2003)
Reviewer:	Karen Lechter, J.D., Ph.D.
Reviewing Div:	HFD-410
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Executive Summary

In a label comprehension study of the labeling on the outside and inside of the package, study participants demonstrated good understanding of some concepts and low understanding of a few concepts. Results for other concepts were inconclusive due to the wording of some of the questions and the sponsor's scoring system for open-ended questions. Despite some shortcomings in the questionnaire and some scores that were lower than desirable, the Division of Surveillance, Research, and Communication Support (DSRCS) believes that labeling changes are likely to result in acceptable levels of comprehension. Results of the Actual Use Study should weigh more heavily in evaluating the labeling.

Concepts that received relatively high comprehension scores are the following:

- Plan B is for contraception.
- Plan B does not protect against STD's, including HIV/AIDS.
- Do not take the product while pregnant; Plan B cannot end a pregnancy.
- Do not use Plan B if you are allergic to its ingredients.
- Nausea and vomiting are side effects.

Concepts with moderate levels of understanding include the following:

- Take the first tablet within 3 days of intercourse.
- Get medical help if severe abdominal pain develops.

Concepts that may not be clearly understood or for which the data are inconclusive are the following:

- Plan B is not for regular use for contraception.
- Take the first tablet as soon as possible after intercourse.
- Take the second tablet 12 hours after the first one.
- Do not use Plan B if you have unexplained vaginal bleeding
- Use Plan B **after** intercourse.
- Plan B can be used even if the woman has medical conditions not mentioned on the label. (Asthma was mentioned in the question.)

As a result of these findings, DSRCS believes that comprehension of the critical messages is adequate or would be adequate after changes to the labeling. Therefore, DSRCS has the following recommendations based on the study:

- Strengthen the following messages:
  - Not for regular use (sponsor has bolded this)
  - Timing of first dose
  - Timing of second dose (sponsor has bolded this)
  - If severe abdominal pain develops, seek immediate medical care
  - Do no use if unexplained vaginal bleeding (if kept in the labeling)
- State on the label if there is a window of time for the second tablet, rather than just the 12 hour time already given.

In addition, DSRCS has a recommendation to help women time the second dose appropriately:

- Have a place on the label for the woman to write the time she took the first pill and the time she should take the second pill.

Inclusion of a package insert might be helpful for consumers.

REVIEW

The purpose of this study was to evaluate comprehension of a prototype OTC package label for Plan B emergency contraceptive pills.

Communication Objectives

The study tested 11 Communication Objectives important for safe and effective use of the product:

1. Plan B is indicated for prevention of pregnancy after unprotected sex.
2. Plan B is intended as a back up method and should not be used for regular contraception.
3. Plan B does not prevent sexually transmitted diseases or HIV/AIDS.
4. The first pill should be taken as soon as possible after intercourse.
5. The first pill should be taken within 72 hours after intercourse.
6. The second pill should be taken 12 hours after the first.
7. Plan B should not be used by women who are already pregnant (because it will not be effective).
8. Plan B should not be used by women with unexplained vaginal bleeding.
9. Plan B should not be used by women with allergy to any ingredient in the product.
10. Side effects of Plan B include nausea and vomiting.
11. If severe abdominal pain develops, the user should seek medical care immediately.

Methodology

Participants

Participants were 663 females, age 12-50 years old. Sample size was based on using a 95% confidence interval of ±5 percentage points, conservatively assuming the proportion of correct responses would be 50%. Based on these requirements, a minimum sample size was 385. To ensure adequate demographic representation and a sufficient number of low literacy women for subset analyses, the target sample was increased to 575. In actuality, data for 656 participants were reported.

Distribution by age was as follows:

Age Range	%
12-16	12
17-25	54
26-50	34

Black and Hispanic women were overrepresented with respect to the general population as follows:

Race	Study population %	General population %
Black	24	12
Hispanic	24	13
White	49	75

More than ¾ of participants were sexually experienced. Most of them had had unprotected intercourse despite a desire not to become pregnant. More than half of participants who had used oral contraceptive pills reported having missed taking pills, and 40% of those who had used condoms had had a condom break. At least 82% of the sexually experienced participants had had either a pregnancy scare or sex not adequately protected by contraception. Only 32 of the sexually experienced participants had ever used emergency contraceptive pills.

Literacy levels among those age 18 or older who had not completed college were as follows:

Literacy Level	% (n=395)
3rd grade or less	<1
4th-6th grade	4
7th-8th grade	31
High school	64
Missing	<1

The highest level of school completed was as follows:

Highest grade completed	% (n=656)
6th grade or less	1
7th or 8th grade	4
9th-11th grade	23
High school or GED	30
Vocational/technical school	3
Less than 4 years of college	18
College	16
Graduate school	6
Refused/missing	<1

Procedure

Interviews were conducted in shopping malls and family planning clinics in eight US cities. Minor participants recruited from clinics did not require parental consent to participate.

Before the interviews began, participants who were age 18 or older who had not completed college were tested for literacy level using the Rapid Estimate of Adult Literacy in Medicine (REALM) test.

For the main questionnaire, participants were asked to look at the outside of the Plan B package as if they were thinking about whether to purchase the product. The interviewer then removed the package while the participant answered the first question. The participant was permitted to look at the outside of the package while answering five additional questions. Participants were then told to open the package and review the contents as if they were about to use the product. Participants could refer to the package as well as the contents for the remaining questions.

The only information on the front outside of the package was the name of the product, the statement "Emergency Contraception," and the number and strength of the tablets. On the back was the Drug Facts format containing the most important information about the indication, warnings, directions, and ingredients. The back also included storage and manufacturing information. Additional information that reinforced the Drug Facts information was on the inside of the package.

At the end of the main questionnaire, participants were given a questionnaire asking information about their sexual activities.

Comments: The sponsor did not give the REALM literacy test to women who had graduated college or to participants younger than 18 years. It would have been better to test everyone, to make their study experience similar and to test literacy at all education levels, as all of these women represented potential product users. The sponsor noted that even at the level of some college education, there were some who tested as low literate.

In correspondence with the agency (Serial No. 110), the sponsor explained its decision not to test the younger participants for two reasons: (1) the REALM is designed for adults, and (2) the sponsor assumed that women under the age of 18 would not be well-educated. The college graduates were not tested because the sponsor assumed that college graduates would have at least a 9th grade literacy level. In hindsight, the sponsor notes that this assumption may not have been correct. The sponsor also pointed out that about 25% of the entire study population was either poorly educated or tested in the lower literacy group on the REALM. Twenty-eight aged 17 or younger had not gotten past 8th grade in school, and 139 who were tested were in the lower literate category.

As only the 393 women age 18 or older who had not graduated from college were categorized by literacy level, we do not have results by literacy level for the entire sample. We do not know what effect, if any, this fact had on the results of the analyses by literacy groups. However, because the results suggest a literacy effect for almost all of the communication objectives, we should proceed as if literacy has an effect on almost everything tested, and try to improve those aspects of the label for which the lower literate group seemed to have particular problems.

Questionnaires

Questions included multiple choice and open-ended questions. The latter are questions for which choices are not provided by the questioner. Many questions presented a hypothetical scenario and asked participants if Plan B use would be correct to use in the situation.

Comment: Scenario-type questions require more cognitive processing than more direct questions about information on the labeling because scenario questions require participants to apply the information.

Main Questionnaire

Question 7 was the first question asked about the product. It was asked after only the outside of the package had been read and after the package was removed. Therefore, this response was based on recall. Questions 8-12 were asked with only the outer carton available for reference. For the remaining questions, participants could open the carton and inspect the contents before responding.

At the end of the questioning about the labeling, participants were asked for demographic information and took a self-administered test ("Confidential Information Questionnaire") about sexual and contraceptive history.

Comments: The scenario questions asked, in essence, if the hypothetical person was using the product correctly or not. Many questions were of the yes/no or correct/incorrect variety. Such questions have a 50% chance of a correct response by chance. It would have been better to follow all of these questions with a probe asking

participants why they answered as they did. We therefore do not know if participants answered correctly by chance or because they knew the information.

Personal information questions about marital status and income did not seem useful to ask for comprehension purposes.

Confidential Information Questionnaire
This questionnaire asked about the participants' experience with sex and birth control. Results were used to further analyze responses to the main questionnaire by categorizing participants according to their responses to these questions.

Comment: The question "Have you ever had sex?" (Q. 1) would have benefited from providing a definition for "sex." Without such a definition, we must assume participants knew it meant sexual intercourse, but we cannot be sure. Q. 6 asked if the participant had ever used birth control pills and had missed taking two or more from one pack. The results were used to conclude that participants responding affirmatively to this question might have experienced anxiety about the possibility of being pregnant. Q. 10 asked if the woman had ever used emergency contraceptive pills. It would have been best to exclude these women from the study, as their experience, possibly with Plan B, might have raised their scores artificially. However, the results showed that there were only 32 in this group, and thus, they may have had little influence on the overall results. An analysis by the sponsor showed no effect of this prior experience on understanding the Communication Objectives. However, the small size of this group may be responsible for the lack of apparent effect. Thus, we cannot conclude that women with prior experience with emergency contraception would not understand the information better than others.

Results by Communication Objective

Results for the total sample were provided for each question. In addition, results for each Communication Objective were provided based on the following characteristics: literacy level, age, race, ethnicity, interview location, type of site (mall or clinic), income, education, previous sexual experience, sexual experience in the past three months, experience with pregnancy scare (condom break, missed pills, unprotected intercourse, worry about unwanted pregnancy), and experience using emergency contraceptive pills. Literacy level and location of the interview had an effect on most responses. Literacy level affected nine of the Communication Objectives. Location affected all of them. Other characteristics had far fewer effects. Any significant findings based on particular characteristics are mentioned in the appropriate sections that follow. The sponsor did not make adjustments for multiple confidence interval estimations.

The sponsor determined whether Communication Objectives had been met by participants based on formulas that differed among the Communication Objectives. For some objectives, correct responses to only half of the questions under that Communication Objective were deemed sufficient to indicate understanding of that

Communication Objective. For others, 75% or 100% of the questions needed to be correct to satisfy the sponsor's criteria for successful understanding.

Based on the sponsor's scoring method for Communication Objectives, more than 85% of participants understood seven of the 11 Communication Objectives, if both acceptable and correct answers were counted. Ninety-three percent (93%) understood that Plan B is indicated for prevention of pregnancy after unprotected sex (Objective 1), 94% understood it does not prevent HIV or AIDS (Objective 3), and almost all (98%) understood that it should not be used by pregnant women (Objective 7). Less than 80% understood two objectives: 67% understood Objective 2 (Plan B is intended as a back up method and should not be used for regular contraception), and 75% understood objective 8 (Plan B should not be used by women with unexplained vaginal bleeding.). The results by Communication Objective appear in Table 1.

Table 1. Results by Communication Objective.

Communication Objective	**% Understanding*** (N=656)
1. Plan B is indicated for prevention of pregnancy after unprotected sex	90/93**
2. Plan B is intended as a back up method and should not be used for regular contraception	67
3. Plan B does not prevent sexually transmitted diseases or HIV/AIDS	94
4. The first pill should be taken within 72 hours after intercourse	85
5. The first pill should be taken as soon as possible after intercourse	82
4. or 5. The first pill should be taken within 72 hours or as soon as possible after intercourse.	97
6. The second pill should be taken 12 hours after the first	69/85†
7. Plan B should not be used by women who are already pregnant	98
8. Plan B should not be used by women with unexplained vaginal bleeding	75
9. Plan B should not be used by women with allergy to any ingredient in the product	91
10. Side effects of Plan B include nausea and vomiting	89
11. If severe abdominal pain develops, the user should seek medical care immediately	81

*Based on sponsor's criteria of 50%-100% correct on questions relevant to each Communication Objective.
**First number based on correct responses for Q. 7 (Sponsor's interpretation). Second number based on correct/acceptable responses for Q. 7 (Sponsor's interpretation).
† First number based on correct responses for Q. 30. Second number based on correct/acceptable responses for Q. 30. (Sponsor's interpretation.)

More than 80% of lower literate women were able to understand eight of the 11 objectives. Women aged 16 years or younger were less likely than older women to understand many of the objectives, but the differences were not statistically significant in most cases, and more than 80% of the younger women understood seven objectives.

Comment: In correspondence with the Agency (facsimile dated 10/21/03), the sponsor stated that it developed the criteria for each communication objective prior to conducting the study. The sponsor said "it would be inappropriate to require subjects to answer all of the questions related to a particular objective 'right' (i.e., correctly or acceptably) for several reasons." These reasons included the fact that the sponsor knew that some questions and some answers, particularly responses to open-ended questions, would be ambiguous. Other reasons included the fact that "people do not always answer questions

correctly even when they know the correct answer," and that some questions were asked before participants saw the whole package.

In some instances, these criteria made it easier to reach the objective by using correct responses for less than all of the questions in an objective. Because there may be disagreement as to what criteria would be appropriate for each Communication Objective, this review will examine results of questions individually, as well as results by Communication Objective.

DSRCS would not necessarily agree with the scoring of some of the "acceptable" responses. Thus, scores for some Communication Objectives may be lower under DSRCS's scoring.

Of the subgroups, DSRCS is most interested in results by literacy level. As noted earlier, the sponsor did not include all participants in the analyses of Communication Objectives based on literacy levels. Instead, only participants age 18 or older who had not completed college were included. Thus, because we do not have a complete comparison of the entire sample of the lower literate (reading level 8th grade or below) with those of a higher reading level, any conclusions we draw from the literacy analysis should be viewed with the understanding that the sample had limitations. Presumably, many of those below age 18 (at least 12%) would test as lower literate, because they had not completed high school. On the other hand, those who had graduated from college (22%) were more likely to be in the higher literacy group. Thus, we cannot be sure how well the literacy results reflect the range of potential product users.

Communication Objective 1: Plan B is indicated for prevention of pregnancy after unprotected sex. (Q 7, 14, 16, 19) *[Communication Objective satisfied if at least two answered correctly]*

The first question in this set (Q. 7) was open-ended (not multiple choice). The other three were all of the yes/no variety, asking if the hypothetical situation described was a correct use of the product.. For these three questions, the correct response was that it was a correct use.

Q. 7 asked what Plan B is used for. The response was based on recall, as the carton was removed before the question was asked. Forty-five percent (45%) responded that the product is for contraception after sex. Thirty-nine percent (39%) stated only that it is for contraception. The sponsor counted both of these as acceptable responses. Therefore, a total of 84% provided correct or acceptable responses to this question under the sponsor's scoring system. For this question, the lower literate group scored 73%, compared with 87% for the higher literate group.

For this Communication Objective, there was a statistically significant difference between the adult (age 18 or older) lower literate (8th grade or lower) and those with a higher reading level. As noted earlier, participants under age 18 and college graduates were not included in this analysis. The results show that 84% of the adult lower literate

met the sponsor's criterion for success on this objective, while 96% of the adult higher literate were successful. Table 2 summarizes the most common responses to Q.7.

Table 2. Responses to open-ended question about purpose of product (Q.7)

Response	**% Responding** (N = 656)
contraception after sex*	45
contraception**	39
after sex, purpose unspecified	4
STI/HIV	1
emergency (sex not mentioned)	1
other	4
don't know/refused	6

*correct under sponsor's scoring

** acceptable under sponsor's scoring

Comment: For Q. 7, it is not clear that those who mentioned only that the product was for contraception, and did not mention "after sex," truly understood the full nature of the indication. It would have been better if this question had probed for more responses by asking if there was anything else the participant wanted to add. Therefore, the total figure of acceptable responses for that question of 84% may be overstating the level of understanding of the participants on this issue. On the other hand, it is likely that some, perhaps many, of those who mentioned only contraception actually understood that the product is used after sex, but failed to mention that detail. We should keep in mind that Q. 7 was answered without participants being able to refer to the carton. For that reason, the relatively low totally correct score (contraception after sex) for this item should not be cause for concern, particularly when viewed in conjunction with other questions about specific uses for the product.

Q. 14 was a scenario about a woman who wanted to use Plan B after a condom broke. Participants were asked if this was an appropriate use according to the package. Ninety-one percent (91%) responded correctly that it was an appropriate use. Eighty-one percent (81%) of the lower literate were correct, while 95% of the higher literate were correct.

Q. 16 stated that a woman with asthma had unprotected sex and took Plan B the next day to prevent pregnancy. Participants were asked if this was a correct use. Sixty-three percent (63%) responded correctly that it was an appropriate use.

Q. 19 asks about using the product two days after unprotected sex. Eighty-seven percent (87%) correctly stated that it was an appropriate use. For this question, 78% of the lower literate and 90% of the higher literate were correct.

Table 3 summarizes responses to the three scenario questions for these Communication Objectives for the total sample.

Table 3. Correct responses to scenario questions about the indication

Question	**% Correct** (N = 656)
14. condom broke	91
16. asthma/unprotected sex	63
19. unprotected sex 2 days ago	87

The sponsor stated that 90% of participants met the criterion for understanding this Communication Objective. The criterion for success was to answer at least two of the four questions correctly or acceptably.

Comment: The relatively low rate of correct responses for the question about the woman with asthma suggests that there may be a tendency for participants to be confused if other medical conditions are mentioned. This may be due to an inclination to respond conservatively to the questions, so that when in doubt, the participant would state that product should not be used. In correspondence with the Agency (Serial No. 110), the sponsor speculates that some women may not fully understand the term "asthma" and some women may have been flustered by this question. Further study would be necessary to determine what caused so many incorrect responses for the question mentioning asthma. Asking participants why they responded as they did might have clarified the situation.

Overall, results for this Communication Objective suggest the following:

- *About 90% understand some specific situations in which it is appropriate to use the product.*
- *There is a tendency to state, incorrectly, that certain medical conditions might preclude use. However, incorrect responses may be an artifact of the testing situation. Moderately high proportions of participants were able to identify two situations under this Communication Objective in which the product would be appropriate.*
- *Many participants did not clearly express the full indication for the product when asked from memory without further prompting.*
- *The sponsor's criterion for success on this Communication Objective (two of the four responses correct or acceptable) seems rather low. With a higher criterion for success, fewer than 90% would have been considered to have answered correctly.*

Communication Objective 2: Plan B is intended as a back-up method and should not be used for regular contraception. (Q. 9, 21, 22, 25) [*Communication Objective satisfied if at least three answered correctly]*

For this series of questions, the three scenarios all depict inappropriate uses, and one question is direct. Q. 9 asks the direct question whether Plan B should be used as regular birth control. Eighty-five percent (85%) answered correctly. Only 71% of the lower literate were correct, while 93% of the higher literate were correct.

Q. 21 presents a scenario in which a woman's husband complains about using condoms and asks if it is correct to use Plan B in this situation. The correct response is that it is not an appropriate use. Only 47% correctly responded here. The sponsor suggests this may be due to the fact that some of the questions used to define this objective "may have required excessively strict or unrealistic interpretation of the concept of 'emergency' contraception." The intent of Q. 21 was that the woman should find another contraceptive method or refuse to have sex when her husband refuses to use condoms. The sponsor stated that this choice might be improbable in the minds of many women, who may have assumed unprotected sex was inevitable and therefore using Plan B would be appropriate. The sponsor will bold the label text "Plan B should not be used in place of regular contraception" to emphasize this point. The lower literate scored 37% for this question, while the higher literate scored 53%.

Q. 22 is a scenario about someone who inappropriately uses Plan B daily instead of usual birth control. Ninety-one percent (91%) were correct on this question. The lower literate scored 76%; the higher literate scored 95%.

Q. 25 is about a couple that wants to use Plan B as the main contraceptive method. Only 68% answered this one correctly. The lower literate scored 50%; the higher literate scored 78%.

The sponsor concluded that the Communication Objective was met by a participant if three of the four questions were answered correctly. Sixty-seven percent (67%) of participants met this criterion. There was a statistically significant difference between the lower and higher literacy participants for this Communication Objective. Forty-six percent (46%) of the adult lower literate met the criterion for success, while 78% of the adult higher literate were successful. Table 4 presents the results for these four questions for the total sample.

Table 4. Correct responses to scenario questions about Using Plan B for regular contraception

Question	**% Correct** (N = 656)
9. Direct question about use for regular birth control	85
21. Husband complains about condoms	47
22. Use Plan B daily instead of usual birth control	91
25. Couple uses Plan B as main contraceptive method	68

Comment: Results for these questions would have been easier to interpret if each question had been followed by another question asking why the woman responded as she did. We do not know if correct responses were correct for the right reasons, or if the incorrect ones were incorrect due to misunderstanding or for some other reason.

In response to the direct question about use for regular contraception, a respectable proportion of participants (85%) answered correctly. However, far fewer were correct about use if one's partner does not want to use protection. The scenario for that question (Q.21) stated that "This time she plans to use plan B." The implication could be that this is a one-time event. Thus, it may not be unreasonable for the women to believe that Plan B is appropriate. Therefore, the relatively low results of this question (Q.21) should not be counted heavily.

However, there does not seem to be a clear rationale for the relatively low scores (68%) for the scenario about using Plan B as the main contraceptive method (Q.25), despite the fact that many more (85%) were correct in saying the product should not be used for regular birth control (Q.9), and a high proportion (92%) answered correctly for a different scenario (Q. 22) that the product should not be used daily instead of usual birth control. In correspondence with the Agency (Serial No. 110), the sponsor suggests that Q. 25 required "more extended thought processes" than the other questions, which may have contributed to the lower correct response rate.

Even using the sponsor's criterion for achieving the Communication Objective (3/4 correct), a relatively low number of participants (67%) seemed to understand clearly and consistently that the product is not to be used as the main form of contraception. Even fewer lower literate participants seemed to understand this concept.

The conflicting results for questions under this Communication Objective suggest that the message that this product is not for regular use should be strengthened on the label.

Communication Objective 3: Plan B does not prevent sexually transmitted diseases or HIV/AIDS. (Q. 13 and 27) *[Communication Objective satisfied if both answered correctly.]*

The two questions in this group include a scenario question and a direct question. Responses to both of these questions should be that Plan B does not protect against STD's. Q. 13 is a scenario about a woman using Plan B to avoid STD's. Ninety-six percent (96%) answered correctly. Among the lower literate, 88% were correct, while among the higher literate, 99% were correct. Q. 27 is a direct question asking if Plan B protects against HIV and other STD's. Ninety-eight percent (98%) answered this correctly.

For this Communication Objective, there was a statistically significant difference between the lower literate and higher literate. Eighty-four percent (84%) of the adult lower literate met the sponsor's criterion for success for this question, while 99% of the adult higher literate were successful. Table 4. summarizes these results for the total sample.

Table 5. Correct responses to questions about use for STD's

Question	**% Correct** (N = 656)
13. scenario about use to avoid STD's	96

27. direct question about protection against HIV and other STD's	98

Comment: Participants understood at high rates that Plan B cannot protect against STD's. Although the lower literate scored lower than the higher literate, scores for the lower literate were not very low.

Communication Objective 4: The first pill should be taken within 72 hours after intercourse. (Q. 10, 29, 19, 20) *[Communication Objective satisfied if at least two answered correctly: 10 (if response mentions 72 hours or 3 days), 29, (19 and 20)]*

Q. 10 asks what the best time is to take the first pill. If the participant has not already said both "within 3 days" **and** "as soon as possible," Q. 10 also includes a second part that asks if the label says anything more specific. The correct answer is "as soon as possible **and** within 72 hours or three days." Twenty-three percent (23%) gave this response. Acceptable responses were the following: "within 72 hours or three days" (31%), **or** "as soon as possible" (26%). Thus, a total of 80% had correct or acceptable responses. An additional 10% said "72 hours or 3 days." These responses were not scored as correct because they did not indicate that was the maximum time.

Q. 29 asks how many days is the longest after sex that a woman should wait before taking the first pill. Ninety-one percent (91%) correctly responded 72 hours. Eighty-four percent (84%) of the lower literate and 95% of the higher literate were correct on this question.

Q. 19 applies also to the first Communication Objective, discussed earlier. Eighty-seven percent (87%) correctly said it was correct to use Plan B if the woman had unprotected sex two days earlier.

Q. 20 asks about use if unprotected sex was a week ago. Ninety-five percent (95%) correctly stated that this was an incorrect use.

The sponsor scored this objective as having been met if participants answered at least two of the four questions correctly. Eighty-five percent (85%) met this criterion. There was a statistically significant difference between the literacy groups in attaining the criterion for success for this Communication Objective. Seventy-one percent (71%) of the adult lower literate and 90% of the adult higher literate met the criterion. Table 6 presents the results for this Communication Objective for the full sample.

Table 6. Correct/acceptable responses to questions about taking the tablet within 72 hours after intercourse

Question	**% Correct/acceptable** (N = 656)
10. Best time to take first tablet	80
29. The longest one should wait before first tablet	91
19. Use 2 days after unprotected sex	87
20. Use 1 week after unprotected sex	95

Comment: If we deem as acceptable for Q. 10 those 10% of responses that mentioned 72 hours or three days, but did not indicate that was the maximum time, then the correct/acceptable score for Q. 10 would be 90%. It is likely that many in this 10% group had the correct understanding, but were sloppy in expressing it. Overall, the results for this Communication Objective suggest moderately high understanding of the timing of the first tablet. However, to be sure that more lower literate women understand this issue, the timing of the first tablet should be emphasized if possible.

Communication Objective 5: The first pill should be taken as soon as possible after intercourse. (Q.10, 26) *[Communication Objective satisfied if either answered correctly, where response to Q. 10 mentions as soon as possible]*

As noted earlier, Q. 10 asked the best time to take the first tablet. Twenty-three percent (23%) scored correctly (as soon as possible **and** within 72 hours or 3 days). A total of 57% scored acceptably (either within 72 hours or 3 days, **or** as soon as possible, without providing a time frame). Acceptable responses included 26% who said as soon as possible. Therefore, for Q. 10, 80% scored correctly or acceptably. Q. 26 asks if Plan B will be more effective if taken one day after unprotected sex or two days after unprotected sex. Seventy-one percent (71%) correctly said one day. Sixteen percent (16%) said both were the same, and 12% incorrectly said two days. Among the lower literate, 64% were correct, compared with 75% of the higher literate.

The sponsor counted people as responding correctly for this Communication Objective if for Q. 10 they mentioned "as soon as possible" or answered correctly to Q. 26. Eighty-two percent (82%) met this criterion. For this Communication Objective, there were no significant differences between the adult lower literate and higher literate participants. Table 7 presents these results.

Table 7. Correct/acceptable responses about timing of the first tablet

Question	**% Correct/acceptable** (N = 656)
10. Best time to take first tablet	80
26. Better to take at 1 days or two?	71

Comment: The moderate overall correct response rate for Q. 10, and the even lower rate among the lower literate, combined with the somewhat lower overall correct response

rate for Q. 26 make it advisable to strengthen the labeling for this issue. Approximately 1/3 seem not to have understood the message about using the product as soon as possible, although there seems to be good understanding, based on other questions, that it should be taken within three days of unprotected intercourse.

Communication Objective 6: The second pill should be taken 12 hours after the first (Q. 30)

Q. 30 asks directly when a woman should take the second tablet. Sixty-nine percent (69%) correctly said 12 hours after the first tablet. The sponsor counted as acceptable those who mentioned 12 hours but said something other than the full correct response. Seventeen percent (17%) responded in this way. An additional person (<1%) gave the response of the next morning, which the sponsor counted as acceptable. Thus, 87% answered correctly or acceptably under the sponsor's scoring system. For this question, there was a statistically significant difference among the literacy groups, with 82% of the adult lower literate and 93% of the higher literate responding correctly or acceptably. Table 8 presents these results for the full sample.

Table 8. Responses about when to take the second tablet (Q. 30)

Response	**% Responding** (N=656)
12 hours after first tablet*	69
12 hours (but did not give full response)*	17
the next morning*	<1
other	12

*Scored as correct or acceptable by sponsor

Comment: It is not clear whether those mentioning 12 hours but not saying "12 hours after the first tablet" truly understood the concept. It is possible that some of them did not, but it is also likely that many of them did. In correspondence with the Agency (facsimile of 10/21/03), the sponsor stated that "…some participants had difficulty communicating in standard English." The sponsor counted as acceptable "responses we suspected were probably correct but were slightly ambiguous, so we could not be sure." They included answers such as "after 12 after the first one," "before your 12 hours is up," "up to 12 hours after the first," "within 12 hours." Thus, it is possible that some responses scored as acceptable by the sponsor did not reflect correct understanding. Also, although it is a minor point, DSRCS would not have scored " the next morning" as an acceptable response. We do not know when the first pill was taken in that case.

Based on only the completely correct responses, only 69% conveyed clear understanding of when to take the second pill. Because it is possible a number of those participants who were scored as acceptable for this question did not truly understand, the timing of the second pill should be emphasized in the materials. We recommend also that the label state what to do if the dose is not taken at exactly 12 hours. If possible, the label should indicate if there is a window of time in which the second dose can be taken.

To assist women in determining exactly when to take the second tablet, we suggest there be a space on the package for the woman to fill in with the time when she took the first tablet and the time when she should take the second tablet.

Q. 23 was not specifically associated with this Communication Objective. However, it is related to the timing of the second dose. Q. 23 asked if it was correct for a woman to take both tablets at the same time. Ninety-six percent (96%) answered correctly that it was not correct.

Comment: A more detailed scenario providing the reasons why the woman might have taken both at the same time would have been more realistic and perhaps would have provided a better question to test this concept.

Communication Objective 7: Plan B should not be used by women who are already pregnant (because it would not be effective). (Q. 11 or Q. 17) *[Communication objective met if either answered correctly.]*

Q. 11 asks whether a woman who is two months pregnant should use Plan B. Ninety-two percent (92%) correctly responded. Q. 17 asks if it was correct for a pregnant woman to use Plan B because she didn't want to become pregnant. Eighty-nine percent (89%) answered this question correctly. Ninety-eight percent (98%) answered at least one of these correctly, which was the sponsor's criterion for having understood the concept. While scores for both literacy groups were high, there was a statistically significant difference between them. The adult lower literate scored 95% on this criterion for success, while the adult higher literate scored 99%.

Q. 12 was not associated with a specific Communication Objective by the sponsor. It is a follow-up to Q. 11, which asked if a woman who is two months pregnant should use Plan B. Q. 12 asks for the reason behind the response to Q. 11. Ninety-four percent (94%) responded correctly that she was already pregnant, the product won't work, or it is too late to use it. Table 9 presents the results for questions related to this Communication Objective.

Table 9. Correct/acceptable responses about use by pregnant women

Question	**% Correct/Acceptable** (N=656)
11. Use by woman 2 months pregnant	92
12. Reason for response to Q. 11	94
17. Use if have positive pregnancy test	89

Comment: As stated in the protocol, one aspect of this Communication Objective was that the product is not effective in pregnant women. This issue was not specifically tested, but it did surface in responses to Q. 12. It appears that a relatively high proportion of participants understood that the product is not appropriate during pregnancy. Responses to Q. 12 suggest that the reasoning for responses to Q. 11 is appropriate.

Communication Objective 8: Plan B should not be used by women with unexplained vaginal bleeding. (Q. 15)

Q. 15 is a scenario about a woman who had unusual vaginal bleeding during the week and who took Plan B to prevent pregnancy after unprotected sex. Participants were asked if this was a correct use of Plan B. Seventy-six percent (76%) answered correctly. Again, there was a statistically significant difference between the literacy groups. The adult lower literate scored 69%, while the adult higher literate scored 82%.

Comment: Clearly, this concept was not highly understood. If it is kept in the labeling, it should be emphasized further, either by bolding or by explaining its importance, or both.

Communication Objective 9: Plan B should not be used by women with allergy to any ingredient in the product. (Q. 18)

Q. 18 is a scenario about a woman allergic to an ingredient in Plan B who used it because she noticed that her partner's condom broke during sex. When asked if this was a correct use of Plan B, 91% answered properly that it was an incorrect use. The differences between literacy groups were statistically significant. The adult lower literate scored 82%, while the higher literate scored 96%.

Communication Objective 10: Side effects of Plan B include nausea and vomiting. *(Q. 32-37) [Communication Objective satisfied if correct on Q. 32 and Q. 34, or nausea/vomiting mentioned in answer to Q. 37. Scored as not meeting Objective if she answered "yes" to all of Q. 32-36.]*

Q. 32-35 ask if different symptoms can be side effects of Plan B (32-nausea; 33-trouble breathing; 34-vomiting; 35-fever). Q. 36 asks if there are any other possible side effects, and Q. 37 asks participants to name one of the possible side effects.

The sponsor considered participants as having understood the Communication Objective if they answered Q. 32 and Q. 34 correctly or if nausea and vomiting were mentioned in answer to Q. 37, unless all of Q. 32-36 were answered "yes." Based on these criteria, 89% understood this Communication Objective. For this Communication Objective, there were statistically significant literacy differences. The adult lower literate scored 84%, while the adult higher literate scored 96%. For Q. 37, 81% of the lower literate were correct and 93% of the higher literate were correct.

When those who said there were other possible side effects were asked to name one additional side effect, 87% provided a correct response. Table 10 presents the results for this set of questions.

Table 10. Correct responses to side effects questions.

Question	**% Correct** (N = 656)
32. nausea a side effect?	99
33. trouble breathing a side effect?	83
34. vomiting a side effect?	96
35. fever a side effect?	80
36. other possible side effects?	94
37. name one other side effect	87

Comment: These results show that participants generally understand the side effects of vomiting and nausea. However, there is a slight tendency to say that everything is a side effect, as evidenced by incorrect scores of about 15-20% for the questions about symptoms that are not real side effects. Such a tendency may have slightly elevated the scores for the nausea and vomiting items. The question asking for another side effect does not seem to contribute much to our understanding of participants' knowledge of the full range of side effects. However, there were no Communication Objectives addressing specific side effects other than nausea and vomiting

Communication Objective 11: If severe abdominal pain develops, the user should seek medical care immediately. (Q. 31)

The question for this Communication Objective presented a scenario asking what a woman should do if she gets severe stomach pain after using Plan B. Seventy percent (70%) said to see or call a doctor, with no time frame mentioned. Eleven percent (11%) said to see or call a doctor immediately. Four percent (4%) said to see a doctor, but not immediately, and 10% said to stop using the product. The sponsor scored as correct responses to see or call a doctor immediately or to see a doctor with the time not mentioned. On that basis, 81% responded acceptably. There were no differences between literacy groups. Table 11 presents the results.

Table. 11. Responses about what to do for severe abdominal pain (Q. 31)

Response	**% Responding** (N=656)
See/call a doctor (time not specified)*	70
See/call a doctor immediately*	11
See/call a doctor, not immediately	4
Stop using	10
Other	1
call number on box	<1

*Scored as correct or acceptable.

Comment: Based on these results, it is not clear that participants understand that they should get immediate medical help for severe abdominal pain. However, as the sponsor suggests, perhaps in real life, it is likely that women who experience this pain would seek medical help quickly. The sponsor should consider emphasizing this message.

Additional Results

Some questions were not associated by the sponsor with particular Communication Objectives. Q. 8 asks if Plan B is the same or different from ordinary birth control pills. Eighty two percent (82%) answered correctly. For this question, 73% of the lower literate and 87% of the higher literate answered correctly.

Comment: Unfortunately, the questionnaire did not ask how this product is different, to enable us to further understand the responses.

Q. 24 was eliminated by the sponsor. It asked "A woman stopped taking her birth control pills a week ago and then she had sex with no other birth control method. She then used Plan B to prevent pregnancy. Was this a correct use of Plan B?" The sponsor said the question was "excluded from the analysis because it was recognized to have been ambiguous after the survey was concluded." No additional explanation was provided.

Comment: We do not know why the sponsor dropped this question, yet retained Q. 21, which also may have been ambiguous. A better explanation of the criteria used to drop a question would have been helpful here.

Q. 28 was a multiple choice question that asked when a woman should expect her next period after taking Plan B. The correct response, at about the normal time, was given by 79% of participants. The sponsor considered the response of one week later as acceptable because the label said **"…your next period should come at the normal time, or a few days early or late. If your period is more than one week late, you may be pregnant."** An additional 10% gave the acceptable response, making a total of 89% correct or acceptable. Five percent (5%) said she should expect her period immediately, and about 1% said she never should expect it. Table 12 shows these results.

Table 12. Responses to when to expect the next period (Q. 28)

Response	**% Responding** (N = 656)
About normal time*	79
1 week late*	10
immediately	5
refused	5
never	1

*Correct or acceptable

Comment: These results suggest a fairly good understanding of the effect of the medication on women's menstruation. The choice of "never" seemed unlikely to be correct on its face, and should have been replaced with another choice.

Results by demographic characteristics

Age. Using the sponsor's criteria for demonstrating comprehension of each Communication Objective, age made a statistically significant ($p \leq .05$) difference for four of the objectives. Table 13 presents those differences.

Table 13. Statistically significant differences for Communication Objectives by age

Communication Objective	**Age 12-15 Correct/ acceptable (%) (n=76)**	**Age 17-25 Correct/ acceptable (%) (n=355)**	**Age 26-50 Correct/ acceptable (%) (n=255)**	**Total Correct/ acceptable (%) (n=656)**
1. Plan B indicated for prevention of pregnancy after unprotected sex*	86	93	95	93
3. Plan B does not prevent sexually transmitted diseases or HIV/AIDS	93	96	92	94
6. Second pill should be taken 12 hours after the first**	77	90	82	86
10. Side effects include nausea and vomiting	90	93	84	89

*includes correct and acceptable responses for Q. 7
**includes correct and acceptable responses for Q. 30

Comment: We should keep in mind that there were no adjustments for multiple comparisons. Therefore, some of these apparently statistically significant differences might have occurred by chance. For 3/4 of these Communication Objectives, the youngest age group scored lowest. For 3/4 of the objectives, the oldest age group scored lower than the middle group. Thus, there is no clear linear effect of age on increasing or decreasing comprehension. It is possible that there is a quadratic relationship, with the youngest and oldest understanding less than those in the mid-range. It is likely that because of the varying age ranges for the three age categories, particularly the very wide (26-50) range for the oldest group, some age-related differences were not detected. Even with these differences, the youngest group (Age 12-15) did not score extremely low.

Race. For three of the Communication Objectives, race made a statistically significant difference. Table 14 presents these results. There was not a consistent trend for any

particular racial group to do better than others. In two of the thee objectives, whites did better than blacks. However, in another, blacks did better than whites and the "other" group.

Table 14. Statistically significant differences for Communication Objectives by race

Communication Objective	**White % Correct/ Acceptable**	**Black % Correct/ Acceptable**	**Other % Correct/ Acceptable**	**Total % Correct/ Acceptable**
2. Plan B is intended as a back up method and should not be used for regular contraception	75	57	61	67
8. Plan B should not be used by women with unexplained vaginal bleeding	77	68	79	75
11. If severe abdominal pain develops, the user should seek medical care immediately	79	88	81	81

Literacy. Literacy level had a statistically significant effect on nine of the 11 Communication Objectives. Table 15 presents the Communication Objectives that showed these differences.

Table 15. Statistically significant differences for Communication Objectives by literacy level.

Communication Objective	**Lower Literate** % Correct/Acceptable (N=139)	**Higher Literate** % Correct/Acceptable (N=254)	**Total** (N=393)
1. Plan B is indicated for prevention of pregnancy after unprotected sex*	84	96	92
2. Plan B is intended as a back up method and should not be used for regular contraception	46	78	67
3. Plan B does not prevent sexually transmitted diseases or HIV/AIDS	84	99	93
4. The first pill should be taken within 72 hours after intercourse	71	90	83
6. The second pill should be taken 12 hours after the first**	82	92	89
7. Plan B should not be used by women who are already pregnant	95	99	98
8. Plan B should not be used by women with unexplained vaginal bleeding	69	81	77
9. Plan B should not be used by women with allergy to any ingredient in the product	82	95	90
10. Side effects of Plan B include nausea and vomiting	84	96	92

*Includes correct and acceptable responses for Q. 7.
**Includes correct and acceptable responses for Q. 30.

In addition to literacy differences by Communication Objective, there were many instances of differences between the literacy groups for the individual questions. Differences between the groups for correct and acceptable responses varied from 1 percentage point to 28 percentage points, with a mean of 11 points. In all cases, the lower literate group scored lower than the higher literate group. The sponsor did not report which of these differences may have been statistically significant. Responses for the two literacy groups are reported in Table 16.

Table 16. Correct/acceptable results for questions by literacy groups.

Question	Lower Literate % Correct/Acceptable (N=139)	Higher Literate % Correct/Acceptable (N=254)
7. Tell what Plan B is used for	73	87
8. Different from ordinary birth control?	73	87
9. Should Plan B be used as regular birth control?	71	93
10. Best time to take 1st tablet	21/75*	26/83*
11. Use if 2 months pregnant	88	93
13. Correct to use to avoid STD's?	88	99
14. Use after condom broke	81	95
15. Use if unusual vaginal bleeding	69	82
16. Use if have asthma	61	66
17. Use if positive pregnancy test	84	92
18. Use if allergic and condom broke	82	96
19. Use 2 days after sex	78	90
20. Use after 1 week	88	96
21. Husband complains about condoms; woman wants to use Plan B	37	54
22. Use Plan B every day instead of usual birth control pills	76	95
23. Take both tablets together	89	98
25. Couple wants to use Plan B as main contraceptive method	50	78
26. Is plan B more effective 1 day or 2 days after sex?	64	75
27. Protection against STD's	94	100
28. When expect next period	65/84*	85/91*
29. What is longest woman can wait to take first tablet?	84	95
30. When take second tablet?	64/82*	77/93*
31. What do if severe stomach pain?	7	10
32. Nausea a side effect?	96	100
33. Trouble breathing a side effect?	78	88
34. Vomiting a side effect?	97	98
35. Fever a side effect?	77	82
36. Other side effects not mentioned?	91	95
37. Name other side effects not mentioned in previous questions	81	93

*First number correct; second number correct plus acceptable by sponsor's scoring

Comment: Literacy level had a definite effect on the results of the study. For most Communication Objectives and for most questions, there were substantial differences in scores between the two literacy groups. Comprehension among the lower literate was

particularly low for Communication Objective 2, concerning use of Plan B as a back up method and not for regular contraception. These results suggest that any strengthening of the messages in the labeling might increase comprehension among the lower literate, but particular attention should be paid to messages about not using the product for regular contraception and not using it if there is unexplained vaginal bleeding, as the lower literate scores were the worst for these two concepts.

We should keep in mind that the only participants included in the literacy analyses were those who were age 18 or older who had not graduated from college. Therefore, all college graduates were eliminated, as were teen-agers. Twenty-two percent (22%) of the full sample had graduated college, and more than 12% were under age 18. (The sponsor reported age ranges of 12-16, 17-25, and 26-50. Therefore, we do not know exactly how many were below age 18.) As a result of this analysis of fewer than the full sample, the literacy results may be atypical, as only adults who had not graduated from college were included. Because college graduates were excluded, it is possible that the higher literacy group had lower literacy than a typical higher literate group taken from the population as a whole, and differences between the literacy groups may therefore be minimized. However, balancing that possibility is the possibility that participants under age 18 would lower the literacy level of the lower literate group, again widening the differences between the groups.

It would have been better to include all participants in the literacy analyses to get a better picture of how literacy would affect the full range of potential product users. Nevertheless, the results do show that literacy had an effect on almost every Communication Objective, making it apparent that lower literate women may have more trouble in understanding the labeling than higher literate women.

Previous sexual experience. There were no statistically significant differences based on whether or not the participants had had sexual experience.

Experience using emergency contraceptive pills. There were not statistically significant differences based on pervious use of emergency contraception.

Comment: As there were only 32 in this group, we should not conclude that they would not answer differently than other women if there had been a larger sample.

Location of interview. There were statistically significant differences based on geographic interview location for all of the Communication Objectives.

Comment: This result is not surprising, as locations are chosen to add variety to the socioeconomic and demographic characteristics of participants.

Other demographic and location effects. Race had an effect on three Communication Objectives, and ethnicity on two. Income affected three Communication Objectives and education affected four. Previous sexual experience had no effect, and experience with a

pregnancy scare and sex within the past three months affected only one Communication Objective, as did site (mall vs. clinic).

Comment: These differences were too few to lead to conclusions that there were systematic effects of these participant characteristics.

Discussion and Conclusions

Based on the sponsor's assessment, two Communication Objectives were understood by less than 80% of the sample. One was that Plan B is intended as a back up method and should not be used for regular contraception. The sponsor attributes this as possibly due to the wording of the questions. However, to help communicate this message, the sponsor will bold the text "Plan B should not be used in place of regular contraception." The other Communication Objective that was understood by less than 80% stated that the product should not be used by women with unexplained vaginal bleeding. The sponsor does not believe this contraindication is appropriate and has stated that it will seek to remove it from the label.

Based on the sponsor's analyses of Communication Objectives, two objectives were understood by 80% and 85% of participants. One was that the first pill should be taken as soon as possible after intercourse and the other one was about what to do if severe abdominal pain develops. The sponsor states that the timing of the first pill should not be viewed in isolation, as the product is still highly effective if use is delayed up to 72 hours. Almost all (97%) understood the product should be used within 72 hours, or as soon as possible after sex. The sponsor believes that failing to demonstrate understanding of what to do if there is severe abdominal pain is not of "extreme clinical concern," because women "do not need written instructions to know that they should see a doctor if severe pain develops." The sponsor plans to bold "as soon as possible" and "a serious medical problem (describing ectopic pregnancy) in the next version of the labeling.

Comment: DSRCS does not agree with the sponsor's scoring of some responses as acceptable. Further, some of the Communication Objectives could be satisfied if fewer than 100% of the questions in the objective were answered correctly. Thus, the sponsor's overall conclusions about the level of comprehension based on Communication Objectives are probably higher than those of DSRCS.

However, DSRCS believes that comprehension of critical messages was generally adequate or could be improved by label changes. Misunderstandings about regular use would be affected by the cost of the product and would not present public health issues.

The following summarizes DSRCS's findings for each Communication Objective:

1. Participants tended to understand that the product is for contraception. However, it was not clear if it was on the top of their mind that the product is for use **after** sex. As the question asked for information from memory and participants who gave partial responses were not probed for further information, it is possible that many

participants may have known that the product was for use after sex but did not express that fact.

Participants understood a variety of situations in which to use the product, but there was a tendency to say that it should not be used if one has other medical conditions. This tendency may have been an artifact of the questioning situation.

2. There were inconsistent responses about use for regular contraception. These conflicting results may be due to weaknesses in the questionnaire rather than to lack of comprehension.
3. There is a high level of understanding that Plan B does not protect against STD's, including HIV/AIDS.
4. There is moderate to high understanding of when to take the first tablet. About 90% understood that users should wait no more than 3 days.
5. The fact that the first pill should be taken as soon as possible after intercourse was not understood at high levels. Of the two questions in this Communication Objective, one scored 80% and the other 71%.
6. The fact that the second tablet should be taken 12 hours after the first was not highly understood, or the results are ambiguous.
7. A fairly high majority understood not to take the product while pregnant and that the product could not end a pregnancy.
8. There was relatively low understanding (76%) not to use the product if there is unexplained vaginal bleeding. The sponsor stated that it plans to request that this information be removed from the label.
9. There is fairly high understanding not to use the product by persons allergic to its ingredients.
10. There is high understanding of nausea and vomiting as side effects.
11. There is moderate (81%) understanding that one must get medical help if severe abdominal pain develops. The sponsor states that women "do not need written instructions to know they should see a doctor if severe pain develops."

This study suggests that there may be some lack of clarity about some issues. Failure to attain high scores for some questions may be due to actual knowledge deficits or to shortcomings of the questionnaire. As we cannot be sure of the source of the lower scores, we recommend stressing the messages that did not score in the high ranges. Messages in the labeling that may not have been communicated at the highest levels include the following:

- Do not use for regular contraception
- Use after intercourse
- Timing of doses
- Do not use if experiencing unexplained vaginal bleeding
- Get medical help for severe abdominal pain

Based on the results of this study, the sponsor has recognized some of the shortcomings of the label and stated that it planned to bold certain information in the label in an effort to communicate that information more effectively.

Results of this study and the ensuing changes to the label to emphasize information that had not been understood at very high levels should be viewed in conjunction with the Actual Use Study. That study provides insight as to whether the revised labeling was sufficient to enable women in the use trial to use the product appropriately.

Recommendations

Based on these results, DSRCS has the following recommendations for changes to the label that had been used in this study:

- Strengthen the following messages:
    - Not for regular use (sponsor has bolded this)
    - Timing of first dose
    - Timing of second dose (sponsor has bolded this)
    - If severe abdominal pain develops, seek immediate medical care
    - Do no use if unexplained vaginal bleeding (if kept in the labeling)
- State if there is a window of time for the second tablet, rather than just the 12 hour time.

In addition, DSRCS has a recommendation to help women time the second dose appropriately:

- Have a place on the label for the woman to write the time she took the first pill and the time she should take the second pill.