EVALUACION DE LA EFICACIA, SEGURIDAD Y ACEPTABILIDAD DE LA MIFEPRISTONA Y EL MISOPROSTOL PARA INDUCIR EL ABORTO EN LA MUJERES EN ESTADO DE EMBARAZO CON AMENORREA HASTA 63 DIAS DE DURACION

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El objetivo del presente estudio es determinar la seguridad, eficacia y aceptabilidad de la mifepristona con misoprostol para terminar el embarazo en mujeres que hayan tenido el primer día de su último período mensual hace 63 días o menos. Tres grupos de mujeres con menos de 50 días; de 50 a 56 días y de 57 a 63 días desde el primer día del último período mensual se incluirán en el estudio. Este estudio se está llevando a cabo como un requisito para la registración de la mifepristona con misoprostol en la Administración de Alimentos y Medicinas de los Estados Unidos (Food and Drug Administration - FDA) para que estos productos se puedan usar para terminar embarazos en los Estados Unidos.

2. Visitas a la clínica

Tengo entendido que en mi primera visita (visita 1) seré asesorada sobre este método y se obtendrá una muestra de mi orina y sangre para asegurarse que estoy embarazada. Se me hará un examen médico, se examinará mi pelvis y tomarán mi historia clínica. Se determinará la duración de mi embarazo utilizando un ultrasonido vaginal, que es una sonda pequeña que se coloca dentro de la vagina. También, se me hará un análisis de sangre para ver si tengo el factor Rh en mi sangre. Si tengo el tipo de sangre Rh negativo, me pondrán una inyección durante la segunda visita para evitar que se desarrollen anticuerpos que pudiesen poner en peligro cualquier embarazo futuro. Entiendo que me pueden pedir muestras de sangre adicionales (como 2 cucharaditas) para medir los niveles de diferentes substancias que se encuentran normalmente en la sangre así como para determinar las características normales de mi sangre. Si decido no permitir que me saquen más muestras de sangre, todavía puedo seguir participando en el estudio.* Para poder terminar mi embarazo, tomaré por vía oral tres tabletas de mifepristona (el primer medicamento) en presencia del personal del estudio.Dos días después regresaré a la clínica (visita 2) aunque yo piense que he abortado y me tomaré por vía oral dos tabletas de misoprostol (segundo medicamento) si no he abortado. Si me tomo el segundo medicamento, la duración de mi estancia en la clínica durante la segunda visita será de aproximadamente cuatro horas. Durante ese tiempo seré cuidadosamente vigilada por el equipo del estudio. Durante este tiempo hay una oportunidad de un 60%-80% de que ocurra el aborto. Si vengo a la clínica en carro, me aseguraré de tener a alguien que me regrese a la casa después de esta visita. Entiendo que yo no puedo ir guiando hasta mi casa.

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Entiendo que si el aborto no ocurre en la clínica, ese muy probable que ocurra en la casa y puede que siga sangrando por el útero durante varios dias. Entiendo que la cantidad de sangre puede ser parecida a la que ocurre durante un aborto espontáneo (esto es, más que durante una regla mensual fuerte). El riesgo de un sangramiento fuerte aumenta después que hayan pasado más de 49 días desde el primer día de mi última menstruación.** Debo usar almohadillas sanitarias hasta que deje de sangrar del útero o que las manchas terminen y no debo usar tampones. Al igual que con un aborto quirúrgico, no puedo volver a hacerme lavados vaginales ("douching") hasta que deje de sangrar (de 10-12 días). No debo volver a tener relaciones sexuales hasta después de ocho a diez días de haber tomado la prostaglandina, pues después de ese tiempo la mayoría de los abortos han terminado.

Yo entiendo que es posible que vea el producto de la concepción en la almohadilla sanitaria o en el excusado. Esto puede suceder en la clínica, en la casa o en el trabajo. Hasta la séptima semana después de la concepción este producto se llama un embrión; es más pequeño que una moneda de veinticinco centavos y generalmente está incrustado dentro de un coágulo de sangre. Aunque yo vea el producto de la concepción, no podré darme cuenta si el método ha tenido éxito ya que puede quedarse parte de la placenta en el útero. Por esto es importante regresar a la clínica para el seguimiento, la visita 3, para que los empleados de la clínica puedan determinar si el aborto ha sido completo.

Se me dará una cita para que regrese a la clínica dos semanas después de haber tomado la primera tableta (visita 3) para estar seguros que el tratamiento ha tenido efectividad. Entiendo que me pueden pedir de nuevo que de muestras de sangre (como 2 cucharaditas) para medir los niveles de diferentes substancias en mi sangre y para determinar las características de mi sangre. Si decido no permitir que me saquen más muestras de sangre, aún puedo seguir participando en el estudio.* Si el tratamiento no ha tenido efectividad, entonces en ese momento se llevará a cabo un procedimiento quirúrgico llamado aspiración al vacío o dilatación y curetaje para terminar el aborto. Este es el mismo

**Enmienda 3 de fecha 2 de mayo de 1995
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procedimiento quirúrgico que hubiese recibido si hubiese decidido hacerme un aborto quirúrgico desde el principio. Estaré segura de tener a alguien que me lleve para la casa en carro después de esta visita y entiendo que yo misma no puedo manejar. Si me doy cuenta que después del tratamiento tengo un flujo vaginal que tiene olor, puede indicar una infección. Me pondré en contacto con mi médico para hacer una cita.

Entiendo que la sangre puede continuar después de mi tercera visita. Si esto sucede, la clínica se pondrá en contacto telefónico conmigo para determinar si ya ha parado o si necesito tratamiento adicional.

Yo entiendo que hasta ahora no ha habido indicaciones que el uso una antiprogestina para terminar un embarazo no ha evitado ni ha dañado la capacidad de una mujer de tener un bebé en el futuro. La mujeres que han tomado mifepristona han podido concebir después y han tenido hijos saludables. Ya que es posible volver a quedar embarazada después del aborto, se me pedirá que seleccione un método para evitar los hijos.

3. Beneficios

Entiendo que la ventaja del método para terminar un embarazo utilizando mifepristona/misoprostol es que evita un procedimiento quirúrgico. No hay riesgos relacionados con la anestesia no riesgo de perforación del útero o de lesiones al conducto cervical que ocurre raras veces después de terminar un embarazo de forma quirúrgica. Otro beneficio es la satisfacción de participar en el estudio que hará que las mujeres de los Estado Unidos tengan disponibles la mifepristona/misoprostol.

4. Riesgos y molestias

Entiendo que cuando me saquen la sangre para los análisis en la primera visita y la tercera visita puedo sentir molestia, tener moretones y puede ocurrir una infección en el sitio de donde se sacó la sangre. Entiendo que la experiencia que existe hasta ahora con la combinación de drogas y el terminar un embarazo de poco tiempo indica que esta terapia tiene pocas reacciones secundarias. La frecuencia de complicaciones de corta duracion se puede comparar con la que se observa después de un aborto quirúrgico hecho con aspiración al vacío. La queja más común durante el tratamiento (en particular después de la administración del segundo medicamento) es dolor en el bajo vientre o retorcijones parecidos a los que se relacionan con un período mensual fuerte. Recibiré el medicamento apropiado contra el dolor cuando sea necesario.

Entiendo que no debo tomar aspirina, Motrin®, ibuprofen (Advil®) o cualquier otra droga que se sabe bloque la acción de las prostaglandinas. Sin embargo, puedo tomar Tylenol® y mi médico me puedo recetar medicamentos más fuertes contra el dolor. Entiendo que los retorcijones y los dolores abdominales es una parte del proceso del aborto normal y esperada. Se ha observado la existencia de nauseas, vómitos y diarrea después de la administración del segundo medicamento. Por lo tanto, es necesario quedarse en la clínica bajo la supervisión apropiada en la segunda visita durante alrededor de cuatro horas antes de regresar a la casa. Entiendo que la cantidad de sangre puede ser parecida a la que ocurre durante un aborto espontáneo (esto es, más que durante una regla mensual fuerte). El riesgo de un sangramiento fuerte aumenta después que hayan pasado más de 49 días desde el primer día de mi última menstruación.** En raras ocasiones, puede haber mucha sangre del útero que cause la necesidad de hacer un aborto quirúrgico y/o una transfusión de sangre.

Entiendo que no es aconsejable dejar que siga un embarazo después de haber tomado mifepristona y/o misoprostol, ya que se desconocen los efectos completos de la mifepristona en el feto y la administración del misoprostol al principio del embarazo se ha asociado al desarrolló anormal del feto. Entiendo que, con base en estudios anteriores y en información obtenida recientemente, el aborto después de la mifepristona/misoprostol tiene éxito en terminar el embarazo en aproximadamente el 95% de las mujeres tratadas que tuvieron el primer día de su última menstruación no más de 49 días antes de recibir la mifepristona. Entre las mujeres que tuvieron el primer día de su última menstruación de 50 a 63 días antes de recibir la mifepristona, tantas como una de cada cuatro pueden necesitar algún tipo de intervención quirúrgica según sugiere esta nueva información.**

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Entiendo que no es aconsejable dejar que siga un embarazo después de haber tomado mifepristona y/o misoprostol, ya que se desconocen los efectos completos de la mifepristona en el feto y la administración del misoprostol al principio del embarazo se ha asociado al desarrollo anormal del feto. Entiendo que el aborto después de la mifepristona/misoprostol tiene éxito en terminar el embarazo en aproximadamente el 95% de las mujeres tratadas. Cuando el aborto no es completo, se recomienda la aspiración al vació o la dilatación y curetaje para dejar de sangrar y evitar la anemia. Cuando no ocurre el aborto, se recomienda terminar el embarazo de forma quirúrgica debido al riesgo posible para el feto. Yo he estado de acuerdo de antemano con este procedimiento.

No han habido problemas cardíacos graves en las 52,000 mujeres que han utilizado la combinación de drogas en el estudio sobre la terminación del embarazo. Sin embargo, ocurrieron complicaciones cardiovasculares graves, incluyendo un ataque al corazón mortal, durante abortos médicos utilizando una combinación de drogas diferente. Estos problemas cardíacos han ocurrido generalmente en mujeres que fuman mucho o que tienen gran cantidad de lípidos (grasas) en la sangre, diabetes, presión arterial alta o historia familiar de enfermedades del corazón. Este riesgo también aumentó en las mujeres mayores de 35 años de edad. Estas complicaciones sólo se han observado después de una prostaglandina inyectada y son raras (una en 20,000 casos). Hasta la fecha no hay pruebas que la prostaglandina oral (misoprostol) que yo tomaré en este estudio y que ha sido de amplio uso durante largos períodos de tiempo para el tratamiento de las úlceras estomacales, esté relacionada con esas reacciones cardiovasculares secundarias.

5. Declaración alterna

Se que se puede terminar mi embarazo pode medio de un aborto hecho por medio de cirugía (dilatación y curetaje o aspiración al vacío). Las posibles ventajas y desventajas de terminar el embarazo de forma quirúrgica en lugar de con medicamentos se me ha explicado. Las ventajas de terminar el embarazo de forma quirúrgica es que es un procedimiento de un día. Los riesgos relacionados con un aborto quirúrgico son mínimos. Esto incluye el riesgo del procedimiento anestésico. En los Estados Unidos, menos del 1% de las pacientes que se hacen un aborto quirúrgico tienen complicaciones graves relacionadas con el procedimiento tales como infección grave de la pelvis, cuello del útero rajado, sangre excesiva que necesite una transfusión o cirugía inesperada de mayor importancia (para una perforación del útero).

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6. Declaración sobre lesiones físicas

Si necesito recibir tratamiento médico como resultado de una lesión física que ocurriera debido a mi participación en este estudio, se me ofrecerá la asistencia médica y tratamiento esencial a corto plazo de inmediato según lo determinen los médicos de este estudio sin cargo adicional ninguno para mi. No recibiré ninguna otra compensación monetaria para ninguna otra asistencia, pero tendré a mis disposición asesoramiento médico y servicios de referencia. Puedo obtener más información sobre la disponibilidad de la asistencia médica y tratamiento para cualquier lesión física que haya resultado de mi participación en este estudio del Investigador, Dr. Sue Haskell a 515-280-7000 or 1-800-568-2404.

7. A quién llamar en caso de emergencia

Comprendo que si sangro por el útero de forma excesiva o tengo dolores abdominales o si se me presenta cualquier otra emergencia médica, se lo informaré inmediatamente a Planned Parenthood of Greater Iowa, 851 19th Street, Des Moines, Iowa 50314. Además, me pondré en contacto con el Dr. Haskell a 515-280-7000. Si no me puedo poner en contacto con él o ella cuando exista una emergencia relacionada con el éstudio, puedo ponerme en contacto con el ——— a 515-280-7000 or 1-800-568-2404.

8. Ofrecimiento de responder preguntas y libertad de retirarse del estudio.

Se me ha dicho que me puedo retirar del estudio en cualquier momento sin poner en peligro la asistencia médica que yo recibo o vaya a recibir en el futuro del hospital o la clínica. Si me retiro, se me ofrecerá un aborto quirúrgico. Se me ha dicho que me puedo poner en contacto con el Dr. Haskell ot ——— a 515-280-7000 tengo alguna pregunta sobre la investigación. Estos médicos pueden nombrar a sus asociados para que respondan mis preguntas.

También comprendo que el Investigador Principal me puede pedir que me retire del estudio si en su juicio clínico es de mejor interés para mi salud o si se me hace imposible seguir el procedimiento experimental de este estudio.

Yo comprendo que si mi tratamiento bajo el estudio no da como resultado un aborto, y si rehuso recibir un aborto quirúrgico y sigo con el embarazo, yo me arriesgo y la criatura puede tener el riesgo de complicaciones incluyendo deformidades del feto o de la criatura.

9. Confidencialidad

Entiendo que la información obtenida en este estudio será transmitida de forma que no se pueda relacionar conmigo y que todos los récords se mantendrán en un gabinete con cierre.

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Comprendo que el Consejo sobre la Población (Population Council) o los observadores nombrados por ellos así como la Administración de Alimentos y Drogas de los Estados Unidos pueden solicitar el acceso a mis récords médicos.

Comprendo que se me puede solicitar que un representante del patrocinador me entreviste. Esta entrevista se llevará a cabo en el idioma que yo hablo y verificará que yo comprendo los riesgos, beneficios, procedimientos y naturaleza experimental del estudio. Si no estoy de acuerdo en ser entrevistada, esto no afectará mi asistencia médica actual o futura en el hospital o la clínica o mi participación en el estudio. Yo comprendo que puedo cambiar mi decisión en cualquier momento. Toda la información se mantendrá confidencial.

10. Declaración del sujeto

A mi, la infrascrita, se me han explicado los riesgos y beneficios de este estudio en un idioma que yo entiendo. Estoy de acuerdo en participar en este estudio como voluntaria.

_____

Fecha Firma de la voluntaria

11. Declaración del investigador

Yo, el infrascrito (la infrascrita) le explicado a la voluntaria en el idioma que ella habla, los procedimientos a seguir en este estudio y los riesgos y beneficios relacionados con éste.

_____

Fecha Firma del(a) investigador(a)

_____

Fecha Firma del testigo de las firmas anteriores y explicación

Ngày tháng _____ Chữ ký của người tình nguyện _____

11. Phát biểu của Chuyên viên Nghiên cứu

Tôi, ký tên dưới đây, đã giải thích cho người tình nguyện bằng ngôn ngữ mà họ nói về thủ tục phải theo trong cuộc nghiên cứu này cùng các rủi ro và lợi ích liên quan.

Ngày tháng _____ Chữ ký của chuyên viên nghiên cứu _____

Ngày tháng _____ Chữ lý của chứng nhân cho các chữ ký và giải thích trên _____

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KẾ HOẠCH THÍ NGHIỆM CHI TIẾT SỐ: 166 A

1. Mục đích và các mục tiêu của việc nghiên cứu

Rất có thể gây phá thai nơi phụ nữ có thai mà không muốn có con bằng cách cho dùng mifepristone kết hợp với một prostaglandin (misoprostol). Mifepristone là một loại thuốc ngăn chặn hoạt động của kích thích tố tiết ra bởi noãn sào, một loại kích thích tố cần có để duy trì sự thai nghén. Một trong những hoạt động của Mifepristone là làm gián đoạn sự thai nghén trong các thời kỳ đầu. Prostaglandins là các chất tự nhiên do lớp lót của tử cung sản xuất ra trong lúc có kinh và gây ra sự co rút của tử cung. Tin tức có được gần đây xác minh lời phát biểu cho rằng mifepristone kết hợp với misoprostol gây ra phá thai cho khoảng 95 phần trăm phụ nữ mà ngày đầu tiên của thời kỳ kinh nguyệt cuối cùng đã xảy ra không quá 49 ngày trước khi được cho uống mifepristone. Đối với phụ nữ mà ngày đầu tiên của thời kỳ kinh nguyệt đã xảy ra khoảng từ 50 đến 63 ngày trước khi uống mifepristone, tin tức mới này cho rằng có tới một phần tư phụ nữ cần phải có một thủ tục giải phẫu nào đó. Một số lý do khiến cần phải có một thủ tục giải phẫu như thế gồm có việc thai nghén được tiếp tục, phá thai không hoàn chỉnh, hay chảy máu quá nhiều. Khả năng bị chảy máu nhiều tăng lên với sự gia tăng thời kỳ tắt kinh**. Các lợi ích chính của phương pháp chấm dứt thai nghén này là không cần phải có dụng cụ giải phẫu đẩy vào trong tử cung. Khoảng 150,000 phụ nữ trong 20 nước đã dùng mifepristone và một prostaglandin như một phương pháp y học để chấm dứt thai nghén. Mifepristone và misoprostol đã được trên 50,000 phụ nữ sử dụng ở liều lượng được dùng trong cuộc nghiên cứu này. Liều lượng được nghiên cứu đã được chấp thuận tại Pháp để dùng theo thông lệ cho phụ nữ có thai trong bảy tuần lễ hay ít hơn. Mifepristone phối hợp cùng với prostaglandin cũng đã được chấp thuận cho dùng tại Trung quốc, Anh quốc, và Thụy điển. Tại hai nước sau này, nó được dùng cho phụ nữ có thai trong chín tuần hay ít hơn.

Các mục tiêu của cuộc nghiên cứu hiện nay là xác định tính an toàn, công hiệu, và chấp nhận được của mifepristone cộng với misoprostol để chấm dứt thai nghén nơi phụ nữ đã được tắt kinh tới 63 ngày hay ít hơn kể từ ngày đầu của kỳ kinh nguyệt trước. Ba nhóm phụ nữ có thai, một nhóm ít hơn 50 ngày; một nhóm từ 50 đến 56 ngày; và từ 57 đến 63 ngày kể từ ngày đầu của kỳ kinh nguyệt trước được đưa vào nghiên cứu này. Cuộc nghiên cứu đang được hoàn thành này là một điều kiện để đăng ký thuốc mifepristone cộng misoprostol với Cơ quan Quản Trị Thực phẩm và Thuốc(FDA) để cho các sản phẩm này có thể được dùng để chấm dứt thai nghén tại Hoa kỳ.

2. Khám bệnh để quan sát.

Tôi hiểu rằng vào lần khám bệnh đầu tiên (khám bệnh 1) tôi sẽ nhận được các lời khuyên về phương pháp, và một mẫu nước tiểu và máu sẽ được lấy để chắn chắn rằng tôi đang mang thai. Tôi sẽ được khám sức khỏe, và khám xương chậu, và bệnh sử của tôi được ghi lại. Nhờ dùng một máy dò siêu âm đặt vào âm đạo, thời gian tôi mang thai sẽ được xác định. Tôi cũng sẽ được thử máu để tìm yếu tố Rh trong máu của tôi. Nếu tôi có loại máu với Rh âm, tôi sẽ được chích một mũi thuốc vào lần khám bệnh thứ hai để

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phòng ngừa sự phát sinh những kháng thể có thể làm nguy hại đến sự thai nghén trong tương lai. Tôi hiểu rằng tôi có thể được yêu cầu cho lấy thêm các mẫu máu (khoảng 2 muỗng trà) để đo lường mức độ các chất khác nhau thường thấy trong máu của tôi cũng như để xác định các đặc tính bình thường máu của tôi. Nếu tôi quyết định không cho lấy thêm mẫu máu, tôi vẫn có thể tiếp tục tham gia vào cuộc nghiên cứu này*. Để chấm dứt sự thai nghén của tôi, tôi sẽ uống ba viên mifepristone (lần cho uống thuốc đầu tiên) trước mặt các nhân viên của cuộc nghiên cứu.

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Hai ngày sau, tôi sẽ trở lại bệnh viện (khám bệnh 2) cả khi tôi tin rằng tôi đã phá thai rồi và tôi sẽ uống hai viên misoprostol (cho uống thuốc lần thứ hai) nếu tôi chưa phá thai. Nếu tôi uống thuốc lần thứ hai, thời gian tôi ở lại bệnh viện lần thứ hai sẽ dài chừng khoảng bốn giờ, trong khi đó tôi sẽ được theo dõi thật sát bởi nhóm nghiên cứu. Trong thời gian này, có chừng 60-80% cơ may phá thai sẽ xảy ra. Nếu tôi đến bệnh viện bằng xe, tôi sẽ chắc chắn sắp xếp để cho một người nào khác lái xe cho tôi về nhà từ lần khám bệnh này, và tôi hiểu rằng tôi sẽ không tự mình lái xe về nhà. Tôi hiểu rằng nếu sự phá thai không xảy ra tại bệnh viện, thì rất có thể nó sẽ xảy ra tại nhà và tôi có thể bị tiếp tục chảy máu từ cung giống như thời kỳ kinh nguyệt nặng trong nhiều ngày. Tôi hiểu rằng lượng máu chảy ra cũng tương tự như lượng máu chảy ra khi bị xảy thai tự nhiên (có nghĩa là nhiều hơn thời kỳ kinh nguyệt nặng). Rủi ro chảy máu nhiều tăng lên sau 49 ngày kể từ ngày đầu của thời kỳ kinh nguyệt cuối cùng của tôi**. Tôi sẽ dùng băng kinh nguyệt cho đến khi máu chảy từ tử cung hay máu chảy nhẹ từ âm đạo chấm dứt và không dùng nút bông kinh nguyệt. Cũng như với việc phá thai qua giải phẫu, tôi không thể xối nước lại cho đến khi máu ngưng rỉ (vào khoảng từ 10-12 ngày). Tôi sẽ không làm tình lại trong khoảng từ 8 đến 10 ngày sau khi uống protaglandin mà vào thời gian hầu hết các vụ phá thai đều đã được hoàn thành.

Tôi hiểu rằng tôi có thể thấy sản phẩm của sự thai nghén trên băng vệ sinh hay trong cầu vệ sinh. Điều này có thể xảy ra tại bệnh viện, tại nhà, hay tại sở làm. Cho đến hết tuần thứ bảy sau khi thai nghén, sản phẩm này được gọi là bào thai; nó nhỏ hơn đồng 25 xu và thường thường được lồng trong các cục máu. Dù cho tôi có nhìn thấy sản phẩm thai nghén, tôi sẽ không thể nào nói được rằng phương pháp này có hiệu quả hay không vì một phần của nhau có thể còn ở lại trong tử cung. Vì vậy mà tôi cần phải trở lại bệnh viện để được theo dõi, khám bệnh 3, để nhân viên bệnh viện có thể xác định là phá thai đã hoàn thành hay chưa.

Một buổi hẹn sau này sẽ được dự trù để cho tôi trở lại bệnh viện hai tuần sau khi uống viên đầu tiên (khám bệnh 3), để bảo đảm rằng việc chữa trị có hiệu quả. Tôi hiểu rằng tôi có thể được yêu cầu cho lấy thêm các mẫu máu (khoảng 2 muỗng trà) để đo lường mức độ các chất khác nhau thường thấy trong máu của tôi cũng như để xác định các đặc tính bình thường máu của tôi. Nếu tôi quyết định không cho lấy thêm mẫu máu, tôi vẫn có thể tiếp tục tham gia vào cuộc nghiên cứu này*. Nếu việc chữa trị không có hiệu quả, thì một thủ tục gọi là hút chân không hay việc làm dãn nở và nạo tử cung sẽ được thực hiện để hoàn thành việc phá thai vào lúc đó. Đây cũng giống như thủ tục giải phẫu đáng lẽ đã được thực hiện nếu ngay lúc đầu tôi đã chọn đi theo cách phá thai bằng giải phẫu. Tôi sẽ chắc chắn sắp xếp cho người nào đó lái xe cho tôi về nhà từ lần khám này, và hiểu rằng tôi sẽ không tự lái xe về nhà. Nếu tôi thấy mủ hay huyết trắng từ âm đạo có mùi hôi sau khi chữa trị, điều này có thể chỉ ra một sự nhiễm trùng. Tôi sẽ tiếp xúc với y sĩ để làm hẹn khám.

Tôi hiểu rằng máu chảy có thể tiếp tục qua cả lần khám thứ ba của tôi. Nếu điều này xảy ra, bệnh viện sẽ tiếp xúc với tôi bằng điện thoại để xác định xem máu đã ngừng chảy chưa hay tôi cần phải được chữa trị thêm.

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Tôi hiểu rằng không có một dấu chỉ nào hiện thời cho thấy rằng việc dùng một chất antiprogestin để chấm dứt sự mang thai đã ngăn ngừa hay làm phương hại đến khả năng có con của người phụ nữ trong tương lai. Phụ nữ uống mifepristone đã có thể có khả năng thụ thai và rồi sau đó có con khỏe mạnh. Vì rất có thể có thai lại sau khi phá thai, tôi được yêu cầu phải chọn và dùng một phương pháp ngừa thai nào đó.

3. Các Lợi ích.

Tôi hiểu rằng một lợi ích của phương pháp y học dùng mifepristone/misoprostol để chấm dứt thai nghén là nó tránh được thủ tục giải phẫu. Không có rủi ro liên hệ đến thuốc mê hay rủi ro tử cung bị lủng hay thương tích ở vùng cổ tử cung hiếm hoi quan sát thấy sau khi chấm dứt thai nghén bằng phẫu thuật. Một lợi ích khác là sự hài lòng được tham gia vào cuộc nghiên cứu có thể làm cho mifepristone/misoprostol sẵn sàng để sử dụng cho phụ nữ tại Hoa kỳ.

4. Các rủi ro và khó chịu

Tôi hiểu rằng lấy máu để thử nghiệm vào lần khám bệnh đầu tiên và lần khám thứ ba có thể gây ra khó chịu, bầm tím, và cũng có thể nhiễm trùng tại nơi lấy máu. Tôi hiểu rằng kinh nghiệm thu lượm được cho đến bây giờ trong việc phối hợp thuốc và chấm dứt thai nghén

sớm cho thấy phép thì đều này có tất cả biến chứng. Tần thường xảy ra của các biến chứng ngắn hạn này có thể so sánh được với tính thường xảy ra của các biến chứng quan sát được sau khi phá thai bằng phẫu thuật qua việc dùng hút chân không. Điều than phiền thông thường nhất trong khi chữa trị (nhất là sau khi cho uống thuốc lần thứ hai) là đau ở bụng dưới hay co quắp bắp thịt cũng giống như co quắp liên hệ với một thời kỳ kinh nguyệt nặng. Tôi sẽ nhận được thuốc men thích hợp để chống đau khi cần. Tôi hiểu rằng tôi sẽ không uống thuốc as-pi-rin, Mo-trin*, I-bu-pro-fen (Advil*) hay bất cứ một thứ thuốc gì khác được biết có tác dụng làm tắc nghẽn hoạt động của các prostaglandins. Tuy nhiên, tôi sẽ uống Ty-le-nol* và tôi có thể nhận được từ bác sĩ một liều lượng mạnh hơn để chống đau. Tôi hiểu rằng co quắp bắp thịt và đau bụng dưới là thông thường và là một phần của tiến trình phá thai. Buồn nôn, mửa, và ỉa chảy đã được quan sát thấy tiếp theo lần cho uống thuốc thứ hai. Vì vậy, vào lần khám bệnh thứ hai, tôi cần phải ở lại bệnh viện dưới sự giám sát y tế vào khoảng bốn giờ trước khi trở về nhà. Tôi hiểu rằng chảy máu âm đạo tương tự như chảy máu khi bị xảy thai tự nhiên (nghĩa là nhiều hơn thời kỳ kinh nguyệt nặng), và kéo dài ít nhất một tuần, có thể xảy ra. Rủi ro chảy máu nhiều tăng lên sau 49 ngày kể từ ngày đầu của thời kỳ kinh nguyệt cuối cùng của tôi**. Trong những trường hợp hiếm hoi, chảy máu âm đạo nặng có thể xảy ra đòi hỏi phải phá thai bằng phẫu thuật và/hay truyền máu.

Tôi hiểu rằng không nên để cho sự thai nghén tiếp tục sau khi uống mifepristone và/hay misoprostol, vì những hậu quả đầy đủ của mifepristone trên thai nhi chưa được biết và việc uống misoprostol vào thời kỳ thai nghén lúc đầu đã được kết hợp với sự phát triển bất bình thường của thai nhi. Tôi hiểu rằng căn cứ vào các nghiên cứu trước kia và tin tức có được gần đây, sự phá thai sau khi uống mifepristone/misoprostol đã thành công để chấm dứt thai nghén cho 95 phần trăm phụ nữ mà ngày đầu tiên của thời kỳ kinh nguyệt cuối cùng đã xảy ra không quá 49 ngày trước khi cho uống mifepristone. Đối với phụ nữ mà ngày đầu tiên của thời kỳ kinh nguyệt cuối cùng đã xảy ra khoảng từ 50 đến 63 ngày trước khi uống thuốc mifepristone, tin tức mới này cho rằng có tới một phần tư phụ nữ cần phải có một thủ tục giải phẫu nào đó**.

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Tôi hiểu rằng không nên cho để cho việc thai nghén tiếp tục sau khi dùng mifepristone và/hay misoprostol, vì hiệu quả đầy đủ của mifepristone trên thai nhi không được biết và việc cho thuốc misoprostol vào lúc mới thai nghén đã được liên kết với việc phát triển các thai nhi bất bình thường. Tôi hiểu rằng phá thai sau khi uống mifepristone/misoprostol đã thành công trong việc chấm dứt thai nghén trong 95% số phụ nữ được chữa trị. Khi phá thai không hoàn tất, hút chân không hay làm dãn nở và nạo tử cung được khuyến cáo để chấm dứt chảy máu và ngăn ngừa thiếu máu. *Khi phá thai không xảy ra, chấm dứt thai nghén bằng phẫu*

thuật được khuyến cáo bởi vì có sự rủi ro cho thai nhi. Tôi đã đồng ý trước đây về thủ tục này.

Không có tình trạng tim nghiêm trọng nào trong số 52,000 phụ nữ dùng sự phối hợp thuốc trong thí nghiệm này để chấm dứt thai nghén. Tuy nhiên, có biến chứng nghiêm trọng về tim mạch, kể cả một trường hợp chết vì đau tim trong khi phá thai theo cách y học dùng phối hợp thuốc. Các tình trạng về tim này thường xảy ra nơi phụ nữ hút thuốc nặng hay đã tăng lượng mỡ trong máu, tiểu đường, áp huyết cao, hay có truyền thống bệnh tim trong gia đình. Rủi ro này cũng tăng lên với phụ nữ trên 35 tuổi. Các biến chứng này đã chỉ thấy sau khi chích prostaglandin và rất hiếm xảy ra (một trong 20,000 trường hợp). Cho đến nay không có bằng chứng nào rằng uống prostaglandin (misoprostol) được liên kết với biến chứng về tim mạch mà tôi sẽ uống trong cuộc nghiên cứu này và đã được sử dụng rộng rãi trong những thời gian dài trong để phòng ngừa bao tử bị ung loét.

5. Phát biểu về Cách khác

Tôi biết rằng thai nghén của tôi có thể chấm dứt bằng thủ tục phá thai theo phẫu thuật (làm dãn nở và và nạo vét tử cung hay hút chân không). Những lợi ích và bất lợi có thể có của việc chấm dứt thai nghén bằng phẫu thuật thay vì chấm dứt bằng y học đã được cắt nghĩa cho tôi hiểu. Lợi ích của việc chấm dứt thai nghén bằng phẫu thuật là thủ tục chỉ kéo dài trong 1 ngày. Các rủi ro liên kết với phá thai bằng phẫu thuật là tối thiểu. Các rủi ro này gồm cả rủi ro dùng thuốc mê. Tại Hoa kỳ, chỉ có dưới 1% các bệnh nhân dùng thủ tục phá thai bằng phẫu thuật trải qua một biến chứng quan trọng liên kết với thủ tục này như nhiễm độc nghiêm trọng vùng xương chậu, cổ tử cung bị rách, chảy máu cần phải truyền máu hay phẫu thuật mà không có ý định trước (vì tử cung bị lủng).

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6. Phát biểu về Thương tích gây cho thân thể

Nếu tôi cần phải chữa trị bằng thuốc men vì hậu quả của thương tích về thân thể phát sinh từ việc tôi tham gia vào việc nghiên cứu này, việc chăm sóc thuốc men và chữa trị ngắn hạn, thiết yếu, tức thời như được xác định bởi các y sĩ trong cuộc nghiên cứu này sẽ có sẵn cho tôi mà không gây tổn phí. Sẽ không có một sự đền bù tiền bạc nào cho bất cứ sự chăm sóc nào khác, nhưng việc tham khảo về y tế và các dịch vụ giới thiệu thích hợp vẫn có sẵn. Muốn biết thêm chi tiết về các sự chăm sóc về y tế và chữa trị có sẵn cho thương tích do hậu quả của việc tôi tham gia vào cuộc nghiên cứu này, xin tiếp xúc với chuyên viên nghiên cứu, Bác sĩ Susan Haskell (điện thoại (515) 280-700) hay (1-800) 568-2404.

7. Gọi Ai trong Trường hợp Khẩn cấp

11/16=18/99
EIR
Dr. Susan C. Haskell CFN 19-34550
Des Moines, Iowa 50314
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Tôi hiểu rằng nếu tử cung chảy máu nghiêm trọng, hay đau bụng dưới, hay các trường hợp y tế khẩn cấp khác phát sinh từ sự liên kết với phương pháp này, tôi sẽ báo cáo ngay lập tức cho Chương trình Planned Parenthood of Greater Iowa, 851 19th Street, Des Moines, IA 50314. Thêm nữa, tôi sẽ tiếp xúc với Bác sĩ Haskell (điện thoại số (515) 280-7000. Nếu không thể tiếp xúc được với ông hay bà ta trong trường hợp khẩn cấp liên quan đến cuộc nghiên cứu này, tôi sẽ tiếp xúc với ———————— tại số (515) 280-7000 hay (1-800) 568-2404.

8. Đề nghị Trả lời Câu hỏi và Tự do Rút lui khỏi cuộc Nghiên cứu.

Tôi đã được cho biết rằng tôi có thể rút lui khỏi cuộc nghiên cứu này bất cứ lúc nào mà không làm nguy hại đến sự chăm sóc y tế của bệnh viện trong hiện tại hay tương lai cho tôi. Nếu tôi rút lui tôi sẽ được đề nghị phá thai bằng phẫu thuật. Tôi đã được cho biết để tiếp xúc với Bác sĩ Haskell Điện thoại: (515) 280-7000 hay ———————— Điện thoại : (515) 280-7000 nếu tôi có câu hỏi về cuộc nghiên cứu. Các y sĩ này có thể chỉ định các cộng sự viên để trả lời những câu hỏi của tôi.

Tôi cũng hiểu rằng chuyên viên nghiên cứu chính có thể đòi hỏi tôi rút lui khỏi cuộc nghiên cứu này, nếu theo ý kiến về y khoa của ông hay bà ta việc này tốt nhất cho sức khỏe của tôi hay nếu tôi không thể theo các thủ tục thử nghiệm của cuộc nghiên cứu này nữa.

Tôi hiểu rằng, nếu việc chữa trị cho tôi trong cuộc nghiên cứu này không đem lại kết quả phá thai, và nếu tôi từ khước phá thai bằng phẫu thuật và tiếp tục với việc thai nghén, tôi phải chịu rủi ro và đứa trẻ phải chịu rủi ro, về các biến chứng kể cả thai nhi hay trẻ sơ sinh dị dạng.

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KẾ HOẠCH THÍ NGHIỆM CHI TIẾT SỐ: 166 A

9. Kín đáo

Tôi hiểu rằng các chi tiết có được trong cuộc nghiên cứu này sẽ được chuyển đi dưới một hình thức không thể nhận diện ra tôi, và rằng tất cả các hồ sơ sẽ được giữ trong tủ khóa. Tôi hiểu rằng Hội đồng Dân số hay những người được chỉ định theo dõi, cũng như Sở Quản trị Thực phẩm và Thuốc men của Hoa kỳ có thể yêu cầu tìm đến hồ sơ y bạ của tôi.

10. Phát biểu về Đối tượng

Tôi, ký tên dưới đây , đã đã được cắt nghĩa về những rủi ro và lợi ích trong cuộc nghiên cứu này bằng một ngôn ngữ mà tôi hiểu được. Tôi đồng ý tham gia vào cuộc nghiên cứu này như một đối tượng tình nguyện.

Ngày tháng

Chữ ký của người tình nguyện

11. Phát biểu của Chuyên viên Nghiên cứu

Tôi, ký tên dưới đây, đã giải thích cho người tình nguyện bằng ngôn ngữ mà họ nói về thủ tục phải theo trong cuộc nghiên cứu này cùng các rủi ro và lợi ích liên quan.

Ngày tháng

Chữ ký của chuyên viên nghiên cứu

Ngày tháng

Chữ lý của chứng nhân cho các chữ ký và giải thích trên

INSTITUTIONAL REVIEW BOARD

Under the Auspices of

[redacted]

October 12, 1994

Sue Haskell, D.O.
851 19th Street
Des Moines, Iowa 50314

EIR — 11/16=18/99
Dr. Susan C. Haskell CFN 19-34550
Des Moines. Iowa 50314
Exhibit — Page 1 of 2

Dear Dr. Haskell:

Thank you for your request to this IRB of September 19, 1994 for review and approval to conduct a study under the [redacted] protocol entitled, "[redacted] Acceptability of Mifepristone and Misoprostol in Inducing Abortion in Pregnancies with Amenorrhea of Up to 63 Days" the protocol #166A and #166B. The IRB is aware that both protocols are identical and that ddesignation of investigators to either protocol will be considered an administrative procedure not affecting the conduct of the study.

This will inform you that on October 12, 1994, this IRB, meeting all Federal Regulations for membership requirements and consisting of 7 individuals of different backgrounds and professions met and approved (by majority) your site to conduct the above mentioned study.

The IRB members included the following professions:

Physicians Clergy, School Principal, Nurse, a Community Activist and a Health Charity Executive

The Protocol (revised and dated October 12, 1994, the attached Informed Consent Form to be utilized at your site, your C.V., pre-investigational, and other regulatory documents site visit were reviewed and approved by majority voting.

Please be informed that all documentation required for IRB review to conduct your proposed study has been approved. A copy of the approved consent form is attached.

It is also a regulatory requirement that you promptly inform this IRB of any proposed changes in the approved research during the period for which IRB approval has been given. Furthermore, no such proposed changes may be initiated without IRB review except where necessary to eliminate apparent immediate hazards to the study patients or subjects.

Investigators conducting studies under the surveillance of this IRB are required to report all adverse reactions of either an unusual nature, unusual frequency or unusual severity to the Chairman without delay and in no event later than ten (10) working days after the event.

A further regulatory requirement is that the IRB receives periodic reports on the progress of your study. For the purposes of this IRB such reports must be submitted to the chairman of the IRB at the above address at regular intervals of not more than six (6) months. The initial six month follow-up report is due April 12, 1995. This regulation must be adhered to and is the investigator's responsibility. If the reports are not received within a reasonable length of time from the date required, IRB approval may be withdrawn. Also, the IRB is to be informed of the date of completion (or premature termination giving the reasons for termination) of your study and supplied with a final report at that time. Should your study be completed in less than six months, then a final study report is all that is required.

Your cooperation with the IRB with regard to these regulations will be much appreciated.

Sincerely,

[redacted]

[redacted]

Chairman

Enclosure

11/16=18/99
EIR [redacted]
Dr. Susan C. Haskell CFN 19-34550
Des Moines, Iowa 50314
Exhibit 5 Page 2 of 2

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

1. DISTRICT ADDRESS & PHONE NO
P.O. BOX 15905
LENEXA, KANSAS 66285
(913) 752-2100

TO

2. NAME AND TITLE OF INDIVIDUAL
Dr Susan C. Haskell, Principal Investigator

3. DATE
11/16/99

4. FIRM NAME
Planned Parenthood of Greater IOWA

5. HOUR
10:00 a.m.
— p.m.

6. NUMBER AND STREET
851 19th Street

7. CITY AND STATE & ZIP CODE
Des Moines, IOWA 50314

8. PHONE # & AREA CODE
(515) 280-7000

Notice of Inspection is hereby given pursuant to Section 704(a)(1) of the Federal Food, Drug, and Cosmetics Act [21 U.S.C. 374(a)][1] and/or Part F or G, Title III of the Public Health Service Act [42 U.S.C. 262-264][2]

9. SIGNATURE *(Food and Drug Administration Employee(s))*
/S/

10. TYPE OR PRINT NAME AND TITLE *(FDA Employee(s))*
Investigator

[1]**Applicable portions of Section 704 and other Sections of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 374] are quoted below:**

Sec. 704. (a)(1) For purposes of enforcement of this Act, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are authorized (A) to enter, at reasonable times, any factory, warehouse, or establishment in which food, drugs, devices, or cosmetics are manufactured, processed, packed, or held, for introduction into interstate commerce or after such introduction, or to enter any vehicle being used to transport or hold such food, drugs, devices, or cosmetics in interstate commerce; and (B) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, such factory, warehouse, establishment, or vehicle and all pertinent equipment, finished and unfinished materials, containers, and labeling therein. In the case of any factory, warehouse, establishment, or consulting laboratory in which prescription drugs, nonprescription drugs intended for human use, or restricted devices are manufactured, processed, packed, or held, inspection shall extend to all things therein *(including records, files, papers, processes, controls, and facilities)* bearing on whether prescription drugs, nonprescription drugs intended for human use or restricted devices which are adulterated or misbranded within the meaning of this Act, or which may not be manufactured, introduced into interstate commerce, or sold, or offered for sale by reason of any provision of this Act, have been or are being manufactured, processed, packed, transported, or held in any such place, or otherwise bearing on violation of this Act. No inspection authorized by the preceding sentence or by paragraph (3) shall extend to financial data, sales data other than shipment data, pricing data, personnel data *(other than data as to qualifications of technical and professional personnel performing functions subject to this Act)*, and research data *(other than data relating to new drugs, antibiotic drugs and devices and, subject to reporting and inspection under regulations lawfully issued pursuant to section 505(i) or (k), section 507(d) or (g), section 519, or 520(g), and data relating to other drugs or devices which in the case of a new drug would be subject to reporting or inspection under lawful regulations issued pursuant to section 505(j) of the title)*. **A separate notice shall be given for each such inspection, but a notice shall not be required for each entry made during the period covered by the inspection. Each such inspection shall be commenced and completed with reasonable promptness.**

Sec. 704(e) Every person required under section 519 or 520(g) to maintain records and every person who is in charge or custody of such records shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and to copy and verify such records.

Section 512. (i)(1) In the case of any new animal drug for which an approval of an application filed pursuant to subsection (b) is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to experience, including experience with uses authorized under subsection (a)(4)(A), and other data or information received or otherwise obtained by such applicant with respect to such drug, or with respect to animal feeds bearing or containing such drug, as the Secretary may by general regulation, or by order with respect to such application prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) or subsection (m)(4) of this section. Such regulation or order shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulation or order is applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this subsection to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

[2]**Applicable sections of Parts F and G of Title III Public Health Service Act [42 U.S.C. 262-264] are quoted below:**

Part F - Licensing - Biological Products and Clinical Laboratories and******

Sec. 351(c) "Any officer, agent, or employee of the Department of Health & Human Services, authorized by the Secretary for the purpose, may during all reasonable hours enter and inspect any establishment for the propagation or manufacture and preparation of any virus, serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or other product aforesaid for sale, barter, or exchange in the District of Columbia, or to be sent, carried, or brought from any State or possession into any other State or possession or into any foreign country, or from any foreign country into any State or possession."

Part F - ******Control of Radiation

Sec. 360 A(a) "If the Secretary finds for good cause that the methods, tests, or programs related to electronic product radiation safety in a particular factory, warehouse, or establishment in which electronic products are manufactured or held, may not be adequate or reliable, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are thereafter authorized (1) to enter, at reasonable times any area in such factory, warehouse, or establishment in which the manufacturer's tests *(or testing programs)* required by section 358(h) are carried out, and (2) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, the facilities and procedures within such area which are related to electronic product radiation safety. Each such inspection shall be commenced and completed with reasonable promptness. In addition to other grounds upon which good cause may be found for purposes of this subsection, good cause will be considered to exist in any case where the manufacturer has introduced into commerce any electronic product which does not comply with an applicable standard prescribed under this subpart and with respect to which no exemption from the notification requirements has been granted by the Secretary under section 359(a)(2) or 359(e)."

(b) "Every manufacturer of electronic products shall establish and maintain such records *(including testing records)*, make such reports, and provide such information, as the Secretary may reasonably require to enable him to determine whether such manufacturer has acted or is acting in compliance with this subpart and standards prescribed pursuant to this subpart and shall, upon request of an officer or employee duly designated by the Secretary, permit such officer or employee to inspect appropriate books, papers, records, and documents relevant to determining whether such manufacturer has acted or is acting in compliance with standards prescribed pursuant to section 359(a)."

******

(f) "The Secretary may by regulation (1) require dealers and distributors of electronic products, to which there are applicable standards prescribed under this subpart and the retail prices of which is not less than $50, to furnish manufacturers of such products such information as may be necessary to identify and locate, for purposes of section 359, the first purchasers of such products for purposes other than resale, and (2) require manufacturers to preserve such information.

FORM FDA 482 (3/99) PREVIOUS EDITION IS OBSOLETE NOTICE OF INSPECTION

(Continued on Reverse)

MIF 002218

Amendment 3
May 5, 1995

CONFIDENTIAL

EVALUATION OF THE EFFICACY, SAFETY AND ACCEPTABILITY OF MIFEPRISTONE AND MISOPROSTOL IN INDUCING ABORTION IN PREGNANT WOMEN WITH AMENORRHEA OF UP TO 63 DAYS

PROTOCOL NUMBER: 166A,B

SPONSOR: The Population Council, Inc.
1230 York Avenue
New York, New York 10021

_____

Signature, Principal Investigator

Protocol approved by The Population Council's IRB on September 14, 1994
Amendment No. 1 approved by The Population Council's IRB on November 2, 1994
Amendment No. 2 and 3 approved by The Population Council's IRB on May 5, 1995

1. INTRODUCTION

Mifepristone is a synthetic steroid currently used for medical abortion in France, Sweden, United Kingdom and China. It acts as a competitive blocker of progesterone and cortisol through binding to their receptors. Because of its antiprogesterone activity, mifepristone has been developed primarily as a medical abortifacient. When used alone in different regimens with total doses ranging from 140 to 1600 mg administered over one to ten days, the success rate of abortion in women with amenorrhea of less than 50 days duration usually varied between 64-85%[1].

Subsequent studies demonstrated that when mifepristone (600 mg) was followed two days later by a prostaglandin analog administered either by the intramuscular route (sulprostone, a prostaglandin E_2 analog), or as a vaginal pessary (gemeprost, a prostaglandin E_1 analog), the efficacy rate for complete abortion increased to 95% and above. Based on these observations, mifepristone has been marketed in France since September 1989 as a medical alternative to surgical abortion for the termination of pregnancies in women with amenorrhea of 49 days or less. Recently, this mifepristone - prostaglandin regimen was approved in the United Kingdom, and in Sweden. In the latter two countries, this combination is used in women with amenorrhea of up to 63 days.

In Europe there is now an accumulated experience with over 150,000 subjects who have received mifepristone together with various prostaglandins. Clinical trials have been conducted in several countries and have confirmed the initial experience. Unlike treatment with mifepristone alone where the success rate decreased with advancing duration of amenorrhea, the combination was effective up to 63 days of amenorrhea and in various published studies, the incidence of abortion induction ranged from 92.7% to 99%[1].

The most comprehensive study published to date comprises 16,369 subjects from over 450 clinics[2]. In this study 0.8% of the cases experienced uterine bleeding significant enough to necessitate vacuum aspiration or dilatation and curettage and in 0.07% (11 women), a blood transfusion was required. Significant cardiovascular side effects were reported in four cases following sulprostone administration. In three of these subjects, there was severe hypotension necessitating infusion of macromolecular solutes and in the final subject, a 38 year-old smoker, there was an acute myocardial infarction. In these four subjects, symptoms commenced within one hour of sulprostone administration and all recovered uneventfully. However, in general use, there was a fatal myocardial infarction in one woman, who was a 31-year-old heavy smoker, following sulprostone[3]. No cardiovascular complications have been reported following gemeprost, but this may be related to the fact that this analog has been used less often than sulprostone. Sulprostone is rapidly absorbed into the circulation following intramuscular injection.

therefore it is not unreasonable to assume that this prostaglandin carries a higher risk of cardiovascular problems than preparations that are administered orally or vaginally and are absorbed more gradually. Moreover, gemeprost, unlike sulprostone, is an E_1 analog.

As a consequence, parenteral prostaglandins should be used cautiously in women with heart disease, those over 35 years of age or in heavy smokers. The French health authorities have in fact withdrawn sulprostone as one of the prostaglandin preparations which can be given with mifepristone.

Because of the cardiovascular side effects reported with sulprostone as well as the inconvenience of both sulprostone and gemeprost which both require refrigeration, alternate prostaglandin preparations are now being used. Misoprostol, (methyl 11α, 16-dihydroxy-16-methyl-9-oxoprost-13 E-en-1-oate) is a prostaglandin E_1 analog that has been safely used for the prevention of nonsteroidal anti-inflammatory drug-induced gastric ulcers in patients at high risk for complications from gastric ulcers for many years; for this indication, it is given in an oral dose of 200 μg four times daily. Its effects on uterine tone are similar to those of other prostaglandins. Misoprostol is inexpensive, orally active and stable. In a recently published French study in women with amenorrhea of 49 days or less, one group comprising 505 women received 400 μg misoprostol 48 hours after mifepristone; the success rate for termination of pregnancy was 96.9%[4]. A second group of 390 women initially followed the same protocol, but if pregnancy was not terminated within four hours after misoprostol, the women were offered an additional 200 μg dose of misoprostol. In this second group, the overall success rate was 98.7%. These results indicate that the combination of mifepristone and misoprostol is of equal or greater effectiveness than the combination of mifepristone and either parenteral or vaginal prostaglandin for the termination of early pregnancy.[4] No serious cardiovascular side effects have been observed. Other side effects were neither more frequent nor more severe than after either parenteral or vaginal prostaglandin preparations[4].

A study from Britain reported complete abortion in 92 out of 99 women with amenorrhea of less than 57 days who were given 200 mg mifepristone followed 48 hours later by 600 μg misoprostol. There were three on-going pregnancies and four incomplete abortions. Vomiting was exhibited in 24% and diarrhea in 7% of the women. No analgesia was needed in 62% of the women[5].

In the two studies reported above, approximately 60-80% of women aborted during the four hours following prostaglandin administration. A number of side effects have been observed during this four hour period. These include: uterine pain, nausea, vomiting and diarrhea. In one of these studies the incidence of nausea, vomiting and diarrhea were 43%, 17% and 14% respectively[4]. It is for these reasons that it is recommended that women be monitored in the clinic for four hours following prostaglandin administration.

In Europe, over 50,000 women have received mifepristone followed 48 hours later by misoprostol without serious heart complications.

2. SUMMARY OF STUDY

The aim of the study is to determine the safety, efficacy, acceptability and feasibility of mifepristone plus misoprostol in inducing abortion, within the U.S. health care system setting, when administered to women exhibiting amenorrhea of varying duration (up to 63 days). The duration of amenorrhea will be defined throughout this document as the number of days from the first day of the last menstrual period. In addition to the large pivotal studies, a small initial pilot study will be conducted to enable the investigators to gain first hand experience with the proposed dosing regimen.

A total of 1,050 pregnant subjects will be enrolled in this and an identical sister protocol, to be conducted simultaneously. Thus a total of 2,100 subjects will be enrolled in the two trials. Three groups of subjects will be examined:

Group 1: Amenorrhea of $\leq$ 49 days
Group 2: Amenorrhea of 50 through 56 days
Group 3: Amenorrhea of 57 through 63 days

Analysis will also be conducted on safety, efficacy and acceptability of all subjects taken as a single group, regardless of the duration of amenorrhea. This will be a multicenter trial utilizing a minimum of six centers in each of the two studies. The centers will all perform pregnancy interruption on a regular basis. The centers will have access to facilities for blood transfusion and routine emergency resuscitation techniques. In all the trial centers, the recruitment of subjects will be such that, as closely as possible, equal numbers of subjects will be enrolled into each of the three groups defined above.

Subjects shall visit the study center three times, unless state law requires an additional, initial informational visit with a mandatory waiting period before the process can begin. At the initial visit (Day 1; after any required statutory waiting period), a full history and physical examination will be performed and the duration of amenorrhea will be determined and the reasons for selecting a medical abortion will all be recorded. At this visit, 600 mg of mifepristone (three 200 mg tablets) will be administered. The subject will return to the study center for the second visit on Day 3 to receive oral misoprostol (400 μg as two 200 μg tablets). The subject will be monitored at the center for at least four hours post the administration of the prostaglandin. The third visit will occur on Day 15. At this visit the completeness of the medical pregnancy termination will be assessed. In the event that the pregnancy is on-going at this time, or if the abortion has been incomplete, either vacuum aspiration or dilation and curettage will be performed. Subjects who undergo a surgical abortion at any time during their enrollment in the study

will return to the center two weeks post the surgical procedure for a follow-up assessment.

3. OBJECTIVE

The objective of this trial is to evaluate the effectiveness, safety, acceptability and feasibility of mifepristone plus misoprostol in inducing abortion when given to women, who have experienced up to 63 days of amenorrhea, within the U.S. health care system setting. Prior to initiation of the pivotal studies, a pilot study comprising 15 women will be performed at each of the selected study centers. The purpose of this pilot trial is to give the investigators exposure to the proposed dosing regimen so they will have first hand experience prior to the initiation of the pivotal studies. The results of the pilot trial will be included in the safety analysis for the product, but the efficacy data will be treated as a subgroup analysis relative to the pivotal trials.

Investigators selected to conduct the trials will be experienced abortion providers and medical investigators. They should have access to an IRB able to review the protocol, and will have malpractice insurance as well as general liability insurance for the clinic, hospital or office where the study will be performed. The investigators should be able to complete the study in six months at a maximum.

The investigators will operate in an appropriate study center; the study center will:

a) Provide routine emergency resuscitation such as O_2, Ambu bag and will be staffed with personnel trained in routine emergency care.

b) Have access on a 24 hour a day basis to blood transfusion, D & C and more elaborate resuscitation procedures.

c) Have space to conduct the study including a room where a woman can be monitored for at least four hours after the prostaglandin administration.

d) Have the physician responsible for the study on call on a 24 hour a day basis, or his/her delegate of equal qualification.

e) Have adequate and sufficient trained personnel for counselling of subjects and conduct of the study.

f) Have transvaginal ultrasound available and personnel trained in the use of the equipment as well as the interpretation of the sonograms for the assessment of gestational age in relation to the reported duration of amenorrhea.

g) Investigators and staff will answer a provided questionnaire at the completion of the study.

4. PATIENT SELECTION

4.1 Patient Sample:

4.1.1 Number of patients: A total of 1,050 patients per each of the identical trials for a total of 2,100 subjects will be enrolled at multiple centers.

4.1.2 Age range: 18 years or older.

4.1.3 Residents of the United States.

4.2 Inclusion Criteria:

4.2.1 Good general health.

4.2.2 Age 18 years or older.

4.2.3 Request termination of pregnancy.

4.2.4 Agree to undergo surgical pregnancy termination in case of failure of the medical abortion method being evaluated.

4.2.5 Have an intrauterine pregnancy of known duration which is less than or equal to 63 days of amenorrhea period. The final determined estimated duration of pregnancy should be less than 64 days of amenorrhea, and as confirmed by uterine size on pelvic examination and ultrasonographic examination.

4.2.6 Have a positive urine pregnancy test.

4.2.7 Willing and able to participate in the study after its precise nature and duration have been explained.

4.2.8 Able and willing to sign an informed consent form.

4.2.9 Resident of the United States.

4.3 Exclusion Criteria:

4.3.1 Evidence of the presence of any disorder which represents a contraindication to the use of mifepristone (e.g., chronic corticosteroid administration, adrenal disease) or misoprostol (e.g., asthma, glaucoma, mitral stenosis, arterial hypotension, sickle cell anemia, or known allergy to prostaglandin).

4.3.2 History of severe liver, respiratory, or renal disease or thromboembolism.

4.3.3 Cardiovascular disease (e.g., angina, valve disease, arrythmia, cardiac failure).

4.3.4 Hypertension being treated on a chronic basis or untreated patients who present with: a blood pressure of > 140 (systolic) or > 90 (diastolic).

4.3.5 Anemia (hemoglobin level below 10 g/dL or hematocrit below 30%) at the Day 1 visit.

4.3.6 A known clotting defect or receiving anticoagulants.

4.3.7 Subjects with an IUD in place.

4.3.8 Insulin dependent diabetes mellitus.

4.3.9 More than 63 days of amenorrhea or results of bimanual pelvic examination or vaginal ultrasound which are inconsistent with 63 days or less of amenorrhea.

4.3.10 Breast-feeding.

4.3.11 Adnexal masses or adnexal tenderness on pelvic examination suggesting pelvic inflammatory disease.

4.3.12 Ectopic pregnancy or threatened abortion.

4.3.13 Women 35 years of age or older who smoke more than 10 cigarettes per day and have another risk factor for cardiovascular disease (e.g., diabetes mellitus, hyperlipidemia, hypertension or family history of ischemic heart diseases).

4.3.14 Unlikely to understand or comply with the protocol requirements.

4.3.15 Women who cannot reach the source of emergency medical care that serves the abortion center within ——— from (a) their home or place of work and (b) the abortion center.

5. STUDY MEDICATION

5.1 Assignment of Study Medication

This is a multicenter trial evaluating the effectiveness, safety and acceptability of mifepristone plus misoprostol in inducing abortion when given to women in one of three groups depending upon the duration of amenorrhea. The three groups are:

Group 1 - Amenorrhea of $\leq$ 49 days
Group 2 - Amenorrhea of 50 through 56 days
Group 3 - Amenorrhea of 57 through 63 days

As closely as is possible, equal numbers of subjects will be enrolled into each of the three groups. There may be differing numbers of patients enrolled from center to center, but the number per group per center should be approximately one third into each of the groups.

5.2 Dosage and Administration

There will be three visits to the study center. At the initial visit (Day 1), a full history and physical examination will be performed and the duration of amenorrhea will be determined and the reasons for selecting a medical abortion will all be recorded. At this visit, 600 mg of mifepristone (three 200 mg tablets) will be administered orally. The subject will return to the study center for the second visit on Day 3 to receive oral misoprostol (400 μg as two 200 μg tablets). The subject will be monitored at the center for at least four hours post the administration of the prostaglandin. The third visit will occur on Day 15. At this visit the completeness of the medical pregnancy termination will be assessed and an acceptability questionnaire administered. In the event that the pregnancy is on-going at this time, or if the abortion has been incomplete, either vacuum aspiration or dilation and curettage will be performed. Subjects who undergo a surgical abortion at any time during their enrollment in the study will return to the center two weeks post the surgical procedure for a follow-up assessment.

5.3 Packaging

A) Mifepristone — Mifepristone will be provided as 200 mg tablets of micronized mifepristone.

B) Misoprostol — Misoprostol will be obtained locally by each investigator as 200 μg tablets of commercially available misoprostol.

All study supplies will be kept in a locked, dry cabinet.

5.4 Labeling

A) Mifepristone — Mifepristone will have a label which will include product identification, expiration date, and drug dose. In addition the following will be printed on the labels: CAUTION: New drug. Limited by Federal Law to Investigational Use. All medication packets will be labelled with the protocol number.

B) Misoprostol — Misoprostol will be obtained locally by each investigator as 200 μg tablets of commercially available misoprostol and dispensed from the center pharmacy.

5.5 Concomitant Medications

No salicylates, indomethacin, or any other drug which inhibits prostaglandin synthesis should be taken. If necessary, analgesics belonging to other pharmacologic classes or spasmolytic drugs may be used. Drugs such as trifluoperazine and related phenothiazines (for treatment of nausea and vomiting) that could increase the risk of hypotension must be avoided as should oxytocin and any other prostaglandin preparation.

The use of concomitant medications during the course of this study will be recorded in the Case Report Form, and these data will be analyzed.

6. STUDY PROCEDURES

Each participating study center will record on a daily basis the number of subjects recruited in each of the three groups. All women approached to participate in the study will be recorded in the study data. Those who refuse to participate in the trial will have a special form completed for the database. These data will be communicated to the sponsor on a weekly basis. At each center, the number of subjects recruited into each of the groups will be equal to one-third the total assigned to the center if possible. When any of the groups has been filled, no further recruitment into that particular group will be conducted. Under no circumstances will any member of the study center staff suggest that a subject appearing at the center, with a duration of amenorrhea consistent with a completed group, be deferred in her request for pregnancy termination to allow for enrollment into an open group at a later time.

6.1 VISIT 1 (Admission, Day 1 of Study)

At the time of the subjects enrollment (Day 1), all the following should be done:

- Counseling.
- Medical, obstetrical and gynecological history.
- Medical examination, including: height, weight, blood pressure, and pulse.
- Bimanual pelvic examination.
- Urine pregnancy test.
- Quantitative Serum ßhCG.
- Vaginal ultrasound.
- Determination of Rh status and where routinely collected, the blood group.
- Hemoglobin or hematocrit determination.

Chemistry Panel (4mL)
Which includes:

Aspartate aminotransferase, Alanine aminotransferase, Alkaline phosphatase, Total Bilirubin, Blood urea nitrogen, Phosphate, Creatinine, 24 hour fasting Glucose, Albumin, Lactate dehydrogenase, Potassium, Sodium, Chloride, Bicarbonate, Uric Acid, Calcium, as well as Cholesterol, Triglycerides, and Total Protein

Hematology Panel (3mL)
Which includes:

Hemoglobin, Hematocrit, RBC, WBC with differential, Platelet count*

Food should be withheld for one hour prior to and one hour post administration of the study drug. At admission to the study, the three tablets of mifepristone (600 mg total) will be swallowed by the subject with no more than 240 mL of water in the presence of a member of the center's study staff who will record the date and time of the administration.

Subjects who smoke will be instructed to refrain from smoking until after the administration of misoprostol at Visit 2, and an appointment will be made for Visit 2.

Subjects will be given a copy of the informed consent and patient diary card describing symptoms which require emergency treatment. These include: heavy bleeding, fever, and severe abdominal pain. The subjects will be given the address and 24 hour telephone number of a medical center (including the name of physicians) which cares for patients on a 24 hour a day basis.

A diary will be provided to each of the subjects for recording medications and symptoms, such as pain, nausea, vomiting and diarrhea. The diary will also be used to record the occurrence of vaginal bleeding on each day. The subject will be instructed to record the bleeding relative to their normal menstrual flow (e.g., lighter, the same as or heavier than normal). If the expulsion takes place before Visit 2, the date and time should be recorded on the subjects diary.

* Amendment 2 dated April 27, 1995

6.2 VISIT 2 (Prostaglandin Administration, Day 3 of Study)

Visit 2 will be conducted on Day three (3) of the study. The following will be performed:

- Clinical examination.

- If the patient believes that expulsion occurred prior to Visit 2, the date and time will be recorded on the case report form as they were noted in the subjects diary. Since it is difficult to confirm that an abortion at this time is complete, nearly all subjects will require misoprostol. If however, the physician can verify unequivocally that complete abortion has occurred, the misoprostol will not be administered. If the abortion is incomplete or if there is any uncertainty about the completeness of the abortion, the misoprostol will be administered.

- Brief interview and review of the diary.

- Any adverse events which occurred since Visit 1 will be recorded on the case report form.

- Subject will receive an injection of anti-D globulin if the subject is Rh negative, if indicated.

- Food should be withheld for one hour prior to and one hour post the administration of misoprostol. The two tablets of misoprostol (400 μg total) will be swallowed by the subject with no more than 240 mL of water in the presence of a member of the center's study staff who will record the date and time of the administration.
- The subject will be observed at the study center for the four hour period post the administration of misoprostol at a minimum. The facility should be capable of surgical termination of pregnancy (by vacuum aspiration or dilation and curettage) and have access to blood transfusion and emergency resuscitation.

- During the observation period, the following should be recorded at least hourly:

- Occurrence of nausea, vomiting, or diarrhea. Intensity should be recorded as:

0: none
1: mild
2: moderate
3: severe

Any treatment for these will be recorded as concomitant medications.

- At the onset of any abdominal pain, the following will be recorded:

  Intensity, recorded as: none, mild, moderate, or severe.

  Duration, documenting any treatment as a concomitant medication.

- Blood pressure and heart rate at hourly intervals unless more frequent readings are indicated.

- Time of expulsion, if occurring during the observation period.

- Any unexpected symptom or clinical finding.

The use of intramuscular sulprostone in combination with mifepristone in previous studies has occasionally precipitated an episode of hypotension usually associated with bradycardia. In extremely rare circumstances this previously utilized treatment regimen has been associated with myocardial infarction and ventricular tachycardia. These complications are very unlikely with the combination of misoprostol and mifepristone. However, any significant fall in blood pressure or significant change in heart rate, however transient, following the administration of misoprostol will be recorded and the subject observed for at least three hours after their blood pressure and heart rate have returned to baseline. In case of chest pain, hypotension or cardiac arrhythmia, an ECG should be performed immediately and if required adequate resuscitation should be undertaken.

The cycle immediately following the administration of mifepristone is ovulatory. Therefore, subjects will be counseled to initiate contraception. Barrier contraception may be initiated within three days of misoprostol administration.

- A gynecological examination will be performed to determine if products of conception remain in the vagina or cervix.

- A very active attempt should be made to contact any subject who fails to appear for the Visit 2 appointment. The administration of misoprostol after Day 3 is strongly discouraged. Misoprostol may be administered between 36 and 60 hours after mifepristone administration.

center shall retain its records relating to such subject through the date on which she was last seen at the center for a period of thirty (30) years following such date.

6.3 VISIT 3 (Exit Interview, Day 15 of Study)

Visit 3 will be conducted on Day fifteen (15) of the study. At Visit 3 the following will be performed:

- Clinical and gynecological examination.

- Assessment of severity and duration of uterine bleeding. Subjects who experience bleeding post Day 15 should be followed-up via telephone until the bleeding has stopped or intervention is clinically indicated.

- Assessment of hemoglobin or hematocrit if indicated.

- Blood samples will be collected for:

Chemistry Panel (4mL)
Which includes:

Aspartate aminotransferase, Alanine aminotransferase, Alkaline phosphatase, Total Bilirubin, Blood urea nitrogen, Phosphate, Creatinine, 24 hour fasting Glucose, Albumin, Lactate dehydrogenase, Potassium, Sodium, Chloride, Bicarbonate, Uric Acid, Calcium, as well as Cholesterol, Triglycerides, and Total Protein

Hematology Panel (3mL)
Which includes:

Hemoglobin, Hematocrit, RBC, WBC with differential, Platelet count

A total of twelve (12) subjects per each group of amenorrhea duration, for a total of thirty-six (36) per center will be involved in these assessments at six (6) selected centers. Thus, a total of 216 subjects from the entire study population will participate.*

- Verification of any concomitant medications or other therapeutic measures since Visit 2.

*Amendment 2 dated April 27, 1995

- Assessment of expulsion (history, pelvic examination), as well as date and time of occurrence if appropriate.

- Final evaluation of the treatment outcome through the clinical and gynecological examination. If necessary, perform ultrasonography and/or urine pregnancy test.

- In instances where the medical abortion method has failed, either completely or partially, perform the necessary additional surgical procedure. In the subjects for whom a surgical procedure is required, schedule a follow-up visit as per Section 6.6 below.

- Examine the subject's view of her abortion experience including her view of the experience relative to expectations; assessment of discomforts and side effects; timing and place of abortion; satisfaction with the experience; comparison to any previous abortion experience; best and worst features of the method being assessed in the trial; attitude toward self-administration of prostaglandin at home and preference for home or clinic treatment. All responses will be recorded in the case report forms.

- Assure that the subject's case record forms have been completely, accurately and properly filled in.

- A very active attempt should be made to contact any subject who fails to appear for the Visit 3 appointment.

- If the center is aware of any subject who misses Visit 2 and does not appear for Visit 3, or who otherwise determines to carry her pregnancy to term, the center shall retain its records relating to such subject through the date on which she was last seen at the center for a period of thirty (30) years following such date.

6.4 UNSCHEDULED VISITS

At Visits 1 and 2, subjects will be advised that they may return to the study center at any time if they experience medical problems associated with the medical abortion or for any other medical problem. At any unscheduled visits the following will be recorded:

- Reason for the visit.

- Information regarding utilization of any other medical resources.

- Pregnancy status at onset of visit.

- Temperature, blood pressure, heart rate, and hemoglobin.

- Any medication administered during visit as well as any medications prescribed.

- Any procedures conducted during the visit.

- Results of any pathology testing.

Subjects who have a surgical abortion at any unscheduled visit will have the exit interview (As defined in Section 6.3 above) prior to departure from the study center on the day of the surgical abortion, and will not return for the scheduled Visit 3. However, subjects undergoing surgical abortion will be scheduled for a follow-up visit as outlined in Section 6.6 below.

6.5 MEDICAL ADVISORY COMMITTEE

If serious adverse events occur beyond expectation, the decision of whether or not the study should be discontinued or modified will be taken by the Sponsor in consultation with the Medical Advisory Committee.

6.6 FOLLOW-UP

Subjects who are enrolled and receive either or both drugs in the study and undergo surgical abortion at any time during their enrollment will be scheduled for a follow-up visit. This follow-up visit will be scheduled for two weeks post the date of the surgical abortion. At this visit the following will be recorded:

- Brief medical history and clinical examination.

6.7 EARLY WITHDRAWAL FROM THE TRIAL

Subjects may withdraw from the study at any time at their own request. In all cases, the reasons for the subjects withdrawal must be recorded in detail in the case report forms and in the patients medical records. In all cases of withdrawal the subjects must be encouraged to have surgical abortions. If any subject refuses surgical abortion, the investigator must record that the subject understands the

- [illegible] center or that [illegible] records with respect to a subject who withdraws from the study after ingesting mifepristone and for whom a complete abortion has not been confirmed for a period of at least 30 years following the subject's last visit to the center.

All efforts will be made to contact subjects who fail to return for the necessary visits (telephone, registered mail). The subject will not be given misoprostol if contacted after 60 hours of the study. A subject may not complete the treatment regimen if severe side effects or symptoms develop after mifepristone administration that, in the opinion of the principal investigator, constitute a threat to the woman's health. Any subjects who do not complete the treatment regimen for any reason will be assessed for the completeness of the abortion, if possible. Any subject who has received mifepristone and has at the time of early termination had an incomplete abortion, as described above, will undergo surgical abortion as described in Section 6.3 above, and will be considered a failure.

7. ADVERSE EXPERIENCES

7.1 General Aspects

Adverse Reactions

Subjects will be notified of possible adverse reactions; they will be instructed to immediately report all adverse reactions to the investigator.

Any adverse reaction, noticed by the investigator or reported by the subject, including clinically significant lab abnormalities, will be recorded in the appropriate section of the case report form, regardless of its severity and relationship to study drug.

Serious or unexpected adverse events will be immediately reported by the investigator by telephone to:

Dr. Irving Spitz
Dr. C. Wayne Bardin
The Population Council, Inc.
(800) 327-8730
24 hour answering service outside normal business hours

____ will notify the sponsor, and ensure FDA notification. All serious ("any experience that is fatal or life-threatening, is permanently disabling, incapacitating, requires inpatient hospitalization, or causes a congenital anomaly, cancer or is due to overdose") and/or unexpected ("any adverse experience that is not identified in nature, severity or frequency in the current investigator's brochure for the study") adverse

and a written report must be submitted to the medical monitor within 24 hours.

The initial telephone contact will be followed within 3 days by a detailed report of the event which will include copies of hospital case reports, autopsy reports and other documents, when applicable. The adverse event must be followed through resolution.

The same applies to all subjects who died during the course of the study or within 30 days of completion of treatment irrespective of whether the adverse reaction was judged as related to treatment. In case of a death, copy of the autopsy report should be sent to the sponsor, if performed.

For each adverse reaction, the following information will be entered in the case report form: description of event, onset date, resolution date, severity (1=mild, awareness of sign or symptom, but easily tolerated; 2=moderate, discomfort enough to cause interference with usual activity; 3=severe, incapacitating with inability to do usual activity), drug cause-effect relationship and the outcome of the event. The investigator will also note if any action was taken regarding the test drug (temporarily or permanently discontinued) and if therapy or hospitalization was required.

ETHICAL ASPECTS

A. Informed Consent Form

The purpose of the study, those adverse reactions that are known to occur with the study drugs and the subject's right to withdraw from the study at any time without prejudice, must be explained to each subject in a language she understands. The subject is then required to sign in the presence of a witness an approved informed consent form in a language she understands containing all the above-mentioned information and a statement that the subject will permit examination of his/her study case report forms by a third party. Willing subjects may be interviewed by a representative of the sponsor about her understanding of the risks, benefits, procedures, and the experimental nature of the study.

B. Institutional Review Board

This study will not be initiated until the protocol and informed consent form have been reviewed and approved by a duly constituted Institutional Review Board (IRB) as required by U.S. FDA regulations. It is the responsibility of the investigator to submit the study protocol with its attachments to the IRB for review and approval.

IRB general assurance number must be given to the Sponsor of the study prior to study initiation, along with a signed and dated statement that the protocol and informed consent form have been reviewed and approved by the IRB.

The investigator is committed, in compliance with FDA regulations, to inform the IRB of any emergent problems, serious adverse reactions or protocol amendments.

C. Protocol Amendments

Any amendment to the protocol will be with mutual agreement between the investigator and the Sponsor. All amendments to the protocol will be submitted to the FDA and to the Institutional Review Board (IRB) concerned for review and, if necessary, approval prior to implementation of the changes.

D. Study Monitoring

A pre-study visit will be made by the monitor to the investigative site in order to review the protocol and to ascertain that the facility is adequate for satisfactory conduct of the study, as well as to discuss the obligations of both the sponsor and the investigator.

The investigator will permit a representative of the sponsor or his designate and the FDA, if requested, to inspect all case report forms and corresponding portion of the study subjects original office and/or hospital medical records, at regular intervals throughout the study. These inspections are for the purpose of assessing the progress of the study, verifying adherence to the protocol, determining the completeness and exactness of the data being entered on the case report forms and assessing the status of study drug storage and accountability. During site visits, case report forms will be examined by the study monitor(s) and verified by comparison with corresponding source data (such as hospital and/or office records).

ADMINISTRATIVE ASPECTS

A. Curricula Vitae

The investigator will provide the Sponsor with copies of the curricula vitae of himself/herself and the co-investigators listed on the FDA Form 1572.

A Case Report Form in triplicate will be provided by the sponsor for each subject to be filled in at each visit. Additional forms will be used for screening of the subjects prior to enrollment. In the event of additional visits, extra case report forms for the unscheduled visits will be filled out. At the visits on Days 1 and 15, acceptability questions will be asked, and the data recorded.

Acceptability questions will be asked on the day of surgical abortion for those having a surgical abortion.

One copy of the forms will be retained by the clinical study site, the other copies will be retrieved by the study monitor at the monitoring visits. All forms will be filled in legibly in black ball point pen. All entries, corrections and alterations are to be initialed and dated by the investigator, co-investigator, or study coordinator making the correction. Corrections will be made by crossing through the incorrect data with a single line so that the incorrect information remains visible, and putting the correct information next to the incorrect data. A reasonable explanation must be given by the investigator for all missing data.

C. Data Retrieval

At intervals during the study and at the conclusion of the study, the study monitor will retrieve signed and dated case report forms from the study site for data entry and analysis. The original and one copy of each page will be retrieved by the monitor. The investigator will keep a copy of all original case report forms and source documents.

D. Records Retention

Except as otherwise explicitly set forth herein, pursuant to applicable federal regulations, the investigator must retain copies of all study records for a period of two (2) years following the date a marketing application is approved for the indication for which the drug is being investigated. If no application is filed or if the application is not approved, the study records must be retained until 2 years after the investigation is discontinued and FDA is notified.

E. Study Termination

Either the investigator or the sponsor may terminate the study at any time for well documented reasons, provided a written notice is submitted at a reasonable time in advance of intended termination.

8.1 Population Analyzed

All subjects to whom mifepristone has been administered will be included in the analyses.

A) Efficacy

Efficacy will be determined by each subject's abortion status and history at Visit 3 (Day 15), two weeks post the administration of mifepristone. The pregnancy/abortion status requires a clinical evaluation, including where necessary ultrasonographic and/or urine pregnancy results.

One measure of success will be defined as a pregnancy termination by Visit 3 (Day 15) without the need for surgical or instrumentation procedures except for forceps extraction of ovular tissue fragments extending through the external cervical os. If pregnancy has not been terminated by Visit 3 (Day 15), this will be considered a failure.

FAILURES

Two categories of failures will be recognized. These will be called medical failures and acceptability failures.

Medical failures are of two types:

i) persisting pregnancy at Visit 3 (Day 15).
ii) medically indicated surgical intervention because of:
    a) incomplete expulsion at Visit 3 (Day 15).
    b) serious adverse advents that warrant early surgical interruption of pregnancy.

Acceptability failures are deemed to have occurred when subjects request surgical interruption of a persisting pregnancy before Visit 3 (Day 15) without medical necessity.

In consequences of this distinction between types of failure, there will be two evaluations of success and failure rates.

[illegible] will be determined by life table analysis on a day to day basis from Visit 1 (Day 1) through Visit 3 (Day 15). Women who request surgical abortions before Visit 3 (acceptability failures) will be considered as censored as of mid-day on the day of the surgical abortion. Persisting pregnancies as of Visit 3 are considered failures. The method success rate is 1-MFR for any day or cumulative analysis. Women with persisting pregnancies of less than two weeks post the administration of mifepristone when last observed (e.g., lost to follow-up) will be treated as censored in mid-day of the last observation in the calculation of gross rates.

The *total failure rate* (TFR) will also be determined by life table techniques using the assumption that some of the subjects with persisting pregnancies are last observed before two weeks post the administration of mifepristone. Daily total failure rates are computed under the assumption that subjects with continuing pregnancies last observed before Visit 3 were last observed in the middle of the day of last observation.

Data will be recorded in the case report forms to allow for the distinction between medical and acceptability failures.

All failures will undergo vacuum aspiration or dilation and curettage. Material will be submitted for pathological examination.

B) Safety

Safety will be assessed utilizing the following parameters:

- Duration and severity of uterine bleeding; data obtained from subject diary, determination of hemoglobin, by treatment (e.g., transfusion, surgical procedure) necessary secondary to heavy and prolonged uterine bleeding.

- Occurrence of any adverse event or abnormal clinical finding (e.g., signs of pelvic infection).

- Adverse events linked to drug administration and abortion (e.g., nausea, vomiting, diarrhea, painful uterine contractions).

- Assessment of heart rate and blood pressure during the observation period following the administration of misoprostol.

Safety data will include all safety parameters at all visits both scheduled and unscheduled, as well as data collected in the subject's diary, of all subjects to whom mifepristone has been administered.

Acceptability will be measured by patient interviews at the final discharge visit. The assessments will be made on the basis of answers to questions concerning:

- satisfaction with the information and counseling,
- satisfaction with the procedure,
- comparison to previous abortion experience, where applicable,
- willingness to choose the method again, and,
- willingness to recommend the method to others.

All these variables will be assessed in light of the level of complications, discomforts, and side effects recorded for each patient on both the questionnaire and symptomatology diary.

Acceptability of the regimen will also be determined through a questionnaire for providers.

D) *Feasibility of Use in the U.S. Health Care System*

Variability is built into the study with regard to: Type of abortion site (hospital clinic, Planned Parenthood clinic, feminist health clinic, private practice, free-standing abortion clinic), ethnicity of patient, socioeconomic status (Medicare, self-pay, insurance, help fund, etc.), and location in inner city, small city, suburb, or rural area. The association of these factors with:

- adherence to the protocol
- complications and side effects
- failure (and type of failure)
- patient satisfaction with medical abortion
- provider comfort with medical abortion

will be analyzed.

8.2 ANALYTIC METHODS

8.2.0. A detailed plan, outlining in advance the statistical evaluation of each baseline, safety and efficacy variable, will be submitted to file prior to statistical examination of the data. Essential features of this plan, as presently anticipated, are described below.

[illegible] through the administration of mifepristone will be summarized. All variable pertaining to safety, efficacy and acceptability will be summarized.

8.2.2. Lifetable Analysis of Efficacy: Single and multiple decrement failure rates for each type of failure and for the total failure rate will be analyzed for each amenorrhea duration, and all durations. Failure rates, by duration of amenorrhea, for age, ethnic group, payment status, and service delivery groups will be determined.

8.2.3. Efficacy Analysis: Multinomial logistic models will be employed to evaluate efficacy. Successful abortion, incomplete expulsion, early surgical interruption due to medical necessity and early surgical interruption at the patient's request (no medical necessity) will serve as the outcome categories used to form response vectors for the models. In one model, the response vector will be comprised of the cumulative log odds over the three types of failure (i.e., incomplete expulsion, medical interruption and requested interruption). In another model, the response vector will be the log odds of these individual types of failure *per se*. In all models, the independent vector will be amenorrhea duration ($\leq$ 49 days, 50-56 days and 57-63 days).

The models will be used to test the overall (omnibus) effect of amenorrhea status. Additionally, pairwise contrasts among the amenorrhea groups will be evaluated. Both the overall effect and pairwise effects will be examined using traditional hypothesis tests to assess the *complete response vector* (i.e. all failure categories considered simultaneously). However, *individual response categories* will be examined in two ways. First, a traditional hypothesis test will be used to conduct a test of the overall affect of amenorrhea. Second, the examination of pairwise amenorrhea group contrasts will take the form of an equivalency test.

All traditional tests will be evaluated using a type I error rate of 0.05. Equivalence tests will be performed using 90% confidence intervals (which mathematically correspond to a type I error rate of 0.05) and an equivalence interval of $\pm$ 5 percentage points.

Single and or multiple decrement life table techniques, as appropriate, will be used to display failure rate probabilities by time, for individual amenorrhea group and all groups combined.The various effects examined using the multinomial logistic models will also be exhibited in tables and/or figures.

abortion. Equivalence of Failure will be undertaken by a variety of multivariate techniques. This analysis pertains to aspects of efficacy, safety and acceptability.

8.2.5. Baseline Safety Analysis. Qualitative baseline and safety variables will be systematically summarized in appropriate patient groupings for examination by the medical reviewer. Descriptive statistics for baseline and safety variables that are suitable for quantitative analysis will be displayed in tables and figures. Furthermore, these variable will be evaluated across amenorrhea groups using linear models, applied to continuous or categorical variables. Continuous variables expected to markedly deviate from normality will be rank transformed to obtain nonparametric tests of significance. Any baseline variable found to exhibit a meaningful difference across amenorrhea groups, will be considered for use as covariate or blocking factor in the efficacy analysis. As a conservative measure to increase statistical power, variables exhibiting p-values of 0.20 or less will be singled out to assess their potential relevance to the safety and efficacy of the study drug.

Analysis of variables associated with need for transfusion and with severe cardiovascular adverse events will be undertaken.

8.2.6. Acceptability Analysis: Analysis of variables associated with acceptability within each duration of amenorrhea and overall shall be undertaken using both univariate and multivariate techniques.

9. RISK-BENEFIT ASSESSMENT

Experience gained to date with the use of mifepristone and prostaglandin for the termination of early pregnancy indicates that this has few side effects and a frequency of short-term complications that is comparable to that observed after vacuum aspiration. The most common complaints during treatment, particularly following administration of the prostaglandin, are lower abdominal pain, nausea, vomiting and diarrhea. In addition, bleeding for several days is common. For these complaints, appropriate medication can be prescribed when required. Occasionally, heavy uterine bleeding may necessitate emergency curettage and, very rarely, blood transfusion.

subjects in this trial treated [illegible] will be expected to undergo surgical termination of pregnancy. It is possible the failure rate will be higher in the older pregnancies. Recently obtained information supports the statement that mifepristone plus misoprostol cause abortion in approximately 95 percent of women with amenorrhea of no more than 49 days before administration of mifepristone. In women with amenorrhea of 50 to 63 days before they received mifepristone, this new information suggests that as many as one in four may require some form of surgical procedure. There are a number of reasons for such a surgical procedure including continued pregnancy, incomplete abortion, or excess bleeding. This excess bleeding may be similar to that which occurs during a spontaneous miscarriage (i.e. more than a heavy menstrual period). The possibility of experiencing excess bleeding increases with increasing duration of amenorrhea**.

Following a treatment regimen involving the intramuscular injection of the prostaglandin analog sulprostone, in a very low percentage of cases (one in 20,000), serious cardiovascular complications have been observed, including one case of fatal myocardial infarction. These complications have been most often associated with subjects who were heavy smokers, and still these complications are extremely rare. There is no evidence that misoprostol, a different class of prostaglandin, which is widely prescribed for longterm use in the prevention and treatment of peptic ulcer disease, is associated with any such cardiovascular side effects.

All subjects will be informed as to the potential complications. Centers participating in the trial will ensure that qualified personnel and necessary equipment and supplies are available at all time to deal with any complications.

Studies conducted in mice and rats have shown that mifepristone does not have any teratogenic effects. There are insufficient data to evaluate the effects of mifepristone on the human fetus. In one subject in France who took mifepristone and failed to abort, pregnancy was terminated at 18 weeks because of fetal abnormalities. The precise relationship to mifepristone could not be established. Thus, in the event of a continuing pregnancy, surgical abortion should be performed. Misoprostol has been reported to be teratogenic and is reported to be associated with malformations of the scalp, cranium and other abnormalities[7].

The benefits of this form of medical termination of pregnancy are that most women participating in the study can be expected to have a complete abortion and will not be exposed to the risks associated with surgical abortion, particularly the risks of physical trauma (e.g., cervical laceration, uterine perforation, etc). Nor does medical abortion carry any anesthetic-related risk.

No financial renumeration will be offered to potential study participants.

**Amendment 3 dated May 2, 1995

10. SIGNATURES

I have read the forgoing protocol and agree to conduct the study as outlined.

_____ ____/____/____

Signature of Investigator M D Y

_____ ____/____/____

Signature of Sponsor M D Y

Table 1

	Visit 1	Visit 2	Visit 3
Counseling	X		
Medical, OB-GYN History	X		
Medical Examination	X	X	X
Pelvic Examination	X	X	X
Urine Pregnancy Test	X		X*
Quant. Serum ßhCG	X		X*
Vaginal Ultrasound	X	X*	X*
Blood Typing including Rh	X		
Hemoglobin or Hematocrit Determination	X		X*
Administration of Mifepristone	X		
Administration of anti-D globulin		X*	
Administration of Misoprostol		X	
Interview and Review of Diary		X	X

* - To be conducted if indicated

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APPENDIX I

PROTOTYPE INFORMED CONSENT

EVALUATION OF THE EFFICACY, SAFETY AND ACCEPTABILITY OF MIFEPRISTONE AND MISOPROSTOL IN INDUCING ABORTION IN PREGNANT WOMEN WITH AMENORRHEA OF UP TO 63 DAYS

PROTOCOL NUMBER: 166 B

1. Purpose and aims of the study

It is possible to induce abortion in women with unwanted pregnancies by taking mifepristone in combination with a prostaglandin (misoprostol). Mifepristone is a drug which blocks the action of progesterone, a hormone needed to maintain pregnancy. One of mifepristone's actions is to interrupt pregnancy in its early stages. Prostaglandins are natural substances made by the lining of the womb during menstruation and cause contraction of the womb. **Recently obtained information supports the statement that mifepristone plus misoprostol cause abortion in approximately 95 percent of women whose first day of their last menstrual period occurred no more than 49 days before administration of mifepristone. In women whose first day of their last menstrual period occurred from 50 to 63 days before they received mifepristone, this new information suggests that as many as one in four may require some form of surgical procedure. There are a number of reasons for such a surgical procedure including continued pregnancy, incomplete abortion, or excess bleeding. The possibility of experiencing excess bleeding increases with increasing duration of amenorrhea**** Major advantages of this method of pregnancy termination are that no surgical instruments are pushed into the womb. Over 150,000 women in 20 countries have used mifepristone and a prostaglandin as a medical method of pregnancy interruption. Mifepristone and misoprostol have been used by over 50,000 women at the dose to be used in this study. The dosage to be studied has been approved for routine use in France for women who have been pregnant for seven weeks or less. Mifepristone in combination with a prostaglandin has also been approved for use in China, Britain and Sweden. In the latter two countries, it is used in women who are pregnant for nine weeks or less.

**Amendment 3 dated May 2, 1995

The aims of the present study are to determine the safety, efficacy and acceptability of mifepristone plus misoprostol for pregnancy termination in women who are 63 days or less from the first day of the last menstrual period. Three groups of women who are less than 50 days; 50 through 56 days and 57 through 63 days from the first day of the last menstrual period will be included in the study. This study is being performed as a requirement for registration of mifepristone plus misoprostol with the U.S. Food and Drug Administration (FDA) so that these products can be used for pregnancy termination in the U.S.

2. Clinic visits

I understand that at my initial visit (visit 1) I will receive counseling about the method, and a urine and blood sample will be collected to make sure I am pregnant. I will be given a physical, and a pelvic exam and my medical history will be taken. Using a vaginal ultrasound, which is a small probe that is placed in the vagina, the duration of my pregnancy will be determined. Also I will be given a blood test for the Rh factor in my blood. If I have an Rh negative blood type, I will be given an injection at the second visit to prevent the development of antibodies that could endanger any future pregnancy. I understand that I may be asked for additional blood samples (about 2 teaspoons) to be collected to measure the levels of different substances normally in my blood, as well as determine the normal characteristics of my blood. If I decide not to have additional blood samples taken, I may still continue to participate in the study* . In order to terminate my pregnancy, I will take three tablets of mifepristone (first medication) orally in the presence of study personnel. Two days later, I will return to the clinic (visit 2) even if I believe I have aborted and will take two misoprostol tablets (second medication) by mouth if I have not aborted. If I take the second medication, the duration of my stay at the clinic at the second visit will be approximately four hours, during which time I will be closely monitored by the study team. During this time, there is an 60-80% chance that abortion will occur. If I come to the clinic in a car, I will be sure to arrange for someone else to drive me home from this visit, and understand that I will not drive myself home.

* Amendment 1 dated April 27, 1995

I understand that if the abortion does not occur at the clinic, it is likely to occur at home and I may continue to have uterine bleeding for several days. **I understand that the amount of bleeding may be similar to that which occurs during a spontaneous miscarriage (i.e. more than a heavy menstrual period). The risk of heavy bleeding increases after 49 days since the first day of my last menstrual period**** . I should use sanitary napkins until the uterine bleeding or spotting ends and not use tampons. As with surgical abortion, I cannot resume douching until the bleeding stops (about 10-12 days). I should not resume sexual intercourse for eight to ten days after taking the prostaglandin, by which time most abortions would have been completed.

I understand that I may see the product of conception on my sanitary napkin or in the toilet. This may happen at the clinic, at home or work. Through the seventh week after conception, this product is called an embryo; it is smaller than a quarter and is usually embedded in a blood clot. Even if I see the products of conception, I will not be able to tell whether the method has been effective as part of the placenta may still remain in the uterus. This is why it is important to return to the clinic for a follow-up, visit 3, so that the clinic staff can determine if the abortion is complete.

A further appointment will be made for me to return to the clinic two weeks after taking the first tablet (visit 3), to ensure that the treatment has been effective. **I understand that I may again be asked for additional blood samples (about 2 teaspoons) to be collected to measure the levels of different substances normally in my blood, and to determine the characteristics of my blood. If I decide not to have additional blood samples taken, I may still continue to participate in the study.*** If the treatment has not been effective; then a surgical procedure called vacuum aspiration or dilatation and curettage will be carried out at that time to complete the abortion. This is the same

** Amendment 3 dated May 2, 1995

* Amendment 2 dated April 27, 1995

surgical procedure that would have been used had I elected to undergo surgical abortion in the first instance. I will be sure to have arranged for someone else to drive me home from this visit, and understand that I will not drive myself home. If I notice a vaginal discharge with odor after treatment, this may indicate an infection. I will contact my physician for an appointment.

I understand that bleeding may continue beyond my third visit. If this occurs the clinic will contact me by telephone to determine if it has stopped or if I need additional treatment.

I understand that there are no indications at present that use of an antiprogestin to end a pregnancy has prevented or harmed a woman's ability to have a baby in the future. Women who have taken mifepristone have been able to conceive and subsequently bear a healthy child. Since it is possible to become pregnant again after the abortion, I will be asked to select and use a contraceptive method.

3. Benefits

I understand that an advantage of the mifepristone/misoprostol medical method for pregnancy termination is that it avoids a surgical procedure. There is no anesthesia-related risks or risk of uterine perforation or cervical canal injury which may rarely be observed after surgical termination of pregnancy. Another benefit is the satisfaction of participating in the study that will make mifepristone/misoprostol available to women in the U.S.

4. Risks and discomforts

I understand that drawing blood for the tests at the first and third visits may be associated with discomfort, bruising, and possibly infection at the site of withdrawal. I understand that experience gained so far with the combination of drugs and the termination of early pregnancy indicates that this therapy has few side effects. The frequency of short-term complications are comparable to that observed after surgical abortion performed by vacuum aspiration. The most common complaint during treatment (particularly following administration of the second medication) is lower abdominal pain or cramps which are similar to those associated with a very heavy menstrual period. I will receive appropriate medication for pain when required.

I understand that I should not take aspirin, Motrin®, ibuprofen (Advil®) or any other drug known to block the action of prostaglandins. However, I may take Tylenol® and I may receive stronger medications for pain from my doctor. I understand that cramps and abdominal pains are usual and an expected part of the abortive process. Nausea, vomiting, and diarrhea have been observed following administration of the second medication. Therefore, at the second visit it is necessary to remain at the clinic under appropriate medical supervision for approximately four hours before returning home. I understand that uterine bleeding, similar to that which occurs during a spontaneous miscarriage (i.e. more than a heavy menstrual period) and lasting at least one week, may be expected. The risk of heavy bleeding increases after 49 days since the first day of my last menstrual period** In rare instances very heavy uterine bleeding may occur requiring surgical abortion and/or blood transfusion.

I understand that it is not advisable to allow a pregnancy to continue after taking mifepristone and/or misoprostol, since the full effects of mifepristone on the fetus are not known and misoprostol administration in early pregnancy has been associated with abnormal development of the fetus. I understand that based on prior studies and recently obtained information, abortion after mifepristone/misoprostol is successful in termination of pregnancy in approximately 95% of treated women whose first day of their last menstrual period occurred no more than 49 days before administration of mifepristone. In women whose first day of their last menstrual period occurred from 50 to 63 days before they received mifepristone, this new information suggests that as many as one in four may require some form of surgical procedure.**

**Amendment 3 dated May 2, 1995

When abortion is incomplete, vacuum aspiration or dilatation and curettage are recommended to terminate bleeding and prevent anemia. *When abortion does not occur, surgical termination of pregnancy is recommended because of the possible risk to the fetus. I have previously agreed to this procedure.*

There have been no serious heart conditions in the 52,000 women using the combination of drugs in the study for pregnancy termination. However, serious cardiovascular complications, including one fatal heart attack occurred during medical abortion using a different drug combination. These heart conditions have occurred usually in women who are heavy smokers or have increased blood fats, diabetes, high blood pressure, or family history of heart disease. This risk also increased in women who are over 35 years of age. These complications have been seen only following an injected prostaglandin and are rare (one in 20,000 cases). To date there is no evidence that the oral prostaglandin (misoprostol) that I will be taking in this study and which has been used widely for prolonged periods of time in the prevention of stomach ulcers, is associated with such cardiovascular side effects.

5. Alternative Statement

I know that my pregnancy could be terminated by a surgically performed abortion procedure (dilatation and curettage or vacuum aspiration). The possible advantages and disadvantages of a surgical rather than a medical termination have been explained to me. The advantages of surgical termination of pregnancy is that this is a one day procedure. The risks associated with surgical abortion are minimal. These include the risk of an anesthetic procedure. In the U.S., less than 1% of patients who undergo a surgical abortion experience a major complication associated with the procedure such as a serious pelvic infection, cervical tear, bleeding requiring a blood transfusion or unintended major surgery (for a uterine perforation).

6. Physical Injury Statement

If I require medical treatment as a result of physical injury arising from my participation in this study, immediate, essential, short-term medical care and treatment as determined by the doctors in this study will be made available without charge to me. There will be no monetary compensation for any other care, but medical consultation and appropriate referral services are available. Further information on the availability of medical care and treatment for any physical injury resulting from my participation in this study may be obtained from the Investigator, Dr. _____ (telephone:_____).

7. Whom to Call in an Emergency

I understand that if severe uterine bleeding, or abdominal pain, or any other medical emergency arises in association with this method, I will report immediately to (institute, address, telephone no.) In addition, I will contact Dr. _____

(telephone:_____). If he or she cannot be reached in a medical emergency related to the study, I may contact Dr. _____ (telephone:_____).

8. Offer to Answer Questions and Freedom to Withdraw from the Study

I have been told that I may withdraw from the study at any time without jeopardy to my present or future medical care from the hospital or clinic. If I withdraw I will be offered a surgical abortion. I have been told to contact Dr. _____(telephone:_ _____ or Dr. _____ (telephone:_____ if I have any questions about the research. These physicians may appoint their associates to answer my questions.

I also understand that the Principal Investigator may require me to withdraw from the study, if in his/her medical judgement it is in the best interest of my health or if it becomes impossible for me to follow the experimental procedure of this study.

I understand that, if my treatment under the study does not result in an abortion, and I refuse surgical abortion and continue with my pregnancy, I risk. and the infant may risk. complications, including fetal or infant malformation.

9. Confidentiality

I understand that information obtained in this study will be transmitted only in a form that cannot be identified with me, and that all records will be kept in a locked cabinet. I understand that the Population Council or their designated monitors, as well as the U.S. Food and Drug Administration may request access to my medical records.

I understand that I may be asked to be interviewed by a representative of the sponsor. The interview will be conducted in the language that I speak and will verify that I understand the risks, benefits, procedures, and the experimental nature of the study. If I do not agree to be interviewed, this will not affect my present or future medical care from the hospital or the clinic, or my participation in the study. I understand that I can change my mind at any time. All information will be kept confidential.

EVALUATION OF THE EFFICACY, SAFETY AND ACCEPTABILITY OF MIFEPRISTONE AND MISOPROSTOL IN INDUCING ABORTION IN PREGNANT WOMEN WITH AMENORRHEA OF UP TO 63 DAYS

PROTOCOL NUMBER: 166 B

10. Subject's Statement

I, the undersigned, have had the risks and benefits of this study explained to me in a language that I understand. I agree to participate in this study as a volunteer subject.

_____ _____

Date Signature of Volunteer

11. Investigator's Statement

I, the undersigned, have explained to the volunteer in the language which she speaks the procedures to be followed in this study and the risks and benefits involved.

_____ _____

Date Signature of Investigator

_____ _____

Date Signature of Witness to the Above Signatures and Explanation

APPEARS THIS WAY ON ORIGINAL

Protocol:

Cover Sheet:	Change:	The Population Council to The Population Council, Inc.
	Change:	Written authorization from The Population Council, to written authorization **of** The Population Council
Table of Contents: 6.5:	Change:	SAFETY ASSESSMENT COMMITTEE **to** MEDICAL ADVISORY COMMITTEE
P. 3: First paragraph:	The word either was added in reference to parenteral or vaginal prostaglandins in combination with mifepristone	
P. 3: Last paragraph:	Change:	heart condition **to** heart complications
P. 4: Third paragraph:	Change:	as close as possible to as **closely** as possible
P. 4: Last paragraph:	Add:	Subject shall visit the study center three times **unless state law requires an additional, initial informational visit with a mandatory waiting period before the process can begin.**
	Add:	At the initial visit (Day 1); **after any required statutory waiting period.**
P. 5: second paragraph:	Change:	institutional insurance **to** general liability insurance
P. 6:	Add: 4.1.3	**Residents of the United States**
P. 6:	Add: 4.2.9	**Resident of the United States**
P. 7: 4.3.2	delete	~~[redacted]~~
P. 7: 4.3.5	Add:	**or hematocrit below 30%**
P. 7: 4.3.7	Delete :	~~[redacted]~~
	Add:	**Subjects with an IUD in place.**
P. 7: 4.3.15	Change to:	Women who cannot reach the source of emergency medical care that serves the abortion center within ~~[redacted]~~ from (a) their home or place or work and (b) the abortion center.

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P. 8: Section 5.2		Change:	[illegible] orally
P. 9: Section 5.3	A)	Change to:	Mifepristone will be provided as 200 mg tablets of micronized mifepristone
	B)	Change to:	Misoprostol will be obtained locally be each investigator as 200 µg tablets of commercially available misoprostol.
P. 9: Section 5.4:	A)	Change to:	Mifepristone will have a label which will include product identification, expiration date, and drug dose. In addition the following will be printed on the labels: CAUTION: New drug. Limited by Federal Law to Investigational Use. All medication packets will be labelled with the protocol number.
	B)	Change to:	Misoprostol will be obtained locally by each investigator as 200 µg tablets of commercially available misoprostol and dispensed from the center pharmacy.
P. 9: Section 5.5 paragraph 1		Change:	hypertension to hypotension
		Change:	should be avoided to **must** be avoided
P. 10: Section 6.1:		Change:	Serum βhCG test to quantitative serum βhCG.
		Change:	Determination of blood group and Rh status to Determination of Ph status and where routinely collected, the blood group.
P. 10: Last paragraph:		Add:	**No more than** 240 ml.
P. 11: Second paragraph:		Change:	Subjects will be given written information **to** Subjects will be given a copy of the informed consent and patient diary card.
		Change:	.... which receives patients ..... **to which cares** for patients.
Section 6.2:		Add:	**If the patient believes that expulsion occurred prior to Visit 2, the date and time will be recorded on the case report form as they were noted in the subjects diary. Since it is difficult to confirm that an abortion at this time is complete, nearly all subjects will require misoprostol. If however, the physician can verify unequivocally**

			that complete abortion has occurred, the misoprostol will not be administered. If the abortion is incomplete or if there is any uncertainty about the completeness of the abortion, the misoprostol will be administered.
	Last paragraph:	Delete:	~~———~~
		Add:	**, if indicated.**
P. 12:	First paragraph:	Add:	**No more than** 240 ml
	Second paragraph: Last sentence	Delete:	~~———~~
P. 13:	Section 6.2: Second to Last paragraph	9/6/94 last paragraph Change to:	A very active attempt should be made to contact any subject who fails to appear for the Visit 2 appointment. The administration of misoprostol after Day 3 is strongly discouraged. Misoprostol may be administered between 36 and 60 hours after mifepristone administration.
P. 13:	Section 6.2:	Add:	**If the center is aware of any subject who misses Visit 2 and does not appear for Visit 3, or who otherwise determines to carry her pregnancy to term, the center shall retain its records relating to such subject through the date on which she was last seen at the center for a period of thirty (30) years following such date.**
P. 13:	Section 6.3:	Add:	**Subjects who experience bleeding post Day 15 should be followed-up via telephone until the bleeding has stopped or intervention is clinically indicated.**
P. 14:	after last paragraph:	Add:	**If the center is aware of any subject who misses Visit 2 and does not appear for Visit 3, or who otherwise determines to carry her pregnancy to term, the center shall retain its records relating to such subject through the date on which she was last seen at the center for a period of thirty (30) years following such date.**
P. 15:	Section 6.5:	Change Heading:	Safety Assessment Committee to Medical Advisory Committee.
		Change Body:	Safety Assessment Committee to Medical Advisory Committee

P. 16:	Section 6.7: first paragraph	Add:	A center must retain its records with respect to a subject who withdraws from the study after ingesting mifepristone and for whom a complete abortion has not been confirmed for a period of **at least 30 years following the subject's last visit to the center.**
P. 16:	Section 6.7: Second paragraph	Change:	Day 6 to 60 hours
P. 18:	Section A:	Change:	study drug to study drugs.
P. 20:	Section D:	Add:	**Except as otherwise explicitly set forth herein,**
P. 21:	Seventh paragraph:	Change:	submitted for histological examination to submitted for pathological examination
P. 27:		Add:	**Hemoglobin or Hematocrit Determination, Quant. Serum βhCG**
		Change:	Administration of ~~——~~ to Administration of anti-D globulin

Informed Consent:

Section 1	Change:	Approximately ~~——~~ to over 150,000
Section 2 Clinic Visits: Second paragraph last sentence:	Change:	or third visit to, visit 3,
Section 2 Clinic Visits:	Add:	paragraph 4

I understand that bleeding may continue beyond my third visit. If this occurs the clinic will contact me by telephone to determine if it has stopped or if I need additional treatment.

Section 8: After last paragraph

Add: **I understand that, if my treatment under the study does not result in an abortion, and I refuse surgical abortion and continue my pregnancy, I risk, and the infant may risk, complications including fetal or infant malformation.**

AMENDMENT #2

The protocol is being amended in order to determine if any changes occur in the blood chemistry or hematology parameters of subjects following the administration of mifepristone and/or misoprostol. Blood samples will be collected as outlined below.

The following additions to the protocol are indicated.

Blood samples will be collected prior to the administration of mifepristone at Visit 1 for the following: ***(page 10 of protocol)***

Chemistry Panel (4m*L*)
Which includes:

Aspartate aminotransferase, Alanine aminotransferase, Alkaline phosphatase, Total Bilirubin, Blood urea nitrogen, Phosphate, Creatinine, 24 hour fasting Glucose, Albumin, Lactate dehydrogenase, Potassium, Sodium, Chloride, Bicarbonate, Uric Acid, Calcium, as well as Cholesterol, Triglycerides, and Total Protein

Hematology Panel (3m*L*)
Which includes:

Hemoglobin, Hematocrit, RBC, WBC with differential, Platelet count

Blood samples will again be collected at Visit 3 (Day 15) for the ***same measurements listed (page 13 of protocol)*** above.

A total of twelve (12) subjects per ***each*** group ***of amenorrhea duration,*** for a total of thirty-six (36) per center will be involved in these assessments at six (6) selected centers. ***Thus,*** a total of 216 subjects from the entire study population will participate.

The notification process (contact and telephone number) Section 7.1 is modified to remove ~~telephone number~~ and

insert: **Dr. Irving Spitz or Dr. C. Wayne Bardin**
The Population Council, Inc.
(800) 327-8730

AMENDMENT #1 (INFORMED CONSENT)

The informed consent text was modified to reflect the additional blood collections for chemistry and hematology. ***(on pages 30, 31, 32)***.

Section 2 Clinic Visits

1st paragraph

..... could endanger any future pregnancy. *I understand that I may be asked for additional blood samples (about 2 teaspoons) to be collected to measure the levels of different substances normally in my blood as well as determine the normal characteristics of my blood. If I decide not to have additional blood samples taken, I may still continue to participate in the study.* In order to.....

3rd paragraph

..... treatment has been effective. *I understand that I may again be asked for additional blood samples (about 2 teaspoons) to be collected to measure the levels of different substances normally in my blood, and to determine the characteristics of my blood. If I decide not to have additional blood samples taken, I may still continue to participate in the study.* If the treatment.....

Section 4 Risks and Discomforts

1st paragraph, 1st sentence

..... for the tests at the first ***and third visits*** may be.....

APPEARS THIS WAY ON ORIGINAL

The protocol is being amended in order to reflect the recent data indicating an increased need for surgical procedures in Groups 2 and 3

The additions to the protocol and informed consent are indicated.

Informed Consent

Page 25 add:

Recently obtained information supports the statement that mifepristone plus misoprostol cause abortion in approximately 95 percent of women with amenorrhea of no more than 49 days before administration of mifepristone. In women with amenorrhea of 50 to 63 days before they received mifepristone, this new information suggests that as many as one in four may require some form of surgical procedure. There are a number of reasons for such a surgical procedure including continued pregnancy, incomplete abortion, or excess bleeding. This excess bleeding may be similar to that which occurs during a spontaneous miscarriage (i.e. more than a heavy menstrual period). The possibility of experiencing excess bleeding increases with increasing duration of amenorrhea.

Page 29 delete:

During the early stages of pregnancy, mifepristone plus misoprostol cause abortion in approximately 95 percent of women.

Page 29 add:

Recently obtained information supports the statement that mifepristone plus misoprostol cause abortion in approximately 95 percent of women whose first day of their last menstrual period occurred no more than 49 days before administration of mifepristone. In women whose first day of their last menstrual period occurred from 50 to 63 days before they received mifepristone, this new information suggests that as many as one in four may require some form of surgical procedure. There are a number of reasons for such a surgical procedure including continued pregnancy, incomplete abortion, or excess bleeding. The possibility of experiencing excess bleeding increases with increasing duration of amenorrhea.

Page 31: Section 2

Add:

I understand that the amount of bleeding may be similar to that which occurs during a spontaneous miscarriage (i.e. more than a heavy menstrual period). The risk of heavy bleeding increases after 49 days since the first day of my last menstrual period.

AMENDMENT #3 (cont'd)

Page 33: Section 4

Add:

I understand that uterine bleeding, similar to that which occurs during a spontaneous miscarriage (i.e. more than a heavy menstrual period) and lasting at least one week, may be expected. The risk of heavy bleeding increases after 49 days since the first day of my last menstrual period.

last paragraph

Add:

I understand that based on prior studies and recently obtained information, abortion after mifepristone/misoprostol is successful in termination of pregnancy in approximately 95% of treated women whose first day of their last menstrual period occurred no more than 49 days before administration of mifepristone. In women whose first day of their last menstrual period occurred from 50 to 63 days before they received mifepristone, this new information suggests that as many as one in four may require some form of surgical procedure.

APPEARS THIS WAY
ON ORIGINAL

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
001	11/02/94	11/04/94	11/16/94	NAUSEA	11/02/94	11/02/94	3	1	3	1
				INTERMITTENT HEADACHE	11/02/94	11/03/94	2	2	2	1
				CRAMPING	11/02/94	11/03/94	2	1	3	1
				INTERMITTENT NAUSEA AND VOMITING	11/03/94	11/04/94	3	1	3	1
				HEAVY BLEEDING	11/04/94	11/04/94	3	1	5	1
				CRAMPING	11/04/94	11/04/94	3	1	7	1
				HEADACHE	11/05/94	11/05/94	2	2	4	1
				CRAMPING	11/06/94	11/07/94	2	2	6	1
				HEAVY BLEEDING	11/07/94	11/07/94	3	1	6	1
				HEADACHE	11/11/94	11/11/94	1	2	1	1
002	11/02/94	11/04/94	11/16/94	MOOD SWING	11/02/94	11/02/94	2	1	2	1
				LOOSE STOOLS	11/03/94	11/04/94	2	1	2	1
				HEAVY BLEEDING	11/03/94	11/05/94	3	1	3	1
				LOSS OF APPETITE	11/04/94	11/07/94	3	1	6	1
				CRAMPING	11/04/94	11/08/94	2	2	7	1
003	11/02/94	11/04/94	11/16/94	VAGINAL INFECTION		11/03/94	1	2	1	1
				BLADDER INFECTION		11/09/94	2	2	1	1
				CRAMPING	11/03/94	11/04/94	2	2	3	1
				HEAVY BLEEDING	11/04/94	11/04/94	3	1	7	1
				CRAMPING	11/04/94	11/04/94	3	1	7	1
				ALLERGIES NASAL CONGESTION	11/05/94	11/05/94	1	2	1	1
				CRAMPING	11/05/94	11/05/94	1	1	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
004	11/02/94	11/04/94	11/17/94	CRAMPING	11/02/94	11/03/94	1	1	3	1
				HEADACHE	11/03/94	11/03/94	2	2	1	1
005	11/02/94	11/04/94	11/16/94	CRAMPING	11/02/94	11/04/94	1	1	2	1
				CRAMPING	11/04/94	11/04/94	3	2	7	1
				CRAMPING	11/04/94	11/04/94	1	1	7	1
				HEADACHE	11/08/94	11/08/94	2	2	1	1
				HEADACHE	11/11/94	11/11/94	2	2	1	1
006	11/07/94	11/09/94	11/21/94	DIZZINESS	11/07/94	11/07/94	1	1	2	1
				CRAMPS	11/08/94	11/09/94	1	1	3	1
				CRAMPS	11/09/94	11/10/94	2	2	7	1
007	11/07/94	11/09/94	11/21/94	SPOTTING	11/08/94	11/08/94	1	1	3	1
				CRAMPING	11/08/94	11/08/94	1	1	3	1
				CRAMPS	11/09/94	11/11/94	2	2	7	1
				HEAVY BLEEDING	11/09/94	11/11/94	2	1	7	1
				CRAMPS	11/12/94	11/12/94	1	1	6	1
008	11/07/94	11/09/94	11/21/94	VOMITING	11/07/94	11/08/94	2	1	3	1
				NAUSEA	11/07/94	11/08/94	2	1	3	1
				CRAMPING	11/09/94	11/09/94	2	1	7	1
				HEAVY BLEEDING	11/10/94	11/13/94	3	1	7	1
				CRAMPS	11/10/94	11/11/94	2	1	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
008 (Cont.)				VOMITING	11/10/94	11/10/94	1	1	7	1
009	11/07/94	11/09/94	11/23/94	NAUSEA	11/07/94	11/07/94	2	1	3	1
				CRAMPS	11/07/94	11/07/94	2	2	3	1
				VOMITING	11/07/94	11/09/94	2	1	3	1
				CRAMPING	11/09/94	11/09/94	3	2	7	1
				VOMITING	11/09/94	11/09/94	2	2	3	1
010	11/07/94	11/09/94	11/21/94	HEADACHE	11/07/94	11/09/94	2	2	4	1
				SHOOTING PAINS IN LOWER STOMACH	11/08/94	11/08/94	3	1	3	1
				CRAMPING	11/09/94	11/09/94	2	1	7	1
				FATIGUE	11/10/94	11/10/94	2	1	4	1
011	11/07/94	11/09/94	11/21/94	NAUSEA	11/08/94	11/08/94	2	1	3	1
				HEAVY BLEEDING	11/09/94	11/09/94	1	1	7	1
				VOMITED	11/09/94	11/09/94	1	1	7	1
				DIARRHEA	11/09/94	11/09/94	1	1	7	1
				HA	11/09/94	11/10/94	2	2	6	1
				CRAMPING	11/09/94	11/09/94	2	1	7	1
012	11/07/94	11/09/94	11/29/94	CRAMPS	11/08/94	11/09/94	2	1	3	1
				NAUSEA	11/08/94	11/09/94	3	1	3	1
				VOMITING	11/08/94	11/09/94	3	1	3	1
				HEAVY BLEEDING	11/09/94	11/10/94	3	1	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
012 (Cont.)				CRAMPING	11/09/94	11/09/94	3	2	7	1
				NAUSEA	11/09/94	11/09/94	3	1	7	1
				CRAMPS	11/10/94	11/10/94	3	1	7	1
				CRAMPS	11/12/94	11/13/94	3	2	7	1
				INTER. CRAMPS	11/14/94	11/17/94	2	2	6	1
013	11/07/94	11/09/94	11/21/94	CRAMPS	11/07/94	11/07/94	1	1	2	1
				NAUSEA	11/08/94	11/09/94	2	2	3	1
				HEAVY BLEEDING	11/08/94	11/09/94	2	1	3	1
				ABDOMINAL PAIN	11/08/94	11/09/94	3	2	3	1
				VOMITING	11/08/94	11/09/94	2	2	3	1
				DIZZINESS	11/09/94	11/09/94	1	1	2	1
				LOWER BACK PAIN	11/09/94	11/09/94	3	1	7	1
				NAUSEA	11/09/94	11/09/94	3	2	7	1
				HEADACHE	11/09/94	11/09/94	1	1	2	1
				CRAMPING	11/09/94	11/09/94	3	1	7	1
				CRAMPS	11/10/94	11/11/94	2	2	6	1
				SEVERE HA	11/12/94	11/12/94	3	2	6	1
				(R) SIDE ABDOMINAL PAIN	11/12/94	11/12/94	3	1	6	1
014	11/07/94	11/09/94	11/21/94	CRAMPING	11/07/94	11/07/94	1	1	3	1
				FATIGUE	11/08/94	11/08/94	1	1	2	1
				LARGE APPETITE	11/08/94	11/08/94	2	1	2	1
				CRAMPS	11/08/94	11/08/94	2	1	3	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
014 (Cont.)				VOMITING	11/09/94	11/09/94	2	2	2	1
				CRAMPS	11/09/94	11/13/94	2	2	7	1
				NAUSEA	11/09/94	11/09/94	2	2	2	1
				CRAMPS	11/15/94	11/21/94	1	2	6	1
015	11/08/94	11/10/94	11/25/94	NAUSEA	11/09/94	11/09/94	3	2	3	1
				INSOMNIA	11/09/94	11/09/94	3	1	2	1
				CRYING / SADNESS	11/09/94	11/09/94	3	1	2	1
				CONGESTION	11/09/94	11/09/94	1	2	2	1
				HEAVY BLEEDING	11/10/94	11/11/94	3	1	7	1
				CRAMPS	11/10/94	11/13/94	3	1	7	1
				CRAMPING	11/10/94	11/10/94	3	2	7	1
				CRAMPS	11/17/94	11/19/94	1	1	6	1
016	11/08/94	11/10/94	11/22/94	VAGINAL INFECTION		11/09/94	1	2	1	1
				NAUSEA	11/08/94	11/09/94	1	1	3	1
				CRAMPS	11/08/94	11/09/94	1	1	3	1
				CRAMPING	11/10/94	11/10/94	1	1	3	1
				CRAMPING	11/10/94	11/10/94	3	2	7	1
017	11/08/94	11/10/94	11/22/94	HEADACHE	11/08/94	11/08/94	1	2	1	1
				BACKACHE	11/09/94	11/09/94	2	2	1	1
				NAUSEA	11/09/94	11/09/94	2	1	3	1
				DRY HEAVES	11/10/94	11/10/94	1	1	2	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
017 (Cont.)				CRAMPING	11/10/94	11/10/94	3	2	7	1
				TOOTHACHE	11/11/94	11/20/94	2	2	1	1
018	11/09/94	11/11/94	11/23/94	CRAMPING	11/09/94	11/13/94	2	2	3	1
				NAUSEA	11/11/94	11/11/94	1	1	2	1
				CRAMPING	11/11/94	11/11/94	3	1	7	1
				NAUSEA	11/11/94	11/11/94	3	1	7	1
019	11/09/94	11/11/94	11/23/94	CRAMPS	11/11/94	11/13/94	1	1	7	1
				CRAMPS	11/11/94	11/11/94	2	1	7	1
				PASSING CLOTS	11/11/94	11/11/94	2	1	7	1
				CRAMPS	11/23/94	11/26/94	2	2	6	1
020	11/14/94	11/16/94	11/28/94	CRAMPS	11/16/94	11/18/94	3	2	7	1
				ABDOMINAL PAIN	11/16/94	11/16/94	2	2	7	1
021	11/14/94	11/16/94	11/28/94	CRAMPING	11/16/94	11/16/94	1	1	7	1
022	11/14/94	11/16/94	11/28/94	CRAMPING	11/14/94	11/15/94	2	1	3	1
				VOMITING	11/15/94	11/16/94	2	1	3	1
				HEAVY BLEEDING	11/16/94	11/19/94	2	1	7	1
				CRAMPING	11/16/94	11/18/94	3	2	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
023	11/14/94	11/16/94	11/29/94	VAGINAL INFECTION		11/15/94	2	2	1	1
				CRAMPS	11/14/94	11/16/94	2	1	3	1
				VOMITING	11/14/94	11/16/94	3	1	3	1
				HEAVY BLEEDING	11/16/94	11/20/94	3	1	7	1
				NAUSEA	11/17/94	11/17/94	2	1	7	1
024	11/14/94	11/16/94	12/12/94	NAUSEA	11/15/94	11/16/94	2	1	3	1
				FATIGUE	11/15/94	11/16/94	1	1	2	1
				ABDOMINAL PAIN	11/16/94	11/16/94	1	1	7	1
025	11/14/94	11/16/94	11/28/94	SLEEPLESSNESS	11/14/94	11/14/94	2	2	2	1
				CRAMPS	11/15/94	11/16/94	1	1	2	1
				CRAMPS	11/16/94	11/19/94	2	2	7	1
				HEAVY BLEEDING	11/16/94	11/18/94	3	1	7	1
				SLEEPLESSNESS	11/18/94	11/18/94	2	2	6	1
026	11/14/94		11/28/94	STOMACH PAIN / CRAMPS	11/15/94	11/15/94	1	2	3	1
				NAUSEA	11/15/94	11/15/94	1	1	2	1
				CRAMPING	11/18/94	11/19/94	1	1	3	1
027	11/14/94	11/16/94	01/09/95	HEAVY BLEEDING	11/16/94	11/16/94	2	1	7	1
				ABDOMINAL PAIN	11/16/94	11/16/94	3	2	7	1
				CRAMPS	11/16/94	11/18/94	2	1	6	1
				LIGHTHEADED	11/29/94	12/02/94	3	2	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
027 (Cont.)				EXCESSIVE BLEEDING	11/29/94	11/29/94	3	3	7	1
				LOW HEMOGLOBIN	11/30/94	Ongoing	2	2	7	3
028	11/14/94	11/16/94	11/28/94	NAUSEA	11/14/94	11/14/94	1	1	3	1
				CRAMPING	11/16/94	11/17/94	2	1	7	1
				NAUSEA	11/16/94	11/16/94	1	1	7	1
029	11/15/94	11/17/94	11/29/94	NAUSEA	11/15/94	11/18/94	1	1	3	1
				HEAVY BLEEDING	11/17/94	11/22/94	3	1	7	1
				CRAMPS	11/17/94	11/18/94	2	2	7	1
				HEMORRHOID	11/18/94	Ongoing	2	1	6	3
030	11/15/94	11/17/94	11/29/94	CRAMPS	11/16/94	11/16/94	1	1	2	1
				HEAVY BLEEDING	11/17/94	11/17/94	3	1	3	1
				HEADACHE	11/17/94	11/17/94	1	2	6	1
				CRAMPING	11/17/94	11/17/94	2	1	7	1
				HEADACHE	11/18/94	11/18/94	2	2	1	1
031	11/15/94	11/17/94	11/29/94	CRAMPING	11/16/94	11/23/94	1	2	3	1
				CRAMPING	11/17/94	11/23/94	2	2	7	1
				LOWER BACK PAIN	11/17/94	11/17/94	2	2	7	1
				EXTREME EMOTIONS	11/18/94	11/20/94	2	1	6	1
				UTI	11/27/94	Ongoing	3	2	6	3

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
032	11/15/94	11/17/94	11/29/94	NAUSEA	11/15/94	11/16/94	2	2	3	1
				HEAVY BLEEDING	11/17/94	11/19/94	3	1	7	1
				CRAMPS	11/17/94	11/18/94	1	2	7	1
				HEADACHE	11/22/94	11/22/94	1	2	6	1
033	11/16/94	11/18/94	12/03/94	CRAMPING	11/17/94	11/17/94	2	2	3	1
				ABDOMINAL PAIN	11/18/94	11/19/94	3	2	7	1
034	11/16/94	11/18/94	11/30/94	CRAMPING	11/17/94	11/18/94	2	1	3	1
				NAUSEA	11/17/94	11/17/94	2	1	2	1
				NAUSEA	11/18/94	11/18/94	2	1	7	1
				CRAMPING	11/18/94	11/20/94	2	1	7	1
				VOMITING	11/18/94	11/18/94	2	1	7	1
				HEADACHE	11/23/94	11/23/94	2	2	1	1
				COLD	11/29/94	11/29/94	2	2	1	1
035	11/16/94	11/18/94	11/30/94	NAUSEA	11/16/94	11/16/94	1	1	3	1
				VOMITING	11/16/94	11/16/94	1	1	3	1
				CRAMPS	11/17/94	11/18/94	1	1	3	1
				CRAMPING	11/18/94	11/19/94	3	2	7	1
				LOWER BACK PAIN	11/21/94	11/21/94	2	2	6	1
				CRAMPING	11/21/94	11/21/94	2	2	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
036	11/20/94		02/01/95	NAUSEA	11/20/94	11/22/94	3	2	2	1
				VOMITING	11/20/94	11/22/94	3	2	2	1
				HEADACHE	11/20/94	11/20/94	2	2	2	1
				EXCESSIVE BLEEDING	11/21/94	11/22/94	3	4	3	1
				CRAMPING	11/21/94	11/22/94	3	1	3	1
				PASSING OUT X 5	11/22/94	11/22/94	3	2	3	1
				CRAMPING	11/23/94	11/23/94	1	1	3	1
037	11/20/94	11/22/94	02/02/95	CRAMPING	11/22/94	11/22/94	2	1	7	4
				EXCESSIVE BLEEDING	11/22/94	11/23/94	2	1	7	1
				CRAMPING	11/22/94	11/22/94	3	1	7	2
				CRAMPING	11/23/94	11/23/94	1	1	7	1
038	11/20/94	11/22/94	12/06/94	NAUSEA	11/21/94	11/22/94	2	1	2	1
				CRAMPING	11/21/94	11/21/94	1	1	3	1
				CRAMPING	11/22/94	11/22/94	2	2	7	1
039	11/20/94	11/22/94	12/14/94	VOMITED	11/20/94	11/20/94	2	1	1	1
				CRAMPS	11/20/94	11/20/94	1	1	3	1
				VOMITED	11/21/94	11/22/94	1	2	1	1
				HA	11/21/94	11/21/94	1	2	3	1
				INTERMITTENT CRAMPS	11/21/94	11/22/94	2	2	3	1
				EXCESSIVE HEAVY BLEEDING (A PAD SOAKED QH X 3H ABOUT)	11/22/94	11/22/94	3	1	6	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
(Patients with Any Adverse Event)

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
039 (Cont.)				NAUSEA	11/22/94	11/22/94	3	1	5	1
				INTERMITTENT CRAMPS	11/22/94	11/23/94	3	2	6	1
				INTERMITTENT CRAMPS	11/24/94	11/24/94	2	1	6	1
040	11/21/94	11/23/94	12/05/94	CRAMPS	11/23/94	11/23/94	2	1	3	1
				CRAMPING	11/23/94	11/23/94	3	1	7	1
				NAUSEA	11/23/94	11/23/94	1	1	7	1
				CRAMPS	11/24/94	11/26/94	1	1	7	1
				HEADACHE	11/28/94	11/29/94	1	1	1	1
				SORE THROAT	11/28/94	11/29/94	1	1	1	1
				ACHING NECK GLANDS	11/28/94	11/29/94	1	1	1	1
041	11/21/94	11/23/94	12/06/94	FATIGUE	11/21/94	11/23/94	1	1	2	1
				NAUSEA	11/22/94	11/23/94	1	2	3	1
				CRAMPING	11/23/94	11/24/94	3	1	7	1
				HEAVY BLEEDING	11/25/94	11/26/94	3	1	7	1
				CRAMPS	11/25/94	11/26/94	3	2	7	1
042	11/21/94	11/23/94	01/26/95	CRAMPS	11/22/94	11/22/94	1	2	3	1
				CRAMPS	11/23/94	11/23/94	3	2	7	1
				CRAMPS	11/24/94	11/24/94	1	1	7	1
				NAUSEA	11/25/94	11/26/94	1	1	6	1
				HOT FLASHES	11/25/94	11/26/94	1	1	6	1
				CRAMPS	11/27/94	11/27/94	2	1	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
042 (Cont.)				CRAMPS	11/28/94	11/29/94	3	2	7	1
				HYPOVOLEMIC	11/30/94	11/30/94	3	3	7	1
				HYPOTENSION	11/30/94	11/30/94	3	3	7	1
				EXCESSIVE BLEEDING	11/30/94	11/30/94	3	3	6	1
				LOW HEMOGLOBIN	12/01/94	Ongoing	2	2	6	3
043	11/21/94	11/23/94	12/09/94	PAIN / CRAMPS	11/21/94	11/22/94	1	1	3	1
				CRAMPS	11/21/94	11/21/94	3	1	3	1
				PAIN / CRAMPS	11/23/94	11/24/94	3	1	7	1
044	11/21/94	11/23/94	12/05/94	SHORTNESS OF BREATH	11/21/94	11/21/94	1	1	3	1
				TIGHTNESS OF ABDOMINAL MUSCLES	11/21/94	11/22/94	1	1	3	1
				SHORTNESS OF BREATH	11/22/94	11/22/94	1	1	3	1
				PAIN / CRAMPS	11/23/94	11/23/94	3	1	7	1
045	11/21/94	11/23/94	12/05/94	NAUSEA	11/21/94	11/21/94	2	1	3	1
				PAIN / CRAMPS	11/22/94	11/22/94	1	1	3	1
				HEAVY BLEEDING	11/23/94	11/24/94	3	1	7	1
				HEADACHE	11/26/94	11/26/94	3	1	1	1
				HEADACHE	11/30/94	11/30/94	1	1	1	1
046	11/21/94	11/23/94	12/06/94	HA	11/22/94	11/22/94	2	2	2	1
				HA	11/23/94	11/23/94	2	2	6	1
				CRAMPS	11/23/94	11/23/94	2	2	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
(Patients with Any Adverse Event)

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
046 (Cont.)				ABDOMINAL PAIN	11/23/94	11/23/94	1	1	7	1
047	11/21/94	11/23/94	01/10/95	VOMITING	11/21/94	11/22/94	3	1	3	1
				WEIGHT LOSS	11/21/94	11/23/94	2	1	3	1
				WEIGHT LOSS	11/23/94	11/30/94	2	1	7	1
				VOMITING	11/23/94	11/30/94	3	1	7	1
				CRAMPS	11/23/94	11/23/94	3	2	7	1
				CRAMPS	11/24/94	11/25/94	3	1	7	1
048	11/23/94	11/25/94	12/09/94	BACTERIAL VAGINOSIS		11/24/94	1	2	1	1
				CRAMPING	11/25/94	11/28/94	2	1	7	1
				CRAMPING	11/25/94	11/25/94	1	1	3	4
049	11/23/94	11/25/94	12/07/94	CRAMPS	11/23/94	11/23/94	1	1	3	1
				TIRED	11/23/94	11/25/94	2	1	2	1
				LITTLE EMOTIONAL	11/24/94	11/24/94	1	1	3	1
				CRAMPING	11/24/94	11/24/94	2	1	3	1
				CRAMPING	11/25/94	11/25/94	2	2	7	1
				DIARRHEA	11/25/94	11/25/94	2	1	7	1
				FAINTED 3 TIMES	11/25/94	11/25/94	3	1	7	1
				HEAVY BLEEDING (EXCESSIVE)	11/25/94	11/25/94	3	1	7	1
				FEVER	11/25/94	11/27/94	2	2	1	1
				TIRED	11/26/94	11/30/94	1	2	6	1
				LIGHT HEADED	11/26/94	11/26/94	1	1	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
049 (Cont.)				CRAMPS	11/28/94	11/30/94	3	2	7	1
				HEAVY BLEEDING (EXCESSIVE)	11/28/94	11/28/94	3	1	7	1
				HEADACHE	11/30/94	12/01/94	2	1	6	1
				SINUS HEADACHE	12/07/94	12/07/94	1	2	1	1
				ANEMIA	12/07/94	12/30/94	1	2	6	1
050	11/23/94		12/07/94	CRAMPING	11/24/94	11/24/94	1	1	3	1
				NAUSEA	11/24/94	11/24/94	2	1	3	1
				GAS PAINS	11/24/94	11/24/94	2	1	3	1
				SWEATING	11/24/94	11/24/94	2	1	3	1
				CRAMPING	11/25/94	11/26/94	1	1	7	1
				NAUSEA	11/26/94	11/26/94	3	1	7	1
				GAS PAINS	11/26/94	11/26/94	3	1	7	1
				CRAMPING	11/26/94	11/26/94	3	1	7	1
				CRAMPING	11/28/94	11/28/94	1	1	7	1
				CRAMPING	11/29/94	11/29/94	3	2	3	1
				NAUSEA	11/29/94	11/29/94	3	1	3	1
				CRAMPING	11/30/94	11/30/94	1	1	7	1
052	11/23/94	11/25/94	12/07/94	CRAMPS	11/25/94	11/25/94	3	1	7	1
				HEAVY BLEEDING	11/25/94	11/26/94	3	1	7	1
				CRAMPING	11/26/94	11/26/94	2	1	7	1
				CRAMPS	12/01/94	12/01/94	1	1	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
053	11/23/94	11/25/94	12/09/94	CRAMPING	11/25/94	11/25/94	1	1	5	1
				HEADACHE	12/02/94	12/02/94	1	2	1	1
054	11/23/94	11/25/94	12/07/94	CRAMPS	11/23/94	11/23/94	2	1	3	1
				CRAMPS	11/25/94	11/25/94	3	2	7	1
055	11/28/94	11/30/94	12/12/94	COLD	11/28/94	12/09/94	2	2	1	1
				HA	11/28/94	12/02/94	2	2	1	1
				INTERMITTENT CRAMPS	11/30/94	12/10/94	3	1	7	1
				CRAMPING	11/30/94	11/30/94	2	1	7	1
				SORE THROAT	12/04/94	12/09/94	2	2	1	1
056	11/28/94	11/30/94	12/12/94	HA	11/28/94	11/28/94	1	2	1	1
				BODY ACHES	11/28/94	11/28/94	1	2	1	1
				CRAMPING	11/28/94	11/30/94	1	1	3	1
				LOWER ABD PAIN	11/29/94	11/29/94	1	2	3	1
				BACK PAIN	11/29/94	11/29/94	1	2	3	1
				CRAMPS	11/30/94	11/30/94	2	2	7	1
				LOWER BACK PAIN	11/30/94	11/30/94	2	2	7	1
				CRAMPING	11/30/94	11/30/94	1	1	5	4
				CRAMPING	12/01/94	12/03/94	2	1	7	2
				CRAMPING	12/04/94	12/04/94	1	1	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
057	11/28/94	11/30/94	12/12/94	ALLERGY SYMPTOMS	11/28/94	11/28/94	2	2	1	1
				CRAMPING	11/28/94	12/03/94	2	2	7	1
				NAUSEA	11/29/94	11/29/94	1	1	2	1
				VOMITING	11/29/94	11/29/94	1	1	2	1
				NAUSEA	12/05/94	12/05/94	1	1	2	1
				VOMITING	12/05/94	12/05/94	1	1	2	1
				ALLERGY SYMPTOMS	12/13/94	Ongoing	2	2	1	2
058	11/28/94	11/30/94	12/12/94	DIZZINESS	11/28/94	11/28/94	3	1	2	1
				INTERMITTENT CRAMPS	11/28/94	11/30/94	3	2	3	1
				NAUSEA	11/29/94	11/30/94	3	1	2	1
				EXCESSIVE BLEEDING (SOAKED A PAD QH X 3H)	11/30/94	12/02/94	3	1	7	1
				INTERMITTENT CRAMPS	11/30/94	12/04/94	3	1	7	1
				NAUSEA	11/30/94	11/30/94	3	2	7	1
				DIARRHEA	11/30/94	11/30/94	2	1	6	1
				HEADACHE	12/01/94	12/01/94	2	2	6	1
				NAUSEATED (FLU?)	12/09/94	12/11/94	3	2	1	2
				BLOATED	12/14/94	12/14/94	2	1	6	1
				LIGHT HEADEDNESS	12/14/94	12/14/94	2	1	6	1
				DECREASED APPETITE	12/14/94	12/14/94	2	1	6	1
				NAUSEATED	12/14/94	12/15/94	2	1	6	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
059	11/28/94	11/30/94	12/13/94	TIRED	11/28/94	11/28/94	3	1	1	1
				TIRED	11/29/94	11/29/94	3	1	1	1
				CRAMPING	11/29/94	11/29/94	1	1	3	1
				CRAMPING	11/30/94	12/01/94	2	1	7	1
				PASSED OUT - FROM STANDING UP	12/01/94	12/01/94	3	1	1	1
				VOMITED	12/01/94	12/01/94	3	1	1	1
				DIARRHEA	12/01/94	12/01/94	3	1	1	1
				NAUSEA	12/01/94	12/01/94	2	2	7	1
060	11/28/94	11/30/94	12/12/94	CRAMPING	11/29/94	11/29/94	1	1	3	1
				CRAMPING	11/30/94	11/30/94	1	1	7	1
061	11/28/94	11/30/94	12/12/94	BACTERIAL VAGINAL INFECTION		11/29/94	2	2	1	1
				CRAMPING	11/30/94	11/30/94	2	2	7	4
				HEAVY BLEEDING; SOAKS A PAD ~QH X 3H	11/30/94	11/30/94	3	1	7	1
				HA	11/30/94	11/30/94	2	2	7	1
				CRAMPING	11/30/94	11/30/94	3	2	7	1
				DIARRHEA	12/01/94	12/01/94	3	1	7	1
				CRAMPING	12/01/94	12/01/94	3	1	7	1
				DIARRHEA	12/02/94	12/02/94	2	1	7	1
				HA	12/02/94	12/05/94	2	2	7	1
				HEAVY BLEEDING; SOAKS A PAD ~QH X 3H	12/03/94	12/04/94	3	1	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
061 (Cont.)				CRAMPS	12/03/94	12/05/94	3	2	7	1
062	11/28/94	11/30/94	12/12/94	NAUSEA	11/28/94	11/28/94	1	1	1	1
				HEADACHE	11/28/94	11/28/94	2	2	1	1
				HEAD COLD	11/28/94	11/29/94	2	2	1	1
				CRAMPING	11/29/94	11/29/94	1	1	3	1
				CRAMPING	11/30/94	11/30/94	2	2	7	1
				HEAVY BLEEDING	12/02/94	12/03/94	3	1	7	1
				CRAMPING	12/02/94	12/04/94	2	2	7	1
063	11/28/94	11/30/94	12/12/94	VAGINAL INFECTION		11/29/94	2	2	1	1
				CRAMPING	11/30/94	11/30/94	3	2	5	1
064	11/28/94	11/30/94	12/12/94	INTERMITTENT CRAMPS	11/30/94	12/03/94	2	2	7	1
				HEAVY BLEEDING	11/30/94	11/30/94	3	1	7	1
065	11/28/94	11/30/94	12/12/94	LOWER BACK ACHE	11/29/94	11/30/94	1	1	3	1
				DIARRHEA	11/29/94	11/29/94	1	1	3	1
				CRAMPS	11/29/94	11/30/94	1	1	3	1
				NAUSEA	11/30/94	11/30/94	1	1	3	1
				CRAMPS	11/30/94	11/30/94	3	1	7	1
				HEADACHE	12/01/94	12/02/94	1	1	7	1
				HEARTBURN	12/03/94	12/03/94	1	2	6	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
(Patients with Any Adverse Event)

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
066	11/29/94	12/01/94	12/16/94	CHLAMYDIA (POSITIVE)		Ongoing	1	2	1	1
				LIGHT HEADEDNESS	12/01/94	12/01/94	2	1	7	1
				CHICKEN POX	12/11/94	12/16/94	2	1	1	1
				LIGHT HEADEDNESS	12/13/94	12/13/94	1	1	7	1
				TIRED	12/13/94	12/13/94	1	1	7	1
067	11/29/94	12/01/94	12/14/94	BACTERIAL VAGINOSIS		12/01/94	1	2	1	1
				CRAMPING (INTERMITTENT)	11/30/94	11/30/94	2	1	3	1
				INTERMITTENT CRAMPS	12/01/94	12/01/94	3	1	7	1
068	12/05/94	12/07/94	12/19/94	HEADACHE	12/05/94	12/05/94	1	1	1	1
				QUEASY STOMACH	12/06/94	12/06/94	1	1	2	1
				HEADACHE	12/06/94	12/06/94	1	2	1	1
				CRAMPS	12/07/94	12/07/94	2	2	7	1
				DIARRHEA	12/07/94	12/07/94	2	1	7	1
				NAUSEA	12/07/94	12/07/94	2	1	7	1
				HA	12/08/94	12/08/94	2	2	7	1
				CRAMPS	12/11/94	12/11/94	1	1	7	1
				HA	12/18/94	12/18/94	2	2	6	1
069	12/05/94	12/07/94	12/19/94	HEADACHE'S	12/05/94	12/06/94	1	2	3	1
				NAUSEA	12/06/94	12/06/94	1	1	3	1
				CRAMPS	12/07/94	12/07/94	3	2	7	2
				HEADACHES	12/07/94	12/08/94	1	2	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
069 (Cont.)				CRAMPS	12/08/94	12/09/94	1	1	7	1
				HEADACHE	12/09/94	12/09/94	2	2	7	1
				CRAMPS	12/09/94	12/09/94	2	2	7	1
070	12/05/94	12/07/94	02/16/95	BACTERIAL VAGINOSIS		12/05/94	2	2	1	1
				VAGINAL INFECTION		12/20/94	2	2	1	1
				SHOOTING INJURY	01/05/94	Ongoing	2	4	1	3
				CRAMPS	12/05/94	12/06/94	1	1	3	1
				GAS	12/05/94	12/06/94	3	1	2	1
				DIARRHEA	12/05/94	12/06/94	2	1	2	1
				CRAMPING	12/07/94	12/10/94	2	2	7	1
				SHOOTING INJURY	12/31/94	01/04/95	3	3	1	2
				SURGICAL PAIN	12/31/94	01/04/95	3	2	1	2
071	12/05/94	12/07/94	12/19/94	BACTERIAL VAGINOSIS		12/16/94	2	2	7	1
				MUSCLE TENSION	12/06/94	12/06/94	2	2	1	1
				CRAMPS	12/07/94	12/07/94	2	2	7	4
				NAUSEA	12/07/94	12/07/94	2	1	7	1
				LIGHT-HEADED (FAINT)	12/07/94	12/07/94	3	1	1	1
				CRAMPING	12/07/94	12/07/94	3	2	7	1
				HEADACHE	12/08/94	12/08/94	2	2	6	1
				CRAMPING	12/08/94	12/08/94	1	2	7	1
				CRAMPING	12/09/94	12/10/94	2	2	7	1
				DIARRHEA	12/10/94	12/10/94	1	1	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
071 (Cont.)				CRAMPING	12/11/94	12/11/94	1	1	7	1
				CRAMPING	12/12/94	12/13/94	1	1	7	1
				STOMACH PAIN	12/15/94	12/15/94	2	2	7	1
				CRAMPING	12/15/94	12/16/94	1	1	7	1
				STIFF NECK & SHOULDERS	12/17/94	12/17/94	2	2	1	1
				CRAMPING	12/17/94	12/17/94	2	2	7	1
				STOMACH PAIN	12/18/94	12/18/94	2	2	7	1
				CRAMPING	12/18/94	12/18/94	1	1	7	1
072	12/12/94	12/14/94	12/27/94	CRAMPS	12/13/94	12/20/94	2	1	2	1
				BACKACHE	12/18/94	12/18/94	3	2	1	1
073	12/12/94	12/14/94	12/27/94	NAUSEA	12/12/94	12/14/94	2	1	3	1
				CRAMPS	12/12/94	12/15/94	2	1	5	1
				NAUSEA	12/14/94	12/15/94	2	2	7	1
				CRAMPS	12/14/94	12/15/94	2	2	7	1
074	12/12/94	12/14/94	12/27/94	CRAMPS	12/12/94	12/13/94	2	2	3	1
				CRAMPS	12/12/94	12/12/94	1	2	3	4
				CRAMPS	12/14/94	12/16/94	2	2	7	1
				CRAMPING	12/17/94	12/17/94	1	1	7	1
				NAUSEATED	12/17/94	12/17/94	3	1	7	2
				CRAMPS	12/17/94	12/17/94	3	1	7	2
				CRAMPS	12/18/94	12/18/94	1	1	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
074 (Cont.)				NAUSEATED	12/18/94	12/18/94	1	1	7	1
075	12/19/94	12/21/94	01/04/95	CRAMPS	12/21/94	12/22/94	2	1	7	1
076	12/19/94	12/21/94	01/06/95	BACTERIAL INFECTION		12/19/94	2	2	1	1
				CHLAMYDIA INFECTION		01/12/95	2	2	1	1
				NAUSEA	12/19/94	12/19/94	2	1	2	1
				CRAMPING	12/19/94	12/20/94	1	1	3	1
				VOMITING BLOOD	12/20/94	12/20/94	1	1	2	1
				NAUSEA	12/20/94	12/20/94	2	2	2	1
				NOSE BLEED	12/20/94	12/20/94	1	1	2	1
				CRAMPING	12/21/94	12/21/94	2	2	7	1
				CRAMPING	12/22/94	12/23/94	1	2	7	1
077	12/19/94	12/21/94	01/04/95	NAUSEA	12/19/94	12/19/94	1	1	3	1
				CRAMPS	12/20/94	12/21/94	2	2	3	1
				CHILLING	12/21/94	12/21/94	2	1	7	1
				CRAMPING	12/21/94	12/27/94	2	2	7	1
				SHAKEY	12/21/94	12/21/94	2	1	7	1
				HYPOTENSIVE	12/21/94	12/21/94	2	1	7	1
				VOMITING	12/26/94	12/26/94	2	1	1	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
078	12/20/94	12/22/94	01/04/95	CRAMPS	12/22/94	12/22/94	2	1	7	1
				HEAVY BLEEDING	12/22/94	12/23/94	2	1	7	1
079	12/27/94	12/29/94	01/11/95	CRAMPS	12/28/94	12/28/94	2	1	3	1
				CRAMPS	12/29/94	12/29/94	3	2	3	1
				CRAMPS	12/29/94	12/31/94	2	1	7	1
				HEADACHE	12/30/94	12/30/94	2	2	6	1
080	12/27/94	12/29/94	01/11/95	CRAMPING	12/28/94	12/28/94	1	1	3	1
				CRAMPING	12/29/94	12/29/94	1	1	7	1
				CRAMPING	12/30/94	12/30/94	2	2	7	1
081	12/27/94	12/29/94	01/11/95	BACTERIAL VAGINOSIS		12/28/94	2	2	1	1
				CRAMPING	12/27/94	12/29/94	1	1	3	1
				VOMITING	12/27/94	12/29/94	2	1	2	1
				CRAMPING	12/29/94	12/29/94	3	2	7	1
				DIARRHEA	12/29/94	12/29/94	1	1	7	1
				CRAMPING	12/30/94	01/01/95	2	2	7	1
082	12/27/94	12/29/94	01/11/95	CRAMPING	12/27/94	12/29/94	1	1	3	1
				CRAMPING	12/29/94	01/03/95	3	2	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
083	12/27/94	12/29/94	01/11/95	CRAMPING	12/27/94	12/27/94	2	2	3	1
				HA	12/27/94	12/27/94	2	2	2	1
				CRAMPING	12/28/94	12/28/94	1	2	3	1
				CRAMPING	12/29/94	01/01/95	2	2	7	1
				CRAMPING	12/29/94	12/29/94	1	2	7	4
				HA	12/30/94	12/30/94	2	2	7	1
				HA	01/01/95	01/01/95	2	2	7	1
				CRAMPING	01/02/95	01/03/95	1	2	7	1
				CRAMPING	01/04/95	01/07/95	1	1	7	1
084	12/28/94	12/30/94	01/17/95	ABD. PAINS	12/29/94	12/30/94	1	1	3	1
				FATIGUE	12/29/94	01/04/95	2	1	3	1
				NAUSEA	12/30/94	12/30/94	2	2	3	1
				NAUSEA	12/30/94	12/30/94	2	1	7	1
				CRAMPS	12/30/94	12/31/94	3	2	7	1
				ABD PAIN	01/01/95	01/01/95	1	2	6	1
				PAIN (R) LEG FROM HIP DOWN	01/15/95	01/15/95	3	1	6	1
				PAIN (R) LEG FROM HIP DOWN	01/16/95	01/16/95	1	1	6	1
085	01/03/95	01/05/95	01/18/95	VERY THIRSTY	01/03/95	01/03/95	1	1	2	1
				CRAMPS ON-OFF	01/03/95	01/03/95	1	1	3	1
				CRAMPS	01/04/95	01/04/95	2	1	2	1
				CRAMPS	01/05/95	01/09/95	2	2	7	1
				CRAMPS	01/10/95	01/11/95	1	1	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
086	01/03/95	01/05/95	01/18/95	BACTERIAL VAGINOSIS		01/19/95	2	2	1	1
				NAUSEA	01/03/95	01/03/95	3	2	1	1
				VOMITING	01/03/95	01/03/95	1	2	3	1
				SWEATS	01/03/95	01/03/95	3	1	3	1
				CHILLS	01/03/95	01/03/95	3	1	3	1
				CRAMPING	01/04/95	01/04/95	2	1	3	1
				NAUSEA INTERMITTENT	01/04/95	01/05/95	1	2	3	1
				CRAMPING	01/05/95	01/14/95	2	2	7	1
				NAUSEA	01/05/95	01/06/95	1	1	7	1
				VOMITING	01/05/95	01/05/95	2	2	3	1
				NAUSEA	01/05/95	01/05/95	3	1	7	2
				DIARRHEA INTERMITTENT	01/13/95	01/17/95	2	1	1	1
				COUGH & COLD SYMPTOMS	01/17/95	01/26/95	2	2	1	1
087	01/03/95	01/05/95	01/18/95	BACTERIAL VAGINOSIS		01/04/95	1	2	1	1
				FATIGUE	01/03/95	01/03/95	3	1	3	2
				DIZZINESS BUT DIDN'T PASS OUT	01/04/95	01/04/95	2	1	3	1
				HOT FLASHES	01/04/95	01/05/95	1	1	3	1
				FATIGUE	01/04/95	01/15/95	1	1	7	2
				PERSPIRING	01/04/95	01/04/95	2	1	3	1
				CRAMPS	01/05/95	01/05/95	1	1	7	1
				CRAMPS	01/05/95	01/05/95	3	2	7	1
				HOT FLASHES	01/06/95	01/15/95	1	1	6	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
088	01/03/95	01/05/95	01/17/95	CRAMPS	01/03/95	01/03/95	1	1	3	1
				NAUSEA	01/03/95	01/03/95	1	1	3	1
				CRAMPS	01/04/95	01/04/95	2	1	3	1
				BLACKED OUT IN SHOWER	01/04/95	01/04/95	2	1	1	1
				CRAMPING	01/05/95	01/05/95	2	1	7	1
				CRAMPING	01/07/95	01/11/95	1	1	7	1
089	01/04/95	01/06/95	01/20/95	NAUSEA	01/04/95	01/04/95	1	1	3	1
				CRAMPING	01/06/95	01/06/95	2	2	7	1
				FEVER	01/20/95	01/20/95	2	2	6	1
				BODY CHILLS	01/20/95	01/20/95	2	2	6	1
				BACTERIAL VAGINOSIS	01/20/95	Ongoing	2	2	1	3
				VAGINAL INFECTION	01/20/95	Ongoing	2	2	1	3
090	01/09/95	01/11/95	01/23/95	COLD, STUFFY NOSE	01/08/95	01/09/95	2	2	1	1
				LOWER BACK PAIN	01/11/95	01/11/95	3	2	5	1
				CRAMPS	01/11/95	01/12/95	1	1	7	1
				CRAMPS	01/11/95	01/11/95	2	1	7	4
				EXCESSIVE BLEEDING	01/11/95	01/11/95	3	1	7	1
				CRAMPING	01/11/95	01/11/95	3	1	7	1
				LOW BACK PAIN	01/11/95	01/12/95	1	1	7	1
				LOW BACK PAIN	01/11/95	01/11/95	2	1	7	4

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
(Patients with Any Adverse Event)

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
091	01/09/95	01/11/95	01/23/95	NAUSEA	01/09/95	01/10/95	2	1	3	1
				CRAMPS	01/09/95	01/09/95	1	1	3	1
				CRAMPS	01/11/95	01/12/95	3	2	7	1
				NAUSEA	01/13/95	01/13/95	2	1	6	1
				CRAMPS	01/13/95	01/14/95	3	2	7	1
				COLD SWEAT	01/15/95	01/15/95	2	1	1	1
				COLD SWEAT	01/17/95	01/17/95	3	1	1	1
092	01/09/95		01/23/95	CRAMPS	01/10/95	01/10/95	2	2	3	1
				LOW BACK PAIN	01/10/95	01/10/95	2	2	3	1
				MILD CRAMPS	01/11/95	01/11/95	1	2	3	1
				MILD CRAMPS	01/12/95	01/15/95	1	2	3	1
				HEADACHE	01/12/95	01/12/95	2	1	3	1
				CRAMPS	01/16/95	01/19/95	1	2	3	1
				HEADACHE	01/16/95	01/19/95	2	2	3	1
				LOW BACK PAIN	01/16/95	01/19/95	1	2	3	1
093	01/09/95	01/11/95	01/23/95	CRAMPING	01/09/95	01/09/95	1	1	3	1
				CRAMPING	01/10/95	01/10/95	2	1	3	1
				CRAMPING	01/11/95	01/11/95	3	2	7	1
				HEADACHE	01/11/95	01/11/95	2	2	4	1
				HEADACHE	01/13/95	01/13/95	2	2	6	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
094	01/09/95	01/11/95	01/23/95	DEPRESSION	12/27/94	Ongoing	3	1	1	3
				HEADACHE	01/09/95	01/09/95	2	2	3	1
				HEADACHE	01/10/95	01/10/95	2	2	3	1
				INTERMITTENT CRAMPS	01/10/95	01/10/95	1	1	3	1
				HEADACHE	01/11/95	01/13/95	2	2	6	1
				CRAMPS	01/11/95	01/13/95	3	2	7	1
				INSOMNIA	01/11/95	Ongoing	3	1	1	3
				IRRITABILITY	01/11/95	Ongoing	2	1	1	3
095	01/09/95	01/11/95	03/06/95	NAUSEA	01/09/95	01/10/95	3	1	3	1
				VOMITING	01/09/95	01/09/95	2	1	3	1
				CRAMPING	01/10/95	01/10/95	1	1	3	1
				COUGH	01/10/95	01/10/95	3	1	1	1
				SINUS PRESSURE	01/10/95	01/10/95	3	1	1	1
				CRAMPING	01/11/95	01/11/95	3	1	7	1
				CRAMPING	01/12/95	01/12/95	1	1	7	1
				HEARTBURN	02/28/95	02/28/95	2	2	1	1
096	01/11/95	01/13/95	01/30/95	NAUSEA	01/11/95	01/11/95	1	1	3	1
				EXCESSIVE BLEEDING	01/12/95	01/12/95	3	1	3	1
				FELT WEAK	01/12/95	01/12/95	1	2	3	1
				CRAMPING	01/13/95	01/13/95	1	1	7	1
				EXCESSIVE BLEEDING	01/14/95	01/14/95	3	1	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
097	01/16/95		01/30/95	NAUSEA	01/16/95	01/16/95	3	2	3	2
				NAUSEA	01/16/95	01/23/95	2	1	3	1
				CRAMPS	01/18/95	01/18/95	2	1	3	1
				CRAMPS	01/20/95	01/22/95	2	1	3	1
098	01/16/95	01/18/95	01/30/95	DIARRHEA	01/16/95	01/17/95	2	1	3	2
				VOMITING	01/17/95	01/18/95	2	1	3	1
				DIARRHEA	01/18/95	01/18/95	1	1	7	2
				HEAVY BLEEDING	01/18/95	01/18/95	3	1	7	1
				CRAMPING	01/18/95	01/18/95	2	1	7	4
				CRAMPING (BAD)	01/18/95	01/20/95	3	2	7	1
				DIARRHEA	01/19/95	01/19/95	1	1	7	1
				DIARRHEA	01/20/95	01/20/95	1	1	7	1
				BACK PAIN	01/21/95	01/21/95	2	1	7	1
				CRAMPING	01/21/95	01/22/95	2	2	7	1
099	01/16/95	01/18/95	02/02/95	CRAMPING	01/16/95	01/18/95	2	1	3	1
				NAUSEA	01/18/95	01/18/95	2	1	7	1
				VOMITING	01/18/95	01/18/95	2	1	7	1
				CRAMPING	01/18/95	01/18/95	2	1	7	1
				CRAMPING	01/19/95	01/21/95	1	1	7	1
				FEVER	01/30/95	01/31/95	2	2	1	1
				VOMITING	01/30/95	01/31/95	2	1	1	1
				DIARRHEA	01/30/95	01/31/95	2	2	1	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
100	01/16/95	01/18/95	01/30/95	VOMITING	01/17/95	01/17/95	1	1	3	1
				NAUSEA	01/17/95	01/18/95	1	1	3	1
				VOMITING	01/18/95	01/18/95	1	1	3	1
				CRAMPING	01/18/95	01/18/95	1	1	7	4
				CRAMPING	01/18/95	01/19/95	2	1	7	1
				DIARRHEA	01/18/95	01/18/95	2	1	7	1
				NAUSEA	01/18/95	01/18/95	1	1	7	1
				CRAMPING	01/20/95	01/21/95	2	2	7	1
				CRAMPING	01/22/95	01/24/95	2	1	7	1
				NASAL CONGESTION	01/24/95	01/26/95	2	2	1	1
				HEADACHE	01/25/95	01/25/95	2	2	6	1
				HEADACHE	01/28/95	01/29/95	2	2	6	1
				NASAL CONGESTION	01/29/95	01/29/95	2	2	1	1
101	01/16/95	01/18/95	01/30/95	CRAMPS	01/16/95	01/17/95	1	1	3	1
				FUNNY TASTE IN MOUTH	01/17/95	01/17/95	1	1	3	1
				FELT FAINT	01/18/95	01/18/95	2	1	3	1
				CRAMPS	01/18/95	01/18/95	3	2	3	3
				CRAMPING	01/18/95	01/18/95	3	2	7	2
				NAUSEA	01/18/95	01/18/95	2	1	3	1
				CRAMPS	01/19/95	01/19/95	2	2	7	1
				CRAMPS	01/20/95	01/20/95	1	1	7	1
				HEADACHE (SINUS)	01/29/95	01/30/95	2	2	1	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
(Patients with Any Adverse Event)

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
102	01/16/95	01/18/95	01/30/95	BACTERIAL VAGINOSIS		Ongoing	2	1	1	3
				NAUSEA (STOMACHACHE)	01/16/95	01/16/95	2	1	3	1
				VOMITING	01/16/95	01/16/95	1	1	3	1
				VOMITING	01/17/95	01/17/95	2	1	3	1
				CRAMPING	01/18/95	01/18/95	2	2	7	4
				HEADACHE	01/18/95	01/18/95	2	2	6	1
				CRAMPING	01/18/95	01/18/95	3	1	7	1
				FATIGUE	01/18/95	Ongoing	1	1	6	3
				CRAMPING	01/19/95	01/30/95	1	1	7	1
103	01/16/95	01/18/95	01/30/95	BACTERIAL INFECTION		01/18/95	2	2	1	1
				CHLAMYDIA		02/07/95	2	2	1	1
				CRAMPING	01/16/95	01/18/95	1	1	2	1
				HIVES	01/17/95	Ongoing	3	2	1	3
				DIARRHEA	01/17/95	01/17/95	2	1	3	1
				NAUSEA INTERMITTENT	01/18/95	01/25/95	2	1	5	1
				CRAMPING	01/18/95	01/18/95	2	1	7	1
				BODILY BRUISES	01/28/95	01/28/95	2	1	1	1
104	01/17/95	01/19/95	02/08/95	CRAMPS	01/18/95	01/18/95	1	2	3	1
				CRAMPS	01/19/95	01/19/95	2	2	7	4
				CRAMPS	01/20/95	01/20/95	3	2	7	3
				CRAMPS	01/21/95	01/21/95	3	2	7	2
				CRAMPS	01/22/95	01/22/95	2	1	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
105	01/23/95	01/25/95	02/06/95	VOMITING	01/24/95	01/24/95	1	1	3	1
				CRAMPS	01/24/95	01/24/95	1	1	3	1
				NAUSEA	01/24/95	01/24/95	1	1	3	1
				VOMITING	01/25/95	01/25/95	1	1	3	1
				CRAMPS	01/25/95	01/25/95	1	1	7	1
				DIARRHEA	01/25/95	01/25/95	1	1	7	1
				CRAMPS	01/26/95	01/26/95	1	1	3	1
				CRAMPS	01/27/95	01/27/95	2	2	7	1
106	01/23/95	01/25/95	02/06/95	CRAMPING	01/25/95	01/28/95	2	1	7	1
				DIARRHEA	01/25/95	01/25/95	1	1	7	1
				CRAMPING	01/25/95	01/25/95	1	1	7	1
				LEG PAIN	01/27/95	01/28/95	2	1	7	1
107	01/23/95	01/25/95	02/06/95	CRAMPS	01/25/95	01/25/95	1	1	5	1
				BACK PAIN	02/03/95	02/04/95	3	2	6	1
				HEADACHE	02/03/95	02/05/95	2	2	1	1
				ABD PAIN	02/03/95	02/05/95	3	2	1	1
				DIZZINESS	02/03/95	02/05/95	1	1	1	1
				SMELLY BROWN DISCHARGE	02/03/95	02/06/95	2	2	1	1
				HIP PAIN	02/03/95	02/03/95	3	2	1	1
				STOMACH PAIN	02/05/95	02/05/95	3	2	1	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
108	01/23/95	01/25/95	03/05/95	VOMITED	01/23/95	01/23/95	2	1	3	1
				NAUSEA	01/23/95	01/23/95	2	1	3	2
				VOMITED	01/24/95	01/24/95	1	1	3	1
				NAUSEA	01/24/95	01/24/95	1	1	3	3
				CRAMPS	01/24/95	01/24/95	1	1	3	1
				CRAMPS	01/25/95	01/25/95	3	2	7	2
				NAUSEA	01/25/95	01/25/95	1	1	7	1
				CRAMPS	01/25/95	01/27/95	1	1	7	1
109	01/23/95	01/25/95	02/06/95	CRAMPING	01/23/95	01/24/95	1	1	3	1
				VOMITING	01/25/95	01/25/95	2	1	3	1
				CRAMPING	01/25/95	01/26/95	3	2	7	2
				EXCESSIVE BLEEDING	01/25/95	01/25/95	3	1	7	1
				CRAMPING	01/27/95	01/31/95	1	1	7	1
110	01/23/95	01/25/95	02/08/95	VAGINAL INFECTION		01/26/95	2	2	1	1
				CRAMPING	01/23/95	01/24/95	1	1	3	1
				PAIN/TENDERNESS IN HIPS	01/24/95	01/24/95	1	2	2	1
				CRAMPING	01/25/95	01/25/95	2	1	7	1
				CRAMPING/PAIN	01/26/95	01/27/95	3	2	7	2
				CRAMPING/PAIN	01/28/95	01/28/95	2	2	7	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
(Patients with Any Adverse Event)

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
111	01/23/95	01/25/95	02/09/95	CRAMPING	01/24/95	01/24/95	3	2	3	1
				VOMITING	01/25/95	01/25/95	2	2	3	1
				CRAMPING	01/25/95	01/25/95	3	2	5	1
				CRAMPING	01/26/95	01/29/95	2	2	5	1
				NAUSEA	02/07/95	02/07/95	2	1	1	1
				COUGH	02/07/95	02/07/95	2	1	1	1
				FEVER	02/07/95	02/07/95	2	1	1	1
				FEVER	02/09/95	Ongoing	2	2	1	3
				NASAL CONGESTION	02/09/95	Ongoing	2	2	1	3
				COUGH	02/09/95	Ongoing	2	2	1	3
112	01/23/95	01/25/95	02/06/95	HA	01/24/95	01/24/95	2	2	3	1
				CRAMPS	01/25/95	01/26/95	1	1	7	1
113	01/30/95	02/01/95	02/21/95	CRAMPING	01/30/95	02/01/95	1	2	3	1
				CRAMPING	02/01/95	02/02/95	3	2	7	1
				CRAMPING	02/01/95	02/01/95	1	1	7	4
				CRAMPING	02/03/95	02/03/95	1	1	7	1
114	01/30/95		02/15/95	CRAMPING	01/31/95	01/31/95	1	1	3	1
				EXCESSIVE BLEEDING	01/31/95	01/31/95	2	1	3	1
				EXCESSIVE BLEEDING	02/03/95	02/04/95	2	1	3	1
				CRAMPING	02/03/95	02/04/95	2	2	3	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
115	01/30/95	02/01/95	02/14/95	CRAMPS	01/31/95	01/31/95	1	1	3	1
				CRAMPS	02/01/95	02/01/95	1	1	3	1
				NAUSEA	02/01/95	02/01/95	1	1	3	1
				CRAMPS	02/01/95	02/01/95	3	2	7	1
				CRAMPS	02/02/95	02/03/95	2	2	7	1
116	01/30/95	02/01/95	02/14/95	HEADACHE	01/30/95	01/30/95	2	1	2	1
				CRAMPING	02/01/95	02/02/95	3	2	7	1
				SLIGHT DIZZINESS	02/01/95	02/01/95	1	1	2	1
				EXCESSIVE BLEEDING	02/02/95	02/02/95	3	1	7	1
				CRAMPS	02/03/95	02/06/95	1	1	7	1
117	01/30/95	02/01/95	02/14/95	ABDOMINAL PAIN	01/30/95	01/30/95	1	1	3	1
				CRAMPS	01/31/95	01/31/95	2	2	3	1
				CRAMPS	02/01/95	02/01/95	2	2	7	1
				EXCESSIVE BLEEDING	02/01/95	02/01/95	3	1	7	1
				CRAMPS	02/03/95	02/04/95	2	2	7	1
				DIARRHEA	02/04/95	02/04/95	1	1	7	1
				CRAMPS	02/06/95	02/07/95	1	2	7	1
				EXCESSIVE BLEEDING	02/09/95	02/10/95	1	2	7	1
				CRAMPING	02/09/95	02/09/95	1	2	7	1
				HEADACHE	02/10/95	02/12/95	2	2	6	1

[1] Severity: 1=Mild, 2=Moderate, 3=Severe
[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.

Appendix A.1, Table 25 (Continued)
Adverse Events
[Patients with Any Adverse Event]

Center Number: 2

Patient Number	Visit 1 Date	Visit 2 Date	Visit 3 Date	Description	Start Date	Stop Date	Severity [1]	Action [2]	Related [3]	Outcome [4]
118	01/30/95	02/01/95	02/21/95	INSOMNIA	01/30/95	01/30/95	1	1	1	1
				CRAMPS	01/30/95	01/30/95	1	1	1	1
				CRAMPS	02/01/95	02/01/95	2	2	7	1
				EXCESSIVE BLEEDING	02/01/95	02/02/95	3	1	7	1
				CRAMPS	02/02/95	02/02/95	2	1	7	3
				CRAMPS	02/03/95	02/03/95	2	2	7	1
119	01/30/95	02/01/95	02/14/95	CERVICITIS		02/07/95	2	2	1	1
				BACTERIAL INFECTION		02/07/95	2	2	1	1
				CRAMPS	01/31/95	01/31/95	2	2	3	1
				HEADACHE	01/31/95	01/31/95	2	2	1	1
				SWOLLEN (R) ANKLE	01/31/95	01/31/95	2	1	1	1
				CRAMPS	02/01/95	02/02/95	2	2	7	4
				CRAMPS	02/03/95	02/03/95	3	2	7	2
				CRAMPS	02/04/95	02/04/95	2	2	7	1
				CRAMPS	02/05/95	02/06/95	1	1	7	1
120	02/06/95	02/08/95	02/20/95	CRAMPS	02/06/95	02/08/95	2	2	2	1
				NAUSEA (UPSET STOMACH)	02/06/95	02/06/95	1	1	3	1
				CRAMPING	02/08/95	02/08/95	1	1	4	1
				CRAMPING	02/08/95	02/08/95	2	2	7	1
				CRAMPING	02/09/95	02/14/95	2	1	7	1
				RUNNY NOSE	02/10/95	Ongoing	1	1	1	1
				CHEST CONGESTION	02/10/95	Ongoing	1	1	1	1

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[2] Action Taken: 1=None, 2=Drug Therapy, 3=Hospitalization, 4=Other
[3] Study Drug Related: 1=Not Related, 2=Possible w/ Mifepristone, 3=Probable w/ Mifepristone, 4=Possible w/ Misoprostol, 5=Probable w/ Misoprostol, 6=Possible w/ Combination, 7=Probable w/ Combination
[4] Outcome: 1=Recovered, 2=Improved, 3=Unchanged, 4=Worse, 5=Death
[5] Value is unknown.