16.1.3 List of Indpendent Ethics Committees or Institutional Review Boards, Representative Written Information for Subject, and Sample Informed Consent Forms

16.1.3.1 List of Independent Ethics Committee/ Institutional Review Board Members

Independent Investigational Review Board Membership Roster (21 January 2010)

INDEPENDENT INVESTIGATIONAL REVIEW BOARD INC.

The IRB of Choice When the Choice is Yours

IRB MEMBERSHIP ROSTER

PRIMARY MEMBERS	
Frances Conway, RN **CHAIR** (Scientific) *Affiliated* *Member since 2008*	Ms. Conway is a registered nurse with knowledge of regulatory requirements as related to IRB compliance with FDA, DHHS, and EPA regulations.
Julie A. Blasingim, BA, MBA **VICE CHAIR** (Non-Scientific) *Affiliated* *Member since 2009*	Ms. Blasingim comes to the IRB with extensive knowledge of human research protection issues and regulatory compliance. She presents ongoing educational programs and regulatory updates to the IRB members and IIRB staff.
Marcos Rejtman, DO (Scientific) *Unaffiliated* *Member since 2005*	Dr. Rejtman is Board Certified in Family Practice, Geriatric Medicine and Hospice & Palliative Care. Through his experience, Dr. Rejtman is able to evaluate protocols from a scientific perspective with a focus on risks/benefit analysis.
Rabbi Akiva D. Mann, MA (Non-Scientific) *Unaffiliated* *Member since 1997*	Rabbi Mann is the Director of The Institute of Jewish Knowledge and Learning and provides moral and ethical perspectives to the review process.
Edward Wiederhorn (Non-Scientific) *Unaffiliated* *Member since 1995*	Mr. Wiederhorn is a community representative to the IIRB, Inc. He is a member of the American Association of Retired Persons (AARP) and has been involved with Fraternal and Charitable Organizations.
Shari Somerstein, RPh (Scientific) *Affiliated* *Member since 1999*	Ms. Somerstein has extensive experience in clinical pharmacology and the drug development process through analysis of clinical and non-clinical data, with a focus on human research protection.
George J. Garbarino (Non-Scientific) *Unaffiliated* *Member since 2004*	Mr. Garbarino has been an advocate for Labor Union members and brings a wide range of experience in the area of workers' rights.
ALTERNATE MEMBERS *Alternate Members serve as a voting member, when filling the role of an absent voting member. Alternate Scientific Members can serve as a voting alternate member for Frances Conway, but cannot serve as a Chair of the IRB. Alternate Non-Scientific Members can serve as an alternate voting member for Julie Blasingim, but cannot serve as a Vice Chair of the IRB.*	
Ernest Bertha, MD, MBA *(Scientific) *Unaffiliated* *Member since 2009*	Dr. Bertha is a Board Certified Pediatrician specializing in emergency medicine, bringing with him a background of pediatric acute care medicine.
David D. Wells, MD (Scientific) *Unaffiliated* *Member since 1996*	Dr. Wells has served as an Emergency Medicine Department Chairman. He has worked with different ethnic populations, especially migrant workers and brings his sensitivity of the social mores of the underprivileged to the IRB.
Glenn K. Moran, MD, FACOFP (Scientific) *Unaffiliated* *Member since 2004*	Dr. Moran is Board Certified in Family Practice. Through his present practice, he is able to contribute up to date information related to the current medical world. In addition, Dr, Moran is a Professor of Osteopathic Medicine at a local university.
Robert Lettman, Esq (Non-Scientific) *Affiliated* *Member since 2004*	Mr. Lettman is a practicing Attorney providing legal understanding with regard to the rights of research participants.
Levi G. Williams, Esq (Non-Scientific) *Unaffiliated* *Member since 2007*	Mr. Williams is a practicing Attorney with a focus on cultural diversity, including multi-racial and juvenile rights.
Marijke Adams, PharmD, PhD (Scientific) *Unaffiliated* *Member since 2009*	Dr. Adams is an adjunct pharmacology Professor at a local University. She also has extensive experience in pharmaceutical drugs development, protocol development, regulatory requirements, and the conduct of clinical and nonclinical research.
Rev. Pat Alessi (Non-Scientific) *Unaffiliated* *Member since 2010*	Rev. Pat Alessi is an ordained minister serving as an Associate Minister for more than 35 years. Her experience allows her to provide moral and ethical perspectives to research involving humans.

CHANGES FROM PREVIOUS ROSTER (Version: 10/1/09)

Addition of Rev. Pat Alessi, and change in affiliation status for Shari Somerstein, RPh.

Version: 1/21/10

Replaces 10/1/09

Independent Investigational Review Board Membership Roster (1 October 2009)

INDEPENDENT INVESTIGATIONAL REVIEW BOARD INC.
The IRB of Choice When the Choice is Yours

IRB MEMBERSHIP ROSTER

PRIMARY MEMBERS	
Frances Conway, RN **CHAIR** (Scientific) *Affiliated* *Member since 2008*	Ms. Conway is a registered nurse with knowledge of regulatory requirements as related to IRB compliance with FDA, DHHS, and EPA regulations.
Julie A. Blasingim, BA, MBA **VICE CHAIR** (Non-Scientific) *Affiliated* *Member since 2009*	Ms. Blasingim comes to the IRB with extensive knowledge of human research protection issues and regulatory compliance. She presents ongoing educational programs and regulatory updates to the IRB members and IIRB staff.
Marcos Rejtman, DO (Scientific) *Unaffiliated* *Member since 2005*	Dr. Rejtman is Board Certified in Family Practice, Geriatric Medicine and Hospice & Palliative Care. Through his experience, Dr. Rejtman is able to evaluate protocols from a scientific perspective with a focus on risks/benefit analysis.
Rabbi Akiva D. Mann, MA (Non-Scientific) *Unaffiliated* *Member since 1997*	Rabbi Mann is the Director of The Institute of Jewish Knowledge and Learning and provides moral and ethical perspectives to the review process.
Edward Wiederhorn (Non-Scientific) *Unaffiliated* *Member since 1995*	Mr. Wiederhorn is a community representative to the IIRB, Inc. He is a member of the American Association of Retired Persons (AARP) and has been involved with Fraternal and Charitable Organizations.
Shari Somerstein, RPh (Scientific) *Unaffiliated* *Member since 1999*	Ms. Somerstein has extensive experience in clinical pharmacology and the drug development process through analysis of clinical and non-clinical data, with a focus on human research protection.
George J. Garbarino (Non-Scientific) *Unaffiliated* *Member since 2004*	Mr. Garbarino has been an advocate for Labor Union members and brings a wide range of experience in the area of workers' rights.
ALTERNATE MEMBERS *Alternate Members serve as a voting member, when filling the role of an absent voting member. Alternate Scientific Members can serve as a voting alternate member for Frances Conway, but cannot serve as a Chair of the IRB. Alternate Non-Scientific Members can serve as an alternate voting member for Julie Blasingim, but cannot serve as a Vice Chair of the IRB.*	
Ernest Bertha, MD, MBA *(Scientific) *Unaffiliated* *Member since 2009*	Dr. Bertha is a Board Certified Pediatrician specializing in emergency medicine, bringing with him a background of pediatric acute care medicine.
David D. Wells, MD (Scientific) *Unaffiliated* *Member since 1996*	Dr. Wells has served as an Emergency Medicine Department Chairman. He has worked with different ethnic populations, especially migrant workers and brings his sensitivity of the social mores of the underprivileged to the IRB.
Glenn K. Moran, MD, FACOFP (Scientific) *Unaffiliated* *Member since 2004*	Dr. Moran is Board Certified in Family Practice. Through his present practice, he is able to contribute up to date information related to the current medical world. In addition, Dr, Moran is a Professor of Osteopathic Medicine at a local university.
Robert Lettman, Esq (Non-Scientific) *Affiliated* *Member since 2004*	Mr. Lettman is a practicing Attorney providing legal understanding with regard to the rights of research participants.
Levi G. Williams, Esq (Non-Scientific) *Unaffiliated* *Member since 2007*	Mr. Williams is a practicing Attorney with a focus on cultural diversity, including multi-racial and juvenile rights.
Marijke Adams, PharmD, PhD (Scientific) *Unaffiliated* *Member since 2009*	Ms. Adams is an adjunct pharmacology Professor at a local University. She also has extensive experience in pharmaceutical drugs development, protocol development, regulatory requirements, and the conduct of clinical and nonclinical research.

CHANGES FROM PREVIOUS ROSTER (Version: 6/1/09)
Resignation of Kim Lerner as Chair, appointment of Frances Conway, RN as Chair, appointment of Julie Blasingim, BA, MBA as Vice Chair, appointment of Marijke Adams, PharmD, PhD as an alternate IRB Member as well as other minor clarifications.

Independent Investigational Review Board Membership Roster (1 June 2009)

INDEPENDENT INVESTIGATIONAL REVIEW BOARD INC.
The IRB of Choice When the Choice is Yours

IRB MEMBERSHIP ROSTER

PRIMARY MEMBERS	
Kim Lerner, BS, CHAIR (Non-Scientific) *Affiliated* *Member since 1989*	Ms. Lerner is co-founder of the Independent Investigational Review Board, Inc.. Ms. Lerner provides extensive knowledge of regulatory compliance and the research industry. She has incorporated her extensive knowledge of continuous quality improvement into all aspects of the IIRB, Inc.
Frances Conway, RN, VICE CHAIR (Scientific) *Affiliated* *Member since 2008*	Ms. Conway is a registered nurse with knowledge of regulatory requirements as related to IRB compliance with FDA, DHHS, and EPA regulations.
Marcos Rejtman, DO (Scientific) *Unaffiliated* *Member since 2005*	Dr. Rejtman is Board Certified in Family Practice, Geriatric Medicine and Hospice & Palliative Care. Through his experience, Dr. Rejtman is able to evaluate protocols from a scientific perspective with a focus on risks/benefit analysis.
Rabbi Akiva D. Mann, MA (Non-Scientific) *Unaffiliated* *Member since 1997*	Rabbi Mann is the Director of The Institute of Jewish Knowledge and Learning and provides moral and ethical perspectives to the review process.
Edward Wiederhorn (Non-Scientific) *Unaffiliated* *Member since 1995*	Mr. Wiederhorn is a community representative to the IIRB, Inc. He is a member of the American Association of Retired Persons (AARP) and has been involved with Fraternal and Charitable Organizations.
Shari Somerstein, RPh (Scientific) *Unaffiliated* *Member since 1999*	Ms. Somerstein has extensive experience in clinical pharmacology and the drug development process through analysis of clinical and non-clinical data, with a focus on human research protection.
George J. Garbarino (Non-Scientific) *Unaffiliated* *Member since 2004*	Mr. Garbarino has been an advocate for Labor Union members and brings a wide range of experience in the area of workers' rights.
ALTERNATE MEMBERS *Alternate Members serve as a voting member, when filling the role of an absent voting member. Alternate Non-Scientific Members can serve as an alternate voting member for Kim Lerner, but cannot serve as a Chair of the IRB. Alternate Scientific Members can serve as a voting alternate member for Frances Conway, but cannot serve as a Vice Chair of the IRB.*	
Julie A. Blasingim, BA, MBA (Non-Scientific) *Affiliated* *Member since 2009*	Ms. Blasingim comes to the IRB with extensive knowledge of human research protection issues and regulatory compliance. She presents ongoing educational programs and regulatory updates to the IRB members and IIRB staff.
Ernest Bertha, MD, MBA *(Scientific) *Unaffiliated* *Member since 2009*	Dr. Bertha is a Board Certified Pediatrician specializing in emergency medicine, bringing with him a background of pediatric acute care medicine.
David D. Wells, MD (Scientific) *Unaffiliated* *Member since 1996*	Dr. Wells has served as an Emergency Medicine Department Chairman. He has worked with different ethnic populations, especially migrant workers and brings his sensitivity of the social mores of the underprivileged to the IRB.
Glenn K. Moran, MD, FACOFP (Scientific) *Unaffiliated* *Member since 2004*	Dr. Moran is Board Certified in Family Practice. Through his present practice, he is able to contribute up to date information related to the current medical world. In addition, Dr, Moran is a Professor of Osteopathic Medicine at a local university.
Robert Lettman, Esq (Non-Scientific) *Affiliated* *Member since 2004*	Mr. Lettman is a practicing Attorney providing legal understanding with regard to the rights of research participants.
Levi G. Williams, Esq (Non-Scientific) *Unaffiliated* *Member since 2007*	Levi Williams is a practicing Attorney with a focus on cultural diversity, including multi-racial and juvenile rights.

CHANGES FROM PREVIOUS ROSTER (Version: 1/6/09)

Removal of Anita McSharry, RN as Vice Chair, addition of Frances Conway, RN as Vice Chair, addition of Julie Blasingim, BA, MBA as alternate IRB Member, addition of Ernest Bertha, MD, MBA as alternate IRB Member as well as other minor clarifications.

Independent Investigational Review Board Membership Roster (6 January 2009)

INDEPENDENT INVESTIGATIONAL REVIEW BOARD INC.

IRB MEMBERSHIP ROSTER

Name	Earned Degree	Repre-sentative Capacity	Indications of Experience	Relation-ship	Affiliation Status	IRB Posi-tion	Member-ship Status
Kim Lerner (Non-Scientific)	Bachelor of Science (BS)	General	Ms. Lerner is co-founder of the Independent Investigational Review Board and has acted as Chairman for the past 18 years. She has transformed her experience as Director of an IRB at a large teaching hospital into directing a large and diverse independent IRB. Her experience serving as the Director of a Hospital Quality Assurance Program provides the foundation for implementation of the Independent IRB's continuous quality improvement and regulatory compliance programs.	Board of Directors, Secretary/ Treasurer of IIRB, Inc.	Affiliated	Chair	Voting Member
Anita McSharry (Scientific)	Registered Nurse (RN)	General	Ms. McSharry is co-founder of the Independent Investigational Review Board and has acted as President for the past 18 years. She has extensive knowledge of principles of medical research, regulatory compliance and clinical safety. Her previous experience as Clinic Director with the University of Miami, Department of Clinical Pharmacology enables her to view the scientific issues related to research through the experience of the researcher in light of the regulatory compliance requirements.	Board of Directors, President of IIRB, Inc., Institutional Official	Affiliated	Vice Chair	Voting Member
Marcos Rejtman (Scientific)	Doctor of Osteopathic Medicine DO	Geriatrics, Spanish Population	Dr. Rejtman is Board Certified in Family Practice, Geriatric Medicine and Hospice & Palliative Medicine and is presently the Medical and Team Director for VITAS Innovative Health Care (Hospice) and provides in-hospital patient management for a multi-specialty group. He also has recent experience in Emergency Department Medicine. He maintains privileges at local hospitals and is active in the areas of Medical Quality Assurance and Peer Review and other community organizations. He is English-Spanish bilingual.	IRB Member Consultant	Unaffiliated	None	Voting Member
Rabbi Akiva D. Mann (Non-Scientific)	Master of Art (MA)	Ethical	Rabbi Mann is the Director of The Institute of Jewish Knowledge and Learning, an educational institution of adult learning. He has been a member of the Independent IRB for 11 years. Rabbi Mann brings skills in analyzing moral and ethical issues and refined judgment in understanding problems related to research and the rights and needs of individuals participating in research studies. He has served on Mayoral Commissions addressing the issues of Medical Ethics and Geriatric Care, as well as having served on Hospital Ethics Committees.	IRB Member Consultant	Unaffiliated	None	Voting Member
Edward Wieder-horn (Non-Scientific)	No Degree	Elderly population	Mr. Wiederhorn is the community representative to the IIRB, Inc. and is a member of the American Association of Retired Persons (AARP). Mr. Wiederhorn has longstanding experience as a Civic Activist and has been a member of Fraternal and Charitable Organizations. Present he is actively involved in support of the City of Hope. Mr. Wiederhorn has been a member for 13 years and provides a broad perspective and world experience relating to assessment of research issues.	IRB Member Consultant	Unaffiliated	None	Voting Member
Shari Somerstein (Scientific)	Bachelor of Science (BS), Registered Pharmacist (RPh)	Pharmaceu-tical Drug Preparation	Ms. Somerstein has served as a member of the Independent IRB for more than 8 years and has extensive experience in interpretation and assessment of clinical research findings and study design. She brings extensive clinical pharmacy experience from a Hospital setting and in the community. She has broad administrative experience in IRB activities including, protocol review, assessment of adverse drug experiences and informed consent form development.	IRB Member Consultant	Unaffiliated	None	Voting Member

George J. Garbarino (Non-Scientific)	None	Worker's Rights	Mr. Garbarino has been an advocate for Labor Union members and brings a wide range of experience in the area of worker's rights and contract negotiations. He is the Business Manager of the Tile, Marble and Stone Workers Local 121 and is associated with the School Board of Broward County. Mr. Garbarino has served as a member of the Independent Investigational Review Board for 4 years.	IRB Member Consultant	Unaffiliated	None	Voting Member
Frances Conway RN (Scientific)	Registered Nurse (RN)	Elderly population	Ms. Conway has served as a registered nurse in multi-specialty fields including acute care facilities in community hospitals, geriatric facilities, and home health care. Presently she serves as the Chief Operating Officer of the IIRB, Inc. and is knowledgeable of FDA, DHHS, and EPA regulations. Ms. Conway also serves as an advisor to the Institutional Official and assists in the development and implementation of the Human Research Protection Program (HRPP) including outreach programs for human research participants.	IIRB, Inc. Staff Member (Chief Operating Officer)	Affiliated	None	Voting Member
David D. Wells* (Scientific)	Medical Doctor (MD)	Financially Disadv-antaged	Dr. Wells graduated from the University of Havana, is English-Spanish bilingual and brings this international experience to the IRB. He has been a member of the Independent IRB for 12 years. He has served as the Emergency Medicine Department Chairman at a local hospital, has health care Clinic experience working with financially disadvantaged patients and is presently volunteering as a Family Practice Physician serving migrant farm workers. This hands-on experience enables him to clearly assess overall research risks and benefits and understand vulnerable population issues.	IRB Member Consultant	Unaffiliated	None	Alternate for Marcos Rejtman, DO, Shari Somerstein, RPh, Anita McSharry RN**, and Frances Conway, RN
Glenn K. Moran* (Scientific)	Doctor of Osteopathic Medicine DO, Fellow of the American College of Osteopathic Family Physicians, FACOFP	General Medical	Dr. Moran is Board Certified in Family Practice and is presently in private practice and has been a member of the Independent Investigational Review Board for 4 years. He maintains privileges at local hospitals and is active in the areas of Medical Quality Assurance and Peer Review and other community organizations. He participates in numerous Advisory capacities in the medical and educational field and is an Assistant Clinical Professor at Nova Southeastern College of Osteopathic Medicine. He is familiar with current medical research requirements.	IRB Member Consultant also serves as a Board of Directors Member	Unaffiliated	None	Alternate for Marcos Rejtman, DO, Shari Somerstein, RPh, Anita McSharry RN**, and Frances Conway, RN
Robert Lettman* (Non-Scientific)	Esquire (Esq)	Legal rights	Mr. Lettman is a practicing Attorney in South Florida with extensive experience in civil litigation and serves as a resource in the consideration of legal aspects of the informed consent process. He has particular strengths in the areas of confidentiality and protection of the rights of the individual. He has been a member of the Board for 4 years. As a member of the community for 30 years he brings insights and knowledge of the needs of the community.	IRB Member Consultant also serves as IIRB, Inc. Legal Counsel	Affiliated	None	Alternate for Rabbi Akiva D. Mann, Edward Wiederhorn, George J. Garbarino, or Kim Lerner**
Levi G. Williams* (Non-Scientific)	Esquire (Esq)	Legal rights	Levi Williams is a practicing attorney that brings to the Board a background of "diversity issue leadership" within the community. Through his legal practice and volunteer work on many different community-interest Boards and his experience on the School Board he brings expertise in understanding matters related to economic and racial issues. He has been a member of the Independent Investigational Review Board for 1 year. He also has experience with "juvenile rights issues" and brings insight into the protective measures that may be warranted for children participating in research.	IRB Member Consultant	Unaffiliated	None	Alternate for Rabbi Akiva D. Mann, Edward Wiederhorn, George J. Garbarino, or Kim Lerner**

* Serves as a voting member, when filling the role of an absent voting member rather than serving as an alternate.

** Alternate non-scientific members can serve as an alternate voting member for Kim Lerner, but cannot serve as a Chair of the IRB. Alternate scientific members can serve as an voting alternate member for Anita McSharry, but cannot serve as a Vice Chair of the IRB.

NO CHANGES FROM PREVIOUS ROSTER (Version: 9/3/08)

Independent Investigational Review Board Membership Roster (3 September 2008)

INDEPENDENT INVESTIGATIONAL REVIEW BOARD INC.

IRB MEMBERSHIP ROSTER

Name	Earned Degree	Representative Capacity	Indications of Experience	Relationship	Affiliation Status	IRB Position	Membership Status
Kim Lerner (Non-Scientific)	Bachelor of Science (BS)	General	Ms. Lerner is co-founder of the Independent Investigational Review Board and has acted as Chairman for the past 18 years. She has transformed her experience as Director of an IRB at a large teaching hospital into directing a large and diverse independent IRB. Her experience serving as the Director of a Hospital Quality Assurance Program provides the foundation for implementation of the Independent IRB's continuous quality improvement and regulatory compliance programs.	Board of Directors, Secretary/ Treasurer of IIRB, Inc.	Affiliated	Chair	Voting Member
Anita McSharry (Scientific)	Registered Nurse (RN)	General	Ms. McSharry is co-founder of the Independent Investigational Review Board and has acted as President for the past 18 years. She has extensive knowledge of principles of medical research, regulatory compliance and clinical safety. Her previous experience as Clinic Director with the University of Miami, Department of Clinical Pharmacology enables her to view the scientific issues related to research through the experience of the researcher in light of the regulatory compliance requirements.	Board of Directors, President of IIRB, Inc., Institutional Official	Affiliated	Vice Chair	Voting Member
Marcos Rejtman (Scientific)	Doctor of Osteopathic Medicine DO	Geriatrics, Spanish Population	Dr. Rejtman is Board Certified in Family Practice, Geriatric Medicine and Hospice & Palliative Medicine and is presently the Medical and Team Director for VITAS Innovative Health Care (Hospice) and provides in-hospital patient management for a multi-specialty group. He also has recent experience in Emergency Department Medicine. He maintains privileges at local hospitals and is active in the areas of Medical Quality Assurance and Peer Review and other community organizations. He is English-Spanish bilingual.	IRB Member Consultant	Unaffiliated	None	Voting Member
Rabbi Akiva D. Mann (Non-Scientific)	Master of Art (MA)	Ethical	Rabbi Mann is the Director of The Institute of Jewish Knowledge and Learning, an educational institution of adult learning. He has been a member of the Independent IRB for 11 years. Rabbi Mann brings skills in analyzing moral and ethical issues and refined judgment in understanding problems related to research and the rights and needs of individuals participating in research studies. He has served on Mayoral Commissions addressing the issues of Medical Ethics and Geriatric Care, as well as having served on Hospital Ethics Committees.	IRB Member Consultant	Unaffiliated	None	Voting Member
Edward Wiederhorn (Non-Scientific)	No Degree	Elderly population	Mr. Wiederhorn is the community representative to the IIRB, Inc. and is a member of the American Association of Retired Persons (AARP). Mr. Wiederhorn has longstanding experience as a Civic Activist and has been a member of Fraternal and Charitable Organizations. Present he is actively involved in support of the City of Hope. Mr. Wiederhorn has been a member for 13 years and provides a broad perspective and world experience relating to assessment of research issues.	IRB Member Consultant	Unaffiliated	None	Voting Member
Shari Somerstein (Scientific)	Bachelor of Science (BS), Registered Pharmacist (RPh)	Pharmaceutical Drug Preparation	Ms. Somerstein has served as a member of the Independent IRB for more than 8 years and has extensive experience in interpretation and assessment of clinical research findings and study design. She brings extensive clinical pharmacy experience from a Hospital setting and in the community. She has broad administrative experience in IRB activities including, protocol review, assessment of adverse drug experiences and informed consent form development.	IRB Member Consultant	Unaffiliated	None	Voting Member

George J. Garbarino (Non-Scientific)	None	Worker's Rights	Mr. Garbarino has been an advocate for Labor Union members and brings a wide range of experience in the area of worker's rights and contract negotiations. He is the Business Manager of the Tile, Marble and Stone Workers Local 121 and is associated with the School Board of Broward County. Mr. Garbarino has served as a member of the Independent Investigational Review Board for 4 years.	IRB Member Consultant	Unaffiliated	None	Voting Member
Frances Conway RN (Scientific)	Registered Nurse (RN)	Elderly population	Ms. Conway has served as a registered nurse in multi-specialty fields including acute care facilities in community hospitals, geriatric facilities, and home health care. Presently she serves as the Chief Operating Officer of the IIRB, Inc. and is knowledgeable of FDA, DHHS, and EPA regulations. Ms. Conway also serves as an advisor to the Institutional Official and assists in the development and implementation of the Human Research Protection Program (HRPP) including outreach programs for human research participants.	IIRB, Inc. Staff Member (Chief Operating Officer)	Affiliated	None	Voting Member
David D. Wells* (Scientific)	Medical Doctor (MD)	Financially Disadv-antaged	Dr. Wells graduated from the University of Havana, is English-Spanish bilingual and brings this international experience to the IRB. He has been a member of the Independent IRB for 12 years. He has served as the Emergency Medicine Department Chairman at a local hospital, has health care Clinic experience working with financially disadvantaged patients and is presently volunteering as a Family Practice Physician serving migrant farm workers. This hands-on experience enables him to clearly assess overall research risks and benefits and understand vulnerable population issues.	IRB Member Consultant	Unaffiliated	None	Alternate for Marcos Rejtman, DO, Shari Somerstein, RPh, Anita McSharry RN**, and Frances Conway, RN
Glenn K. Moran* (Scientific)	Doctor of Osteopathic Medicine DO, Fellow of the American College of Osteopathic Family Physicians, FACOFP	General Medical	Dr. Moran is Board Certified in Family Practice and is presently in private practice and has been a member of the Independent Investigational Review Board for 4 years. He maintains privileges at local hospitals and is active in the areas of Medical Quality Assurance and Peer Review and other community organizations. He participates in numerous Advisory capacities in the medical and educational field and is an Assistant Clinical Professor at Nova Southeastern College of Osteopathic Medicine. He is familiar with current medical research requirements.	IRB Member Consultant also serves as a Board of Directors Member	Unaffiliated	None	Alternate for Marcos Rejtman, DO, Shari Somerstein, RPh, Anita McSharry RN**, and Frances Conway, RN
Robert Lettman* (Non-Scientific)	Esquire (Esq)	Legal rights	Mr. Lettman is a practicing Attorney in South Florida with extensive experience in civil litigation and serves as a resource in the consideration of legal aspects of the informed consent process. He has particular strengths in the areas of confidentiality and protection of the rights of the individual. He has been a member of the Board for 4 years. As a member of the community for 30 years he brings insights and knowledge of the needs of the community.	IRB Member Consultant also serves as IIRB, Inc. Legal Counsel	Affiliated	None	Alternate for Rabbi Akiva D. Mann, Edward Wiederhorn, George J. Garbarino, or Kim Lerner**
Levi G. Williams* (Non-Scientific)	Esquire (Esq)	Legal rights	Levi Williams is a practicing attorney that brings to the Board a background of "diversity issue leadership" within the community. Through his legal practice and volunteer work on many different community-interest Boards and his experience on the School Board he brings expertise in understanding matters related to economic and racial issues. He has been a member of the Independent Investigational Review Board for 1 year. He also has experience with "juvenile rights issues" and brings insight into the protective measures that may be warranted for children participating in research.	IRB Member Consultant	Unaffiliated	None	Alternate for Rabbi Akiva D. Mann, Edward Wiederhorn, George J. Garbarino, or Kim Lerner**

* Serves as a voting member, when filling the role of an absent voting member rather than serving as an alternate.

** Alternate non-scientific members can serve as an alternate voting member for Kim Lerner, but cannot serve as a Chair of the IRB. Alternate scientific members can serve as an voting alternate member for Anita McSharry, but cannot serve as a Vice Chair of the IRB.

16.1.3.2 Sample Volunteer Information and Consent Form

Sample Volunteer Information and Consent Form - Daytona Beach (13 April 2009)

INFORMED CONSENT AUTHORIZATION TO PARTICIPATE IN A CLINICAL INVESTIGATION

Title: (Protocol #: SM 08-01) A Controlled Study of the Ability of a Traditional Swedish Smokeless Tobacco Product ("Snus") to Increase the Quit Rate Among Cigarette Smokers Who Wish to Stop Smoking

Principal Investigator: H. Frank Farmer Jr. MD, PhD, CPI
(Main Study Doctor)

Site of Investigation: Covance CRU, Inc
1900 Mason Ave Suite 140
Daytona Beach, FL 32117

24 hour Telephone #: (386) 366-6400

Sponsor: Swedish Match AB

Participant's Name:_____

You are being asked to participate in a tobacco-switching research study because you currently smoke cigarettes and desire to stop smoking. Your decision to participate in this study is voluntary. If you decide to participate in the study and then change your mind, you can leave the study at any time. However, before you give your consent to be a volunteer, we want you to read the following and ask as many questions as necessary to be sure that you understand what your participation would involve.

Covance Clinical Research Unit Inc. is paid to test investigational products. The study doctors in this study work for Covance, but do not have a financial interest in the outcome of this study

NATURE AND PURPOSE OF THE STUDY

Snus is a smokeless tobacco product made from ground tobacco leaves, water, and food-allowed additives in a paper sachet (packet) that is placed under the upper lip. The placement of the Snus under the upper lip means that there is no need to spit as in other oral tobacco products. Snus is commonly used in Sweden as an alternative to smoking tobacco.

The purpose of this study is to examine if the use of Snus compared to placebo (inactive ingredients manufactured to appear the same as Snus) can increase the quit rate among cigarette smokers who wish to stop smoking. Withdrawal symptoms will be examined and tobacco dependence will be measured. The safety of Snus compared to placebo will be examined. Blood samples will be collected to study breakdown products of nicotine and biological indicators related to tobacco use. This study is not intended to eliminate your tobacco dependence.

APPROVED BY
Independent IRB
Corrected Document – Dated 4/13/09
Signature 3/16/09 Date

Initials: _____
Date: _____

RESEARCH PARTICIPANT SELECTION

You have been offered an opportunity to participate in this research study because you are a male or female between the ages of 25 and 65 years of age, (inclusive) who has smoked at least 10 cigarettes a day for at least one year and desires to quit smoking. You must otherwise be healthy.

If you are a woman, you must not be pregnant or breast feeding. Women of childbearing potential must have been practicing one of the following methods of birth control for at least one month prior to the start of the study and agree to continue practicing it during the study: hormonal contraceptives, intrauterine device (IUD), spermicide and barrier (i.e., condom, diaphragm or cervical cap with spermicidal foam, gel, film or suppository), spouse/partner sterility; or is practicing abstinence and agrees to continue abstinence or to start an acceptable method of contraception from the above list if sexual activity starts.

It is important that you answer all of the screening questions completely. You must disclose all past and present diseases, allergies and all medications that you are taking, including prescription and non prescription drugs.

Approximately 250 volunteers will be enrolled in this multi site research study.

STUDY DURATION

The duration of your participation in this study is approximately 30 weeks including the screening visit. This study requires 6 outpatient clinic visits (screening, baseline, Weeks 6, 10, 16 and 28) and 8 telephone contacts (Weeks 1, 2, 3, 4, 8, 13, 20 and 24).

STUDY DESIGN

The study consists of four phases: Screening (up to 2 weeks), Study Product Test Period (4 weeks), Intervention Phase (approximately 12 weeks), and a Follow-up Phase (approximately 12 weeks). If you are interested, you will be invited to the clinic to attend an Information Session and Screening visit to determine if you are eligible to participate. During the Baseline visit, you will be randomly (by chance) assigned to receive either Snus or placebo. You will have an equal chance of receiving either Snus or placebo. You will not have a choice as to whether you receive Snus or placebo and neither you nor the study doctor will know which of the study products you are receiving, however, this information can be made available if medically necessary. Over the next 4 weeks, you will become familiar with the product and will try to refrain from cigarettes by using this product when you feel the urge to smoke. The Snus/placebo packet is to be placed under the upper lip and may be held for up to 60 minutes. You will be instructed to use the Snus/placebo when you feel the urge to smoke. If after 15 to 20 minutes of using this product you still feel the urge to smoke, you may do so provided that you remove the Snus/placebo from your mouth. You will be encouraged to gradually substitute as many cigarettes with Snus as possible and to refrain from all cigarettes at the latest by the first day of Week 5. You will use the study product for a total of 12 weeks (study product will be discontinued at the Week 16 visit). You will be asked to what extent you have replaced cigarettes with the study product and your breath will be analyzed for

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Signature
3/16/09
Date

Initials: _____
Date: _____

carbon monoxide (CO), a gas that is found in the breath of smokers. You will receive an educational booklet on the hazards of smoking and will be provided brief counseling at each visit. After the interventional phase, your progress will be followed for an additional 12 weeks.

The Snus/placebo products come in two sizes, a 1 gram size (typically replaces one cigarette) and a 0.5 gram size. You will be encouraged to use at least five 1 gram Snus/placebo sachets per day (or ten sachets if you chose the 0.5 gram sachet). The recommended maximum number of 1 gram sachets per day is 24. However, this number may be increased in heavy smokers (15-20 cigarettes per day) who try to replace all cigarettes with study product.

The Snus/placebo study product is for your use only and is not to be given to anyone else. The Snus/placebo study product should be kept refrigerated. The Snus/placebo study product must be kept out of the reach of children and those of limited mental capacity. Snus will not be provided to you as part of the trial after Week 16 of the Study.

SCREENING

The Screening Phase will consist of an Information Session and Screening Visit (which may be scheduled consecutively at one session at the study doctor's discretion). During the Information Session, you will receive information on the health risks associated with a range of nicotine products including: cigarettes, non-Snus smokeless tobacco, Snus, and nicotine replacement therapy. Possible alternatives to the use of Snus will be described. The effects of nicotine on the body and an account will be given of experience with Snus, including potential health risks associated with different smokeless tobacco products.

At the Screening Visit you will sign this informed consent form after all of your questions have been answered and if you are willing to participate in this study. A complete medical history will be recorded. This will include your history of smoking (i.e., at what age you started to smoke, average number of cigarettes smoked per day during the past year, history of quit attempts, your desire to quit smoking, history of nicotine replacement therapy and/or other drugs or aids used in attempts to quit smoking, history of previous smokeless tobacco use). A physical examination including the inside of your mouth, measurement of your vital signs (blood pressure, heart rate, breathing rate and temperature), and height and weight will be performed. An ECG will be performed. Blood and urine samples will be collected for routine laboratory tests including a screening for drugs of abuse. Women who are able to have children will have a pregnancy test. Women between the ages of 45 and 55 will have a Follicular Stimulating Hormone (FSH) test to verify post-menopausal status. You will receive educational materials on smoking cessation from the National Cancer Institute's "Cleaning the Air" booklet and brief counseling (approximately 10 minutes).

You will be permitted to participate in the study at the discretion of the study doctor if the results of the study screening laboratory tests and other assessments are satisfactory. Screening procedures may need to be repeated in order to qualify for this study. You

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Signature 3/16/09 Date

Initials: _____
Date: _____

will be advised of the study restrictions and when to report to the clinic to begin the study. You may be considered an alternate for this study until such time that you have received study product.

STUDY PROCEDURES

Study Product test Period (Week 1 through Week 4)

Baseline Visit

You will return to the study clinic within 2 weeks of the Screening Visit. At this visit your eligibility to participate in this study will be reviewed. You will exhale into a device that measures the amount of carbon monoxide (CO) in your breath (CO exhaled air test). Blood samples will be collected for analysis of nicotine metabolites and biomarkers of exposure and/or disease related to tobacco use. You will complete two questionnaires related to your nicotine dependence and symptoms of nicotine withdrawal. After a brief counseling session, you will receive a study diary and study product, either Snus or placebo. In the diary you will record the number and size of the study product that you used and the number of cigarettes that you smoked daily. You should gradually decrease the number of cigarettes that you smoke through the use of the study product.

Week 1 through 4

A study staff member will contact you weekly by phone to review your smoking status, use of the study product, and brief behavioral counseling. You will also be asked how you are feeling. You continue to complete your diary during this portion of the study.

Intervention Phase (Week 5 through Week 16)

Throughout the Intervention Phase you will complete clinic visits and telephone contacts. Telephone contacts will occur at Weeks 8 and 13 and will include a review of your smoking status, use of the study product, how you feel, and brief behavioral counseling.

Clinic Visits (Week 6 and Week 10)

At these visits the following procedures will be performed:

- Your vital signs and weight will be measured
- CO exhaled air test
- Blood samples will be collected for biomarker blood tests (Week 6 only)
- You will complete a questionnaire to evaluate any symptoms of nicotine withdrawal that you might have
- You will receive brief behavioral counseling
- You will receive more study product
- You will be asked how you are feeling
- You will be asked if you are still smoking
- Your diary will be reviewed and you will receive a new diary.

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Signature 3/16/09 Date

Initials: _____
Date: _____

Clinic Visit (Week 16)
At this visit the following procedures will be performed:

- Your vital signs and weight will be measured
- A physical examination will be performed
- An examination of your mouth will be performed
- CO exhaled air test
- You will complete a questionnaire to determine your nicotine dependence
- You will complete a questionnaire to evaluate any symptoms of nicotine withdrawal that you might have
- Blood samples will be collected for biomarker tests
- You will receive brief behavioral counseling
- You will be asked if you are still smoking
- You will be asked how you are feeling
- Your diary will be reviewed for information regarding study product use and compliance.

You will not receive any more study product after this study visit.

Upon completion of the trial, if you have been successful in quitting cigarette smoking, but still require nicotine replacement, it is preferred that you switch to another smokeless tobacco product or nicotine replacement product, such as Nicoderm or Nicorette, rather than begin cigarette smoking again.

If you choose to discontinue your participation in this study prior to Week 16, you will be asked to undergo the procedures outlined above.

Follow-up Phase (Week 17 through Week 28)
Telephone contacts will occur at Weeks 20 and 24 and will include a review of your smoking status and brief behavioral counseling. You will also be asked how you are feeling.

Final Clinic Visit (Week 28)
The following procedures will be performed at this visit:

- Physical examination
- Examination of your mouth
- Your vital signs and weight will be measured
- CO exhaled air test
- You will complete a questionnaire to determine your nicotine dependence
- You will complete a questionnaire to evaluate any symptoms of nicotine withdrawal that you might have
- Blood samples will be collected for biomarker tests
- You will receive brief behavioral counseling

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Signature 3/16/09 Date

Initials: _____
Date: _____

- You will be asked if you are still smoking
- You will be asked how you are feeling to assess for adverse events
- You will be asked if you have used over-the counter nicotine replacement therapy, smoking cessation services, smokeless tobacco, or smoking products other than cigarettes since week 16.

If you discontinue your participation in this study after Week 16 but prior to Week 28, you will be asked to undergo the procedures outlined above.

If you should develop a visible side effect, such as a skin rash, we may need to take pictures of it for the study records.
The study doctor may require longer observation in the clinic or additional laboratory testing based on the effects of the study product or the results of the laboratory tests as necessary.

Withdrawal Procedures
If you withdraw early from the study, for any reason, you will be asked to complete the lab testing and discharge procedures outlined in the Week 16 or Week 28 sections listed above as applicable.

RESTRICTIONS

MAY I HAVE...?

- Tobacco or Nicotine-Containing Products: You may continue to use your usual brand of cigarettes according to the study design, however, you may not use any other tobacco or nicotine-containing products throughout the study including: pipes, cigarillos, snuff, and chewing tobacco. Over-the-counter nicotine replacement products are prohibited during the study.

- Drugs for smoking cessation: You must not have used any smoking cessation drugs (i.e., Wellbutrin®, Chantix®) for at least 3 months prior to the start of the study.

- Other Medications: You may use other medications with the knowledge and approval of the study doctor.

Blood Sampling
Blood samples will be taken approximately 5 times throughout the course of the study, (including screening and 6 outpatient clinic visits). Approximately 230 mL of blood, (somewhat less than 1 cup), will be drawn throughout the study. Additional blood samples may be required if any of your lab values are abnormal. It is possible that more than one attempt to obtain a blood sample may be necessary.

For comparison, a standard blood donation at a blood collection center, once in any 56-day period, is about 2 cups of blood. Additional blood samples may be drawn during the

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Independent IRB
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Signature 3/16/09 Date

Initials: _____
Date: _____

study if the study doctor considers it necessary for monitoring your health.

Research Participant Responsibilities
As a research participant you will be asked to complete the study procedures for this study, come to the study clinic for all of your scheduled visits, follow the instructions listed in this informed consent form, and notify the study doctor if any information regarding your health or availability to participate in this study changes.

STUDY DOCTOR AVAILABILITY
In the event of any type of medical emergency, the study doctor will be on call and available, throughout the study.

RISKS AND DISCOMFORTS
There may be risks to you if you participate in this study. According to the Surgeon General and other public health authorities, all tobacco products carry significant risks. There may also be social and/or personal adjustments to switching products or quitting.

Tobacco-burning cigarettes are required by law to carry one of four warning labels. The four warning labels for these products are:

•SURGEON GENERAL'S WARNING: Smoking Causes Lung Cancer, Heart Disease, Emphysema, and May Complicate Pregnancy.
•SURGEON GENERAL'S WARNING: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health.
•SURGEON GENERAL'S WARNING: Smoking by Pregnant Women May Result in Fetal Injury, Premature Birth, and Low Birth Weight.
•SURGEON GENERAL'S WARNING: Cigarette Smoke Contains Carbon Monoxide
.

Oral tobacco products: Snus is an oral tobacco product and is required to carry one of three warnings:
• WARNING: This product may cause mouth cancer.
• WARNING: This product may cause gum disease and tooth loss.
• WARNING: This product is not a safe alternative to cigarettes.

The use of Snus has been associated with oral lesions. The use of Snus may increase your risk of cardiovascular disease including heart attack.

Nicotine Overdose
It is possible that you may experience symptoms of nicotine overdose with excessive use of the Snus particularly if you are still smoking. Typical symptoms include nausea, vomiting, diarrhea, stomach pain, cold sweat, problems with hearing or vision, rapid or uneven heartbeats, and chest pain. In its most severe form nicotine overdose can lead to seizures and death.

Effects of Quitting Smoking
Generally, any risks of smoking cessation are far outweighed by the benefits.

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Signature 3/16/09 Date

Initials: _____
Date: _____

Nevertheless, it is reasonable to prepare for the discomforts of stopping smoking:

- Symptoms of withdrawal are common as patients attempt to stop smoking. Withdrawal symptoms can include insomnia, irritability, frustration or anger, anxiety, difficulty concentrating, restlessness, a decreased heart rate and an intense craving for cigarettes.

- Some people who stop smoking experience depression; this can be severe enough that it requires counseling or antidepressant medication. Symptoms of sleeplessness, emotional irritability, sadness, inattention, or other signs of depression should be discussed with the Study Doctor or study staff.

- Weight gain can occur with smoking cessation because people tend to eat more after quitting. The average weight gain is eight to 10 pounds. An exercise program and dieting can minimize weight gain. The benefits of quitting smoking are much greater than the risk of gaining weight.

Study Procedure Risk

During the collection of blood samples, you may experience pain and/or bruising at the insertion site of the needle. Although rare, localized clot formation and infections may occur. Lightheadedness and/or fainting may also occur during or shortly after the blood draw.

UNKNOWN/UNFORESEEABLE RISKS

In addition to the risks listed above, there may be some unknown or infrequent and unforeseeable risks associated with the use of this study product, including allergic reaction or interaction with medications. You will be informed in a timely manner both verbally and in writing of any new information, findings or changes to the way the research will be performed that might influence your willingness to continue your participation in this study.

RISKS TO THE UNBORN

Pregnancy/Fetal Risks: The Surgeon General's warnings for cigarette smoking state that smoking by pregnant women may complicate pregnancy and may result in fetal injury, premature birth, low birth weight, and therefore **may be hazardous.** The use of Snus was associated with increased risk of preterm delivery and preeclampsia (a dangerous and potentially fatal complication of pregnancy).

If you think that you have become pregnant during the study it is important that you inform the study doctor immediately. If you become pregnant or think that you may be pregnant, you will be removed from the study and the study doctor will refer you to seek obstetric care, the cost of which will be your responsibility. The study doctor may request to track your pregnancy and will report the pregnancy and outcome to the Sponsor and the IRB.

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Independent IRB
Corrected Document – Dated 4/13/09
Signature 3/16/09 Date

Initials: _____
Date: _____

BIRTH CONTROL REQUIREMENTS

Female: Women of childbearing potential must have been practicing one of the following methods of birth control for at least one month prior to the start of the study and agree to continue practicing it during the study: hormonal contraceptives, intrauterine device (IUD), spermicide and barrier (i.e., condom, diaphragm or cervical cap with spermicidal foam, gel, film or suppository), spouse/partner sterility; or is practicing abstinence and agrees to continue abstinence or to start an acceptable method of contraception from the above list if sexual activity starts.

Women that smoke and use hormonal contraceptives (pills, patches, etc.) are at increased risk of blood clots.

BENEFITS

Your participation in this study may help to stop smoking but there is no guarantee that it will decrease your dependence on nicotine.

Participation in this study is purely for research purposes, and participation in this study will not improve your health or treat any medical problem you may have.

You may benefit by having physical examinations. The results of laboratory tests done at the screening visit will be made available to you. However, if you test positive for any unauthorized drugs or alcohol, all the tests may not be completed.

COST

There is no cost for participating in this research study. The study sponsor pays all the study costs.

PAYMENT FOR BEING IN THE STUDY

You will be paid for taking part in this study as outlined below. This is to compensate you for your time and travel. Each portion of the study has a monetary value assigned to it, which accumulates as you participate in this study.

Payment Schedule

Screening Visit	$0.00
Outpatient Clinic Visits $125.00 x 5 visits	$625.00
Telephone contacts $50.00 x 8 contacts	$400.00
TOTAL	$1,025.00

Total compensation for study completion will be $1,025.00. If you choose to withdraw from the study, you will receive payment only for the days that you have completed as outlined above. If it is necessary for you to return to the clinic for additional safety follow up visits, you will be paid $50.00 for each completed visit.

All research participants will be paid within 14 business days of the completion of their participation in the study depending on the number of visits they completed.

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Independent IRB
Corrected Document – Dated 4/13/09
Signature 3/16/09 Date

Initials: _____
Date: _____

In agreeing to participate in this study, you will be acting as an independent contractor, not as an employee of Covance Clinical Research Unit, Inc. Because payments made to you for participating in this study will be reported to the IRS as income, you are required to provide your social security number as required by law. No deductions for any state or federal withholding or any other similar taxes will be made. It is the responsibility of the participant to report this compensation on state and federal tax returns and for the payment of any taxes that are due on this compensation.

The Internal Revenue Service (IRS) requires Covance to deduct 30% from the final payment when participants are foreign nationals who do not have a Social Security or Tax identification number.

TREATMENT ALTERNATIVE

You do not have to participate in this study in order to quit smoking. There are several FDA approved over-the-counter and prescription medications that assist people to quit smoking. Some of these medications include: Nicotine Replacement Therapy (i.e., nicotine gum, lozenges and patches) which can be obtained over-the-counter and prescription medications like Wellbutrin® and Chantix®.

RIGHT TO WITHDRAW OR REMOVAL FROM STUDY

You are free to withdraw from this study at any time, and you agree to inform the study doctor immediately if you intend to withdraw for any reason. To terminate your participation in this study, you must contact the study doctor at the contact information listed on page one of this informed consent form. You may be asked to come to the study clinic or doctor's office to complete some end of study procedures which are listed in the Withdrawal Procedures section of this document. Your decision to participate in this study or to withdraw from this study will not influence the availability of your future medical care and will involve no penalty or loss of benefits to which you are otherwise entitled. You may withdraw from this study at any time.

You agree that the study doctor in charge of the study can remove you from this study without your consent for any reason, including, but not limited to:

a. His/her judgment that any condition or circumstance may jeopardize your welfare such as increased risk, change in potential benefit, or the integrity of the study.
b. Your failure to follow the instructions of the study doctor(s).
c. If the study is stopped by the sponsor and/or doctors participating in the study prior to completion.

OFFER TO ANSWER ANY QUESTIONS ABOUT THIS STUDY

If you have any questions, concerns, or complaints during this study, or if you think you may have experienced a research-related injury, you should contact H. Frank Farmer Jr. MD, PhD, CPI at (386) 366-6400.

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Corrected Document – Dated 4/13/09
Signature 3/16/09 Date

Initials: _____
Date: _____

If you have any questions regarding your rights as a research participant, please contact Kim Lerner, Chair of the Independent Investigational Review Board, Inc. at toll free 1-(877) 888-iirb (4472) during regular working hours. You can also contact the Independent Investigational Review Board, Inc. if you would like to report problems in a research study, express concerns, ask questions, request information, or provide input. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of participants in a research study. For more information about your rights and role as a research participant you can visit the Research Participant section of the IIRB, Inc. website at www.iirb.com.

CONFIDENTIALITY/MEDICAL RECORDS

If you agree to take part in the research, information about your health and your participation will be collected and recorded by the study doctor. This information will contain your full name and address, and may contain other information about you such as your initials and date of birth. Your name will not be disclosed outside the clinic unless required by law.

Sponsor, representatives of the Sponsor, US Food and Drug Administration (FDA), health authorities and the Independent IRB may inspect your medical records which may include your name, address and other personal information that identifies you. If necessary, some or all of your medical records may be copied during these inspections. The purpose of these inspections is to make sure that the study is carried out correctly. We may also have to disclose records when legally required by state law and local agencies (i.e. reportable diseases).

The results of this research may be presented at meetings or in publications. However, you will not be personally identified in any presentations or publications.

Because of the need to use information as noted above, absolute confidentiality cannot be guaranteed.

BUSINESS CONFIDENTIALITY

The information and any materials or items that you are given about or during the study - such as information identifying the research unit, the sponsor, any study drug(s), and/or the type of study being performed - should be considered confidential business information of Covance and the study sponsor. You are of course free to discuss such information under confidence with your doctor or with your friends and family while considering whether to participate in this study or at any time when discussing your present or future healthcare. However, distributing confidential business information as described above to the media or posting it on the internet is prohibited.

IN CASE OF INJURY

Your safety is the major concern of every member of the staff. Please contact the study staff as soon as possible if you have side effects or injuries. The phone number for Covance is (386) 366-6400.

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Corrected Document – Dated 4/13/09

Signature 3/16/09 Date

Initials: _____
Date: _____

Covance will provide immediate medical treatment and follow-up care, without cost to you, for side effects or injuries caused by being in this study. The costs for any other medical problems not caused by being in this study are your responsibility. Financial compensation for such things as lost wages, disability or discomfort due to injury is not available.

You **DO NOT** waive any of your legal rights by signing this form.

CLOSING STATEMENT

You have read the information which has been stated above and have received satisfactory answers to all of the questions which you have asked and you willingly sign and initial each page of this consent form. You will receive a copy of the signed informed consent. You hereby consent to be a participant in this study.

I volunteer to take part in this study of my own free will. I understand that I may withdraw my consent at any time.

SIGNATURES

Please read the following paragraph out loud to the person obtaining the consent.

I have read in a language that I understand well, the above information. The content and meaning of this information has been explained to me. **I have asked the staff any questions I may have and have had enough time to decide if I want to take part in this study.** I hereby voluntarily consent and offer to take part in this study and authorize the use and disclosure of my medical information.

_____	_____	_____
Date/Time	Print Participant Name	Participant Signature

COVANCE STAFF ONLY

Date/ Scientific Time	**Name of Person Conducting Informed Consent Discussion**	**Signature of Person Conducting the Informed Consent Discussion**

Copy of consent form given to subject on (date) _____ by (initials) _____

Independent Investigational Review Board, Inc.
Approved: 11/18/08; Revised: 12/30/08, 1/20/09, 3/16/09

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Signature 3/16/09 Date

Initials: _____
Date: _____

Sample Volunteer Information and Consent Form - Austin (20 July 2009)

INFORMED CONSENT AUTHORIZATION TO PARTICIPATE IN A CLINICAL INVESTIGATION

Title: (Protocol #: SM 08-01) A Controlled Study of the Ability of a Traditional Swedish Smokeless Tobacco Product ("Snus") to Increase the Quit Rate Among Cigarette Smokers Who Wish to Stop Smoking

Principal Investigator: David C. Carter, MD
(Main Study Doctor)

Site of Investigation: Covance CRU Inc.
313 East Anderson Lane, Suites 200 & 300
Austin, TX 78752

Telephone #: (512) 302-6500
24 hour Telephone #: (512) 284-4723

Sponsor: Swedish Match AB

Participant's Name:_____

You are being asked to participate in a tobacco-switching research study because you currently smoke cigarettes and desire to stop smoking. Your decision to participate in this study is voluntary. If you decide to participate in the study and then change your mind, you can leave the study at any time. However, before you give your consent to be a volunteer, we want you to read the following and ask as many questions as necessary to be sure that you understand what your participation would involve.

Covance Clinical Research Unit Inc. is paid to test investigational products. The study doctors in this study work for Covance, but do not have a financial interest in the outcome of this study

NATURE AND PURPOSE OF THE STUDY

Snus is a smokeless tobacco product made from ground tobacco leaves, water, and food-allowed additives in a paper sachet (packet) that is placed under the upper lip. The placement of the Snus under the upper lip means that there is no need to spit as in other oral tobacco products. Snus is commonly used in Sweden as an alternative to smoking tobacco.

The purpose of this study is to examine if the use of Snus compared to placebo (inactive ingredients manufactured to appear the same as Snus) can increase the quit rate among cigarette smokers who wish to stop smoking. Withdrawal symptoms will be examined and tobacco dependence will be measured. The safety of Snus compared to placebo will be examined. Blood samples will be collected to study breakdown products of nicotine and biological indicators related to tobacco use. This study is not intended to eliminate your tobacco dependence.

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Signature 7/20/09 Date

Initials: _____
Date: _____

RESEARCH PARTICIPANT SELECTION

You have been offered an opportunity to participate in this research study because you are a male or female between the ages of 25 and 65 years of age, (inclusive) who has smoked at least 10 cigarettes a day for at least one year and desires to quit smoking. You must otherwise be healthy.

If you are a woman, you must not be pregnant or breast feeding. Women of childbearing potential must have been practicing one of the following methods of birth control for at least one month prior to the start of the study and agree to continue practicing it during the study: hormonal contraceptives, intrauterine device (IUD), spermicide and barrier (i.e., condom, diaphragm or cervical cap with spermicidal foam, gel, film or suppository), spouse/partner sterility; or is practicing abstinence and agrees to continue abstinence or to start an acceptable method of contraception from the above list if sexual activity starts.

It is important that you answer all of the screening questions completely. You must disclose all past and present diseases, allergies and all medications that you are taking, including prescription and non prescription drugs.

Approximately 250 volunteers will be enrolled in this multi site research study.

STUDY DURATION

The duration of your participation in this study is approximately 30 weeks including the screening visit. This study requires 6 outpatient clinic visits (screening, baseline, Weeks 6, 10, 16 and 28) and 8 telephone contacts (Weeks 1, 2, 3, 4, 8, 13, 20 and 24).

STUDY DESIGN

The study consists of four phases: Screening (up to 2 weeks), Study Product Test Period (4 weeks), Intervention Phase (approximately 12 weeks), and a Follow-up Phase (approximately 12 weeks). If you are interested, you will be invited to the clinic to attend an Information Session and Screening visit to determine if you are eligible to participate. During the Baseline visit, you will be randomly (by chance) assigned to receive either Snus or placebo. You will have an equal chance of receiving either Snus or placebo. You will not have a choice as to whether you receive Snus or placebo and neither you nor the study doctor will know which of the study products you are receiving, however, this information can be made available if medically necessary. Over the next 4 weeks, you will become familiar with the product and will try to refrain from cigarettes by using this product when you feel the urge to smoke. The Snus/placebo packet is to be placed under the upper lip and may be held for up to 60 minutes. You will be instructed to use the Snus/placebo when you feel the urge to smoke. If after 15 to 20 minutes of using this product you still feel the urge to smoke, you may do so provided that you remove the Snus/placebo from your mouth. You will be encouraged to gradually substitute as many cigarettes with Snus as possible and to refrain from all cigarettes at the latest by the first day of Week 5. You will use the study product for a total of 12 weeks (study product will be discontinued at the Week 16 visit). You will be asked to what extent you have replaced cigarettes with the study product and your breath will be analyzed for

APPROVED BY
Independent IRB
Signature 7/20/09 Date

Initials: _____
Date: _____

carbon monoxide (CO), a gas that is found in the breath of smokers. You will receive an educational booklet on the hazards of smoking and will be provided brief counseling at each visit. After the interventional phase, your progress will be followed for an additional 12 weeks.

The Snus/placebo products come in two sizes, a 1 gram size (typically replaces one cigarette) and a 0.5 gram size. You will be encouraged to use at least five 1 gram Snus/placebo sachets per day (or ten sachets if you chose the 0.5 gram sachet). The recommended maximum number of 1 gram sachets per day is 24. However, this number may be increased in heavy smokers (15-20 cigarettes per day) who try to replace all cigarettes with study product.

The Snus/placebo study product is for your use only and is not to be given to anyone else. The Snus/placebo study product should be kept refrigerated. The Snus/placebo study product must be kept out of the reach of children and those of limited mental capacity. Snus will not be provided to you as part of the trial after Week 16 of the Study.

SCREENING

The Screening Phase will consist of an Information Session and Screening Visit (which may be scheduled consecutively at one session at the study doctor's discretion). During the Information Session, you will receive information on the health risks associated with a range of nicotine products including: cigarettes, non-Snus smokeless tobacco, Snus, and nicotine replacement therapy. Possible alternatives to the use of Snus will be described. The effects of nicotine on the body and an account will be given of experience with Snus, including potential health risks associated with different smokeless tobacco products.

At the Screening Visit you will sign this informed consent form after all of your questions have been answered and if you are willing to participate in this study. A complete medical history will be recorded. This will include your history of smoking (i.e., at what age you started to smoke, average number of cigarettes smoked per day during the past year, history of quit attempts, your desire to quit smoking, history of nicotine replacement therapy and/or other drugs or aids used in attempts to quit smoking, history of previous smokeless tobacco use). A physical examination including the inside of your mouth, measurement of your vital signs (blood pressure, heart rate, breathing rate and temperature), and height and weight will be performed. An ECG will be performed. Blood and urine samples will be collected for routine laboratory tests including a screening for drugs of abuse. Women who are able to have children will have a pregnancy test. Women between the ages of 45 and 55 will have a Follicular Stimulating Hormone (FSH) test to verify post-menopausal status. You will receive educational materials on smoking cessation from the National Cancer Institute's "Cleaning the Air" booklet and brief counseling (approximately 10 minutes).

You will be permitted to participate in the study at the discretion of the study doctor if the results of the study screening laboratory tests and other assessments are satisfactory. Screening procedures may need to be repeated in order to qualify for this study. You

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Independent IRB
Signature
7/20/09
Date

Initials: _____
Date: _____

will be advised of the study restrictions and when to report to the clinic to begin the study. You may be considered an alternate for this study until such time that you have received study product.

STUDY PROCEDURES

Study Product test Period (Week 1 through Week 4)

Baseline Visit

You will return to the study clinic within 2 weeks of the Screening Visit. At this visit your eligibility to participate in this study will be reviewed. You will exhale into a device that measures the amount of carbon monoxide (CO) in your breath (CO exhaled air test). Blood samples will be collected for analysis of nicotine metabolites and biomarkers of exposure and/or disease related to tobacco use. You will complete two questionnaires related to your nicotine dependence and symptoms of nicotine withdrawal. After a brief counseling session, you will receive a study diary and study product, either Snus or placebo. In the diary you will record the number and size of the study product that you used and the number of cigarettes that you smoked daily. You should gradually decrease the number of cigarettes that you smoke through the use of the study product.

Week 1 through 4

A study staff member will contact you weekly by phone to review your smoking status, use of the study product, and brief behavioral counseling. You will also be asked how you are feeling. You continue to complete your diary during this portion of the study.

Intervention Phase (Week 5 through Week 16)

Throughout the Intervention Phase you will complete clinic visits and telephone contacts. Telephone contacts will occur at Weeks 8 and 13 and will include a review of your smoking status, use of the study product, how you feel, and brief behavioral counseling.

Clinic Visits (Week 6 and Week 10)

At these visits the following procedures will be performed:

- Your vital signs and weight will be measured
- CO exhaled air test
- Blood samples will be collected for biomarker blood tests (Week 6 only)
- You will complete a questionnaire to evaluate any symptoms of nicotine withdrawal that you might have
- You will receive brief behavioral counseling
- You will receive more study product
- You will be asked how you are feeling
- You will be asked if you are still smoking
- Your diary will be reviewed and you will receive a new diary.

Clinic Visit (Week 16)

At this visit the following procedures will be performed:

- Your vital signs and weight will be measured

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Signature 7/20/09 Date

Initials: _____
Date: _____

- A physical examination will be performed
- An examination of your mouth will be performed
- CO exhaled air test
- You will complete a questionnaire to determine your nicotine dependence
- You will complete a questionnaire to evaluate any symptoms of nicotine withdrawal that you might have
- Blood samples will be collected for biomarker tests
- You will receive brief behavioral counseling
- You will be asked if you are still smoking
- You will be asked how you are feeling
- Your diary will be reviewed for information regarding study product use and compliance.

You will not receive any more study product after this study visit.

Upon completion of the trial, if you have been successful in quitting cigarette smoking, but still require nicotine replacement, it is preferred that you switch to another smokeless tobacco product or nicotine replacement product, such as Nicoderm or Nicorette, rather than begin cigarette smoking again.

If you choose to discontinue your participation in this study prior to Week 16, you will be asked to undergo the procedures outlined above.

Follow-up Phase (Week 17 through Week 28)
Telephone contacts will occur at Weeks 20 and 24 and will include a review of your smoking status and brief behavioral counseling. You will also be asked how you are feeling.

Final Clinic Visit (Week 28)
The following procedures will be performed at this visit:

- Physical examination
- Examination of your mouth
- Your vital signs and weight will be measured
- CO exhaled air test
- You will complete a questionnaire to determine your nicotine dependence
- You will complete a questionnaire to evaluate any symptoms of nicotine withdrawal that you might have
- Blood samples will be collected for biomarker tests
- You will receive brief behavioral counseling
- You will be asked if you are still smoking
- You will be asked how you are feeling to assess for adverse events
- You will be asked if you have used over-the counter nicotine replacement therapy, smoking cessation services, smokeless tobacco, or smoking products other than cigarettes since week 16.

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Signature 7/20/09 Date

Initials: _____
Date: _____

If you discontinue your participation in this study after Week 16 but prior to Week 28, you will be asked to undergo the procedures outlined above.

If you should develop a visible side effect, such as a skin rash, we may need to take pictures of it for the study records.

The study doctor may require longer observation in the clinic or additional laboratory testing based on the effects of the study product or the results of the laboratory tests as necessary.

Withdrawal Procedures
If you withdraw early from the study, for any reason, you will be asked to complete the lab testing and discharge procedures outlined in the Week 16 or Week 28 sections listed above as applicable.

RESTRICTIONS

MAY I HAVE...?

- Tobacco or Nicotine-Containing Products: You may continue to use your usual brand of cigarettes according to the study design, however, you may not use any other tobacco or nicotine-containing products throughout the study including: pipes, cigarillos, snuff, and chewing tobacco. Over-the-counter nicotine replacement products are prohibited during the study.

- Drugs for smoking cessation: You must not have used any smoking cessation drugs (i.e., Wellbutrin®, Chantix®) for at least 3 months prior to the start of the study.

- Other Medications: You may use other medications with the knowledge and approval of the study doctor.

Blood Sampling
Blood samples will be taken approximately 5 times throughout the course of the study, (including screening and 6 outpatient clinic visits). Approximately 230 mL of blood, (about 1 cup), will be drawn throughout the study. Additional blood samples may be required if any of your lab values are abnormal. It is possible that more than one attempt to obtain a blood sample may be necessary.

For comparison, a standard blood donation at a blood collection center, once in any 56-day period, is about 2 cups of blood. Additional blood samples may be drawn during the study if the study doctor considers it necessary for monitoring your health.

Research Participant Responsibilities
As a research participant you will be asked to complete the study procedures for this study, come to the study clinic for all of your scheduled visits, follow the instructions listed in this informed consent form, and notify the study doctor if any information

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Independent IRB
Signature 7/20/09 Date

Initials: _____
Date: _____

regarding your health or availability to participate in this study changes.

STUDY DOCTOR AVAILABILITY
In the event of any type of medical emergency, the study doctor will be on call and available, throughout the study.

RISKS AND DISCOMFORTS
There may be risks to you if you participate in this study. According to the Surgeon General and other public health authorities, all tobacco products carry significant risks. There may also be social and/or personal adjustments to switching products or quitting.

Tobacco-burning cigarettes are required by law to carry one of four warning labels. The four warning labels for these products are:

•SURGEON GENERAL'S WARNING: Smoking Causes Lung Cancer, Heart Disease, Emphysema, and May Complicate Pregnancy.
•SURGEON GENERAL'S WARNING: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health.
•SURGEON GENERAL'S WARNING: Smoking by Pregnant Women May Result in Fetal Injury, Premature Birth, and Low Birth Weight.
•SURGEON GENERAL'S WARNING: Cigarette Smoke Contains Carbon Monoxide

Oral tobacco products: Snus is an oral tobacco product and is required to carry one of three warnings:
• WARNING: This product may cause mouth cancer.
• WARNING: This product may cause gum disease and tooth loss.
• WARNING: This product is not a safe alternative to cigarettes.

The use of Snus has been associated with oral lesions. The use of Snus may increase your risk of cardiovascular disease including heart attack.

Nicotine Overdose
It is possible that you may experience symptoms of nicotine overdose with excessive use of the Snus particularly if you are still smoking. Typical symptoms include nausea, vomiting, diarrhea, stomach pain, cold sweat, problems with hearing or vision, rapid or uneven heartbeats, and chest pain. In its most severe form nicotine overdose can lead to seizures and death.

Effects of Quitting Smoking
Generally, any risks of smoking cessation are far outweighed by the benefits. Nevertheless, it is reasonable to prepare for the discomforts of stopping smoking:

- Symptoms of withdrawal are common as patients attempt to stop smoking. Withdrawal symptoms can include insomnia, irritability, frustration or anger, anxiety, difficulty concentrating, restlessness, a decreased heart rate and an intense craving for cigarettes.

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Independent IRB
Signature 7/20/09 Date

Initials: _____
Date: _____

- Some people who stop smoking experience depression; this can be severe enough that it requires counseling or antidepressant medication. Symptoms of sleeplessness, emotional irritability, sadness, inattention, or other signs of depression should be discussed with the Study Doctor or study staff.

- Weight gain can occur with smoking cessation because people tend to eat more after quitting. The average weight gain is eight to 10 pounds. An exercise program and dieting can minimize weight gain. The benefits of quitting smoking are much greater than the risk of gaining weight.

Study Procedure Risk

During the collection of blood samples, you may experience pain and/or bruising at the insertion site of the needle. Although rare, localized clot formation and infections may occur. Lightheadedness and/or fainting may also occur during or shortly after the blood draw.

UNKNOWN/UNFORESEEABLE RISKS

In addition to the risks listed above, there may be some unknown or infrequent and unforeseeable risks associated with the use of this study product, including allergic reaction or interaction with medications. You will be informed in a timely manner both verbally and in writing of any new information, findings or changes to the way the research will be performed that might influence your willingness to continue your participation in this study.

RISKS TO THE UNBORN

Pregnancy/Fetal Risks: The Surgeon General's warnings for cigarette smoking state that smoking by pregnant women may complicate pregnancy and may result in fetal injury, premature birth, low birth weight, and therefore **may be hazardous.** The use of Snus was associated with increased risk of preterm delivery and preeclampsia (a dangerous and potentially fatal complication of pregnancy).

If you think that you have become pregnant during the study it is important that you inform the study doctor immediately. If you become pregnant or think that you may be pregnant, you will be removed from the study and the study doctor will refer you to seek obstetric care, the cost of which will be your responsibility. The study doctor may request to track your pregnancy and will report the pregnancy and outcome to the Sponsor and the IRB.

BIRTH CONTROL REQUIREMENTS

Female: Women of childbearing potential must have been practicing one of the following methods of birth control for at least one month prior to the start of the study and agree to continue practicing it during the study: hormonal contraceptives, intrauterine device (IUD), spermicide and barrier (i.e., condom, diaphragm or cervical cap with spermicidal foam, gel, film or suppository), spouse/partner sterility; or is practicing abstinence and agrees to continue abstinence or to start an acceptable method of contraception from the above list if sexual activity starts.

APPROVED BY
Independent IRB
Signature 7/20/09 Date

Initials: _____
Date: _____

Women that smoke and use hormonal contraceptives (pills, patches, etc.) are at increased risk of blood clots.

BENEFITS

Your participation in this study may help to stop smoking but there is no guarantee that it will decrease your dependence on nicotine.

Participation in this study is purely for research purposes, and participation in this study will not improve your health or treat any medical problem you may have.

You may benefit by having physical examinations. The results of laboratory tests done at the screening visit will be made available to you. However, if you test positive for any unauthorized drugs or alcohol, all the tests may not be completed.

COST

There is no cost for participating in this research study. The study sponsor pays all the study costs.

PAYMENT FOR BEING IN THE STUDY

You will be paid for taking part in this study as outlined below. This is to compensate you for your time and travel. Each portion of the study has a monetary value assigned to it, which accumulates as you participate in this study.

Payment Schedule

Screening Visit	$0.00
Outpatient Clinic Visits $125.00 x 5 visits	$625.00
Telephone contacts $50.00 x 8 contacts	$400.00
TOTAL	$1,025.00

Total compensation for study completion will be $1,025.00. If you choose to withdraw from the study, you will receive payment only for the days that you have completed as outlined above. If it is necessary for you to return to the clinic for additional safety follow up visits, you will be paid $50.00 for each completed visit.

All research participants will be paid within 14 business days of the completion of their participation in the study depending on the number of visits they completed.
In agreeing to participate in this study, you will be acting as an independent contractor, not as an employee of Covance Clinical Research Unit, Inc. Because payments made to you for participating in this study will be reported to the IRS as income, you are required to provide your social security number as required by law. No deductions for any state or federal withholding or any other similar taxes will be made. It is the responsibility of the participant to report this compensation on state and federal tax returns and for the payment of any taxes that are due on this compensation.

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Independent IRB
Signature 7/20/09 Date

Initials: _____
Date: _____

The Internal Revenue Service (IRS) requires Covance to deduct 30% from the final payment when participants are foreign nationals who do not have a Social Security or Tax identification number.

TREATMENT ALTERNATIVE

You do not have to participate in this study in order to quit smoking. There are several FDA approved over-the-counter and prescription medications that assist people to quit smoking. Some of these medications include: Nicotine Replacement Therapy (i.e., nicotine gum, lozenges and patches) which can be obtained over-the-counter and prescription medications like Wellbutrin® and Chantix®.

RIGHT TO WITHDRAW OR REMOVAL FROM STUDY

You are free to withdraw from this study at any time, and you agree to inform the study doctor immediately if you intend to withdraw for any reason. To terminate your participation in this study, you must contact the study doctor at the contact information listed on page one of this informed consent form. You may be asked to come to the study clinic or doctor's office to complete some end of study procedures which are listed in the Withdrawal Procedures section of this document. Your decision to participate in this study or to withdraw from this study will not influence the availability of your future medical care and will involve no penalty or loss of benefits to which you are otherwise entitled. You may withdraw from this study at any time.

You agree that the study doctor in charge of the study can remove you from this study without your consent for any reason, including, but not limited to:

a. His/her judgment that any condition or circumstance may jeopardize your welfare such as increased risk, change in potential benefit, or the integrity of the study.
b. Your failure to follow the instructions of the study doctor(s).
c. If the study is stopped by the sponsor and/or doctors participating in the study prior to completion.

OFFER TO ANSWER ANY QUESTIONS ABOUT THIS STUDY

If you have any questions, concerns, or complaints during this study, or if you think you may have experienced a research-related injury, you should contact David C. Carter, MD at (512) 302-6500.

If you have any questions regarding your rights as a research participant, please contact Kim Lerner, Chair of the Independent Investigational Review Board, Inc. at toll free 1-(877) 888-iirb (4472) during regular working hours. You can also contact the Independent Investigational Review Board, Inc. if you would like to report problems in a research study, express concerns, ask questions, request information, or provide input. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of participants in a research study. For more information about your rights and role as a research participant you can visit the Research Participant section of the IIRB, Inc. website at www.iirb.com.

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Independent IRB
Signature 7/20/09 Date

Initials: _____
Date: _____

CONFIDENTIALITY/MEDICAL RECORDS

If you agree to take part in the research, information about your health and your participation will be collected and recorded by the study doctor. This information will contain your full name and address, and may contain other information about you such as your initials and date of birth. Your name will not be disclosed outside the clinic unless required by law.

Sponsor, representatives of the Sponsor, US Food and Drug Administration (FDA), health authorities and the Independent IRB may inspect your medical records which may include your name, address and other personal information that identifies you. If necessary, some or all of your medical records may be copied during these inspections. The purpose of these inspections is to make sure that the study is carried out correctly. We may also have to disclose records when legally required by state law and local agencies (i.e. reportable diseases).

The results of this research may be presented at meetings or in publications. However, you will not be personally identified in any presentations or publications.

Because of the need to use information as noted above, absolute confidentiality cannot be guaranteed.

BUSINESS CONFIDENTIALITY

The information and any materials or items that you are given about or during the study - such as information identifying the research unit, the sponsor, any study drug(s), and/or the type of study being performed - should be considered confidential business information of Covance and the study sponsor. You are of course free to discuss such information under confidence with your doctor or with your friends and family while considering whether to participate in this study or at any time when discussing your present or future healthcare. However, distributing confidential business information as described above to the media or posting it on the internet is prohibited.

IN CASE OF INJURY

Your safety is the major concern of every member of the staff. Please contact the study staff as soon as possible if you have side effects or injuries. The phone number for Covance is (512) 302-6500 .

Covance will provide immediate medical treatment and follow-up care, without cost to you, for side effects or injuries caused by being in this study. The costs for any other medical problems not caused by being in this study are your responsibility. Financial compensation for such things as lost wages, disability or discomfort due to injury is not available.

You **DO NOT** waive any of your legal rights by signing this form.

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Signature 7/20/09 Date

Initials: _____
Date: _____

CLOSING STATEMENT

You have read the information which has been stated above and have received satisfactory answers to all of the questions which you have asked and you willingly sign and initial each page of this consent form. You will receive a copy of the signed informed consent. You hereby consent to be a participant in this study.

I volunteer to take part in this study of my own free will. I understand that I may withdraw my consent at any time.

SIGNATURES

Please read the following paragraph out loud to the person obtaining the consent.

I have read in a language that I understand well, the above information. The content and meaning of this information has been explained to me. **I have asked the staff any questions I may have and have had enough time to decide if I want to take part in this study.** I hereby voluntarily consent and offer to take part in this study and authorize the use and disclosure of my medical information.

_____	_____	_____
Date/Time	Print Participant Name	Participant Signature

COVANCE STAFF ONLY

Date/ Scientific Time	Name of Person Conducting Informed Consent Discussion	Signature of Person Conducting Informed Consent Discussion

Copy of consent form given to subject on (date) _____ by (initials) _____

Independent Investigational Review Board, Inc.
Approved: 11/18/08; Revised: 12/30/08, 1/20/09, 3/16/09, 7/20/09

APPROVED BY
Independent IRB
Signature 7/20/09 Date

Initials: _____
Date: _____

Sample Volunteer Information and Consent Form - Portland (16 March 2009)

INFORMED CONSENT AUTHORIZATION TO PARTICIPATE IN A CLINICAL INVESTIGATION

Title: (Protocol #: SM 08-01) A Controlled Study of the Ability of a Traditional Swedish Smokeless Tobacco Product ("Snus") to Increase the Quit Rate Among Cigarette Smokers Who Wish to Stop Smoking

Principal Investigator: Keith Klatt, MD
(Main Study Doctor)

Site of Investigation: **Covance** CRU Inc.
5331 SW Macadam Ave., Suite 307, 322, & 344
Portland, OR 97239

24 hour Telephone #: 503-294-7193

Sponsor: Swedish Match AB

Participant's Name:_____

You are being asked to participate in a tobacco-switching research study because you currently smoke cigarettes and desire to stop smoking. Your decision to participate in this study is voluntary. If you decide to participate in the study and then change your mind, you can leave the study at any time. However, before you give your consent to be a volunteer, we want you to read the following and ask as many questions as necessary to be sure that you understand what your participation would involve.

Covance Clinical Research Unit Inc. is paid to test investigational products. The study doctors in this study work for Covance, but do not have a financial interest in the outcome of this study

NATURE AND PURPOSE OF THE STUDY

Snus is a smokeless tobacco product made from ground tobacco leaves, water, and food-allowed additives in a paper sachet (packet) that is placed under the upper lip. The placement of the Snus under the upper lip means that there is no need to spit as in other oral tobacco products. Snus is commonly used in Sweden as an alternative to smoking tobacco.

The purpose of this study is to examine if the use of Snus compared to placebo (inactive ingredients manufactured to appear the same as Snus) can increase the quit rate among cigarette smokers who wish to stop smoking. Withdrawal symptoms will be examined and tobacco dependence will be measured. The safety of Snus compared to placebo will be examined. Blood samples will be collected to study breakdown products of nicotine and biological indicators related to tobacco use. This study is not intended to eliminate your tobacco dependence.

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Independent IRB
Signature — Date: 3/16/09

Initials: _____
Date: _____

RESEARCH PARTICIPANT SELECTION

You have been offered an opportunity to participate in this research study because you are a male or female between the ages of 25 and 65 years of age, (inclusive) who has smoked at least 10 cigarettes a day for at least one year and desires to quit smoking. You must otherwise be healthy.

If you are a woman, you must not be pregnant or breast feeding. Women of childbearing potential must have been practicing one of the following methods of birth control for at least one month prior to the start of the study and agree to continue practicing it during the study: hormonal contraceptives, intrauterine device (IUD), spermicide and barrier (i.e., condom, diaphragm or cervical cap with spermicidal foam, gel, film or suppository), spouse/partner sterility; or is practicing abstinence and agrees to continue abstinence or to start an acceptable method of contraception from the above list if sexual activity starts.

It is important that you answer all of the screening questions completely. You must disclose all past and present diseases, allergies and all medications that you are taking, including prescription and non prescription drugs.

Approximately 250 volunteers will be enrolled in this multi site research study.

STUDY DURATION

The duration of your participation in this study is approximately 30 weeks including the screening visit. This study requires 6 outpatient clinic visits (screening, baseline, Weeks 6, 10, 16 and 28) and 8 telephone contacts (Weeks 1, 2, 3, 4, 8, 13, 20 and 24).

STUDY DESIGN

The study consists of four phases: Screening (up to 2 weeks), Study Product Test Period (4 weeks), Intervention Phase (approximately 12 weeks), and a Follow-up Phase (approximately 12 weeks). If you are interested, you will be invited to the clinic to attend an Information Session and Screening visit to determine if you are eligible to participate. During the Baseline visit, you will be randomly (by chance) assigned to receive either Snus or placebo. You will have an equal chance of receiving either Snus or placebo. You will not have a choice as to whether you receive Snus or placebo and neither you nor the study doctor will know which of the study products you are receiving, however, this information can be made available if medically necessary. Over the next 4 weeks, you will become familiar with the product and will try to refrain from cigarettes by using this product when you feel the urge to smoke. The Snus/placebo packet is to be placed under the upper lip and may be held for up to 60 minutes. You will be instructed to use the Snus/placebo when you feel the urge to smoke. If after 15 to 20 minutes of using this product you still feel the urge to smoke, you may do so provided that you remove the Snus/placebo from your mouth. You will be encouraged to gradually substitute as many cigarettes with Snus as possible and to refrain from all cigarettes at the latest by the first day of Week 5. You will use the study product for a total of 12 weeks (study product will be discontinued at the Week 16 visit). You will be asked to what extent you have replaced cigarettes with the study product and your breath will be analyzed for

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Independent IRB
Signature 3/16/09 Date

Initials: _____
Date: _____

carbon monoxide (CO), a gas that is found in the breath of smokers. You will receive an educational booklet on the hazards of smoking and will be provided brief counseling at each visit. After the interventional phase, your progress will be followed for an additional 12 weeks.

The Snus/placebo products come in two sizes, a 1 gram size (typically replaces one cigarette) and a 0.5 gram size. You will be encouraged to use at least five 1 gram Snus/placebo sachets per day (or ten sachets if you chose the 0.5 gram sachet). The recommended maximum number of 1 gram sachets per day is 24. However, this number may be increased in heavy smokers (15-20 cigarettes per day) who try to replace all cigarettes with study product.

The Snus/placebo study product is for your use only and is not to be given to anyone else. The Snus/placebo study product should be kept refrigerated. The Snus/placebo study product must be kept out of the reach of children and those of limited mental capacity. Snus will not be provided to you as part of the trial after Week 16 of the Study.

SCREENING

The Screening Phase will consist of an Information Session and Screening Visit (which may be scheduled consecutively at one session at the study doctor's discretion). During the Information Session, you will receive information on the health risks associated with a range of nicotine products including: cigarettes, non-Snus smokeless tobacco, Snus, and nicotine replacement therapy. Possible alternatives to the use of Snus will be described. The effects of nicotine on the body and an account will be given of experience with Snus, including potential health risks associated with different smokeless tobacco products.

At the Screening Visit you will sign this informed consent form after all of your questions have been answered and if you are willing to participate in this study. A complete medical history will be recorded. This will include your history of smoking (i.e., at what age you started to smoke, average number of cigarettes smoked per day during the past year, history of quit attempts, your desire to quit smoking, history of nicotine replacement therapy and/or other drugs or aids used in attempts to quit smoking, history of previous smokeless tobacco use). A physical examination including the inside of your mouth, measurement of your vital signs (blood pressure, heart rate, breathing rate and temperature), and height and weight will be performed. An ECG will be performed. Blood and urine samples will be collected for routine laboratory tests including a screening for drugs of abuse. Women who are able to have children will have a pregnancy test. Women between the ages of 45 and 55 will have a Follicular Stimulating Hormone (FSH) test to verify post-menopausal status. You will receive educational materials on smoking cessation from the National Cancer Institute's "Cleaning the Air" booklet and brief counseling (approximately 10 minutes).

You will be permitted to participate in the study at the discretion of the study doctor if the results of the study screening laboratory tests and other assessments are satisfactory. Screening procedures may need to be repeated in order to qualify for this study. You

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Independent IRB
Signature — 3/16/09 Date

Initials: _____
Date: _____

will be advised of the study restrictions and when to report to the clinic to begin the study. You may be considered an alternate for this study until such time that you have received study product.

STUDY PROCEDURES

Study Product test Period (Week 1 through Week 4)

Baseline Visit

You will return to the study clinic within 2 weeks of the Screening Visit. At this visit your eligibility to participate in this study will be reviewed. You will exhale into a device that measures the amount of carbon monoxide (CO) in your breath (CO exhaled air test). Blood samples will be collected for analysis of nicotine metabolites and biomarkers of exposure and/or disease related to tobacco use. You will complete two questionnaires related to your nicotine dependence and symptoms of nicotine withdrawal. After a brief counseling session, you will receive a study diary and study product, either Snus or placebo. In the diary you will record the number and size of the study product that you used and the number of cigarettes that you smoked daily. You should gradually decrease the number of cigarettes that you smoke through the use of the study product.

Week 1 through 4

A study staff member will contact you weekly by phone to review your smoking status, use of the study product, and brief behavioral counseling. You will also be asked how you are feeling. You continue to complete your diary during this portion of the study.

Intervention Phase (Week 5 through Week 16)

Throughout the Intervention Phase you will complete clinic visits and telephone contacts. Telephone contacts will occur at Weeks 8 and 13 and will include a review of your smoking status, use of the study product, how you feel, and brief behavioral counseling.

Clinic Visits (Week 6 and Week 10)

At these visits the following procedures will be performed:

- Your vital signs and weight will be measured
- CO exhaled air test
- Blood samples will be collected for biomarker blood tests (Week 6 only)
- You will complete a questionnaire to evaluate any symptoms of nicotine withdrawal that you might have
- You will receive brief behavioral counseling
- You will receive more study product
- You will be asked how you are feeling
- You will be asked if you are still smoking
- Your diary will be reviewed and you will receive a new diary.

Clinic Visit (Week 16)

At this visit the following procedures will be performed:

APPROVED BY
Independent IRB
Signature
3/16/09
Date

Initials: _____
Date: _____

- Your vital signs and weight will be measured
- A physical examination will be performed
- An examination of your mouth will be performed
- CO exhaled air test
- You will complete a questionnaire to determine your nicotine dependence
- You will complete a questionnaire to evaluate any symptoms of nicotine withdrawal that you might have
- Blood samples will be collected for biomarker tests
- You will receive brief behavioral counseling
- You will be asked if you are still smoking
- You will be asked how you are feeling
- Your diary will be reviewed for information regarding study product use and compliance.

You will not receive any more study product after this study visit.

Upon completion of the trial, if you have been successful in quitting cigarette smoking, but still require nicotine replacement, it is preferred that you switch to another smokeless tobacco product or nicotine replacement product, such as Nicoderm or Nicorette, rather than begin cigarette smoking again.

If you choose to discontinue your participation in this study prior to Week 16, you will be asked to undergo the procedures outlined above.

Follow-up Phase (Week 17 through Week 28)
Telephone contacts will occur at Weeks 20 and 24 and will include a review of your smoking status and brief behavioral counseling. You will also be asked how you are feeling.

Final Clinic Visit (Week 28)
The following procedures will be performed at this visit:

- Physical examination
- Examination of your mouth
- Your vital signs and weight will be measured
- CO exhaled air test
- You will complete a questionnaire to determine your nicotine dependence
- You will complete a questionnaire to evaluate any symptoms of nicotine withdrawal that you might have
- Blood samples will be collected for biomarker tests
- You will receive brief behavioral counseling
- You will be asked if you are still smoking
- You will be asked how you are feeling to assess for adverse events
- You will be asked if you have used over-the counter nicotine replacement therapy, smoking cessation services, smokeless tobacco, or smoking products

APPROVED BY
Independent IRB
Signature 3/16/09 Date

Initials: _____
Date: _____

other than cigarettes since week 16.

If you discontinue your participation in this study after Week 16 but prior to Week 28, you will be asked to undergo the procedures outlined above.

If you should develop a visible side effect, such as a skin rash, we may need to take pictures of it for the study records.

The study doctor may require longer observation in the clinic or additional laboratory testing based on the effects of the study product or the results of the laboratory tests as necessary.

Withdrawal Procedures
If you withdraw early from the study, for any reason, you will be asked to complete the lab testing and discharge procedures outlined in the Week 16 or Week 28 sections listed above as applicable.

RESTRICTIONS

MAY I HAVE...?

- Tobacco or Nicotine-Containing Products: You may continue to use your usual brand of cigarettes according to the study design, however, you may not use any other tobacco or nicotine-containing products throughout the study including: pipes, cigarillos, snuff, and chewing tobacco. Over-the-counter nicotine replacement products are prohibited during the study.

- Drugs for smoking cessation: You must not have used any smoking cessation drugs (i.e., Wellbutrin®, Chantix®) for at least 3 months prior to the start of the study.

- Other Medications: You may use other medications with the knowledge and approval of the study doctor.

Blood Sampling
Blood samples will be taken approximately 5 times throughout the course of the study, (including screening and 6 outpatient clinic visits). Approximately 230 mL of blood, (about 1 cup), will be drawn throughout the study. Additional blood samples may be required if any of your lab values are abnormal. It is possible that more than one attempt to obtain a blood sample may be necessary.

For comparison, a standard blood donation at a blood collection center, once in any 56-day period, is about 2 cups of blood. Additional blood samples may be drawn during the study if the study doctor considers it necessary for monitoring your health.

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Research Participant Responsibilities
As a research participant you will be asked to complete the study procedures for this study, come to the study clinic for all of your scheduled visits, follow the instructions listed in this informed consent form, and notify the study doctor if any information regarding your health or availability to participate in this study changes.

STUDY DOCTOR AVAILABILITY
In the event of any type of medical emergency, the study doctor will be on call and available, throughout the study.

RISKS AND DISCOMFORTS
There may be risks to you if you participate in this study. According to the Surgeon General and other public health authorities, all tobacco products carry significant risks. There may also be social and/or personal adjustments to switching products or quitting.

Tobacco-burning cigarettes are required by law to carry one of four warning labels. The four warning labels for these products are:

•SURGEON GENERAL'S WARNING: Smoking Causes Lung Cancer, Heart Disease, Emphysema, and May Complicate Pregnancy.
•SURGEON GENERAL'S WARNING: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health.
•SURGEON GENERAL'S WARNING: Smoking by Pregnant Women May Result in Fetal Injury, Premature Birth, and Low Birth Weight.
•SURGEON GENERAL'S WARNING: Cigarette Smoke Contains Carbon Monoxide

Oral tobacco products: Snus is an oral tobacco product and is required to carry one of three warnings:
• WARNING: This product may cause mouth cancer.
• WARNING: This product may cause gum disease and tooth loss.
• WARNING: This product is not a safe alternative to cigarettes.

The use of Snus has been associated with oral lesions. The use fo Snus may increase your risk of cardiovascular disease including heart attack.

Nicotine Overdose
It is possible that you may experience symptoms of nicotine overdose with excessive use of the Snus particularly if you are still smoking. Typical symptoms include nausea, vomiting, diarrhea, stomach pain, cold sweat, problems with hearing or vision, rapid or uneven heartbeats, and chest pain. In its most severe form nicotine overdose can lead to seizures and death.

Effects of Quitting Smoking
Generally, any risks of smoking cessation are far outweighed by the benefits. Nevertheless, it is reasonable to prepare for the discomforts of stopping smoking:

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Initials: _____
Date: _____

- Symptoms of withdrawal are common as patients attempt to stop smoking. Withdrawal symptoms can include insomnia, irritability, frustration or anger, anxiety, difficulty concentrating, restlessness, a decreased heart rate and an intense craving for cigarettes.

- Some people who stop smoking experience depression; this can be severe enough that it requires counseling or antidepressant medication. Symptoms of sleeplessness, emotional irritability, sadness, inattention, or other signs of depression should be discussed with the Study Doctor or study staff.

- Weight gain can occur with smoking cessation because people tend to eat more after quitting. The average weight gain is eight to 10 pounds. An exercise program and dieting can minimize weight gain. The benefits of quitting smoking are much greater than the risk of gaining weight.

Study Procedure Risk

During the collection of blood samples, you may experience pain and/or bruising at the insertion site of the needle. Although rare, localized clot formation and infections may occur. Lightheadedness and/or fainting may also occur during or shortly after the blood draw.

UNKNOWN/UNFORESEEABLE RISKS

In addition to the risks listed above, there may be some unknown or infrequent and unforeseeable risks associated with the use of this study product, including allergic reaction or interaction with medications. You will be informed in a timely manner both verbally and in writing of any new information, findings or changes to the way the research will be performed that might influence your willingness to continue your participation in this study.

RISKS TO THE UNBORN

Pregnancy/Fetal Risks: The Surgeon General's warnings for cigarette smoking state that smoking by pregnant women may complicate pregnancy and may result in fetal injury, premature birth, low birth weight, and therefore **may be hazardous.** The use of Snus was associated with increased risk of preterm delivery and preeclampsia (a dangerous and potentially fatal complication of pregnancy).

If you think that you have become pregnant during the study it is important that you inform the study doctor immediately. If you become pregnant or think that you may be pregnant, you will be removed from the study and the study doctor will refer you to seek obstetric care, the cost of which will be your responsibility. The study doctor may request to track your pregnancy and will report the pregnancy and outcome to the Sponsor and the IRB.

BIRTH CONTROL REQUIREMENTS

Female: Women of childbearing potential must have been practicing one of the following methods of birth control for at least one month prior to the start of the study

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Initials: _____
Date: _____

and agree to continue practicing it during the study: hormonal contraceptives, intrauterine device (IUD), spermicide and barrier (i.e., condom, diaphragm or cervical cap with spermicidal foam, gel, film or suppository), spouse/partner sterility; or is practicing abstinence and agrees to continue abstinence or to start an acceptable method of contraception from the above list if sexual activity starts.

Women that smoke and use hormonal contraceptives (pills, patches, etc.) are at increased risk of blood clots.

BENEFITS

Your participation in this study may help to stop smoking but there is no guarantee that it will decrease your dependence on nicotine.

Participation in this study is purely for research purposes, and participation in this study will not improve your health or treat any medical problem you may have.

You may benefit by having physical examinations. The results of laboratory tests done at the screening visit will be made available to you. However, if you test positive for any unauthorized drugs or alcohol, all the tests may not be completed.

COST

There is no cost for participating in this research study. The study sponsor pays all the study costs.

PAYMENT FOR BEING IN THE STUDY

You will be paid for taking part in this study as outlined below. This is to compensate you for your time and travel. Each portion of the study has a monetary value assigned to it, which accumulates as you participate in this study.

Payment Schedule

Screening Visit	$0.00
Outpatient Clinic Visits $75.00 x 5 visits	$375.00
Telephone contacts $50.00 x 8 contacts	$400.00
TOTAL	$775.00

Total compensation for study completion will be $775.00. If you choose to withdraw from the study, you will receive payment only for the days that you have completed as outlined above. If it is necessary for you to return to the clinic for additional safety follow up visits, you will be paid $35.00 for each completed visit.

All research participants will be paid within 14 business days of the completion of their participation in the study depending on the number of visits they completed.

In agreeing to participate in this study, you will be acting as an independent contractor, not as an employee of Covance Clinical Research Unit, Inc. Because payments made to you for participating in this study will be reported to the IRS as income, you are

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Signature — Date: 3/16/09

Initials: _____
Date: _____

required to provide your social security number as required by law. No deductions for any state or federal withholding or any other similar taxes will be made. It is the responsibility of the participant to report this compensation on state and federal tax returns and for the payment of any taxes that are due on this compensation.

The Internal Revenue Service (IRS) requires Covance to deduct 30% from the final payment when participants are foreign nationals who do not have a Social Security or Tax identification number.

TREATMENT ALTERNATIVE

You do not have to participate in this study in order to quit smoking. There are several FDA approved over-the-counter and prescription medications that assist people to quit smoking. Some of these medications include: Nicotine Replacement Therapy (i.e., nicotine gum, lozenges and patches) which can be obtained over-the-counter and prescription medications like Wellbutrin® and Chantix®.

RIGHT TO WITHDRAW OR REMOVAL FROM STUDY

You are free to withdraw from this study at any time, and you agree to inform the study doctor immediately if you intend to withdraw for any reason. To terminate your participation in this study, you must contact the study doctor at the contact information listed on page one of this informed consent form. You may be asked to come to the study clinic or doctor's office to complete some end of study procedures which are listed in the Withdrawal Procedures section of this document. Your decision to participate in this study or to withdraw from this study will not influence the availability of your future medical care and will involve no penalty or loss of benefits to which you are otherwise entitled. You may withdraw from this study at any time.

You agree that the study doctor in charge of the study can remove you from this study without your consent for any reason, including, but not limited to:

a. His/her judgment that any condition or circumstance may jeopardize your welfare such as increased risk, change in potential benefit, or the integrity of the study.
b. Your failure to follow the instructions of the study doctor(s).
c. If the study is stopped by the sponsor and/or doctors participating in the study prior to completion.

OFFER TO ANSWER ANY QUESTIONS ABOUT THIS STUDY

If you have any questions, concerns, or complaints during this study, or if you think you may have experienced a research-related injury, you should contact Keith Klatt, MD at (503) 294-7193.

If you have any questions regarding your rights as a research participant, please contact Kim Lerner, Chair of the Independent Investigational Review Board, Inc. at toll free 1-(877) 888-iirb (4472) during regular working hours. You can also contact the Independent Investigational Review Board, Inc. if you would like to report problems in a research study, express concerns, ask questions, request information, or provide input.

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Initials: _____
Date: _____

The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of participants in a research study. For more information about your rights and role as a research participant you can visit the Research Participant section of the IIRB, Inc. website at www.iirb.com.

CONFIDENTIALITY/MEDICAL RECORDS

If you agree to take part in the research, information about your health and your participation will be collected and recorded by the study doctor. This information will contain your full name and address, and may contain other information about you such as your initials and date of birth. Your name will not be disclosed outside the clinic unless required by law.

Sponsor, representatives of the Sponsor, US Food and Drug Administration (FDA), health authorities and the Independent IRB may inspect your medical records which may include your name, address and other personal information that identifies you. If necessary, some or all of your medical records may be copied during these inspections. The purpose of these inspections is to make sure that the study is carried out correctly. We may also have to disclose records when legally required by state law and local agencies (i.e. reportable diseeases).

The results of this research may be presented at meetings or in publications. However, you will not be personally identified in any presentations or publications.

Because of the need to use information as noted above, absolute confidentiality cannot be guaranteed.

BUSINESS CONFIDENTIALITY

The information and any materials or items that you are given about or during the study - such as information identifying the research unit, the sponsor, any study drug(s), and/or the type of study being performed - should be considered confidential business information of Covance and the study sponsor. You are of course free to discuss such information under confidence with your doctor or with your friends and family while considering whether to participate in this study or at any time when discussing your present or future healthcare. However, distributing confidential business information as described above to the media or posting it on the internet is prohibited.

IN CASE OF INJURY

Your safety is the major concern of every member of the staff. Please contact the study staff as soon as possible if you have side effects or injuries. The phone number for Covance is (503) 294-7193.

Covance will provide immediate medical treatment and follow-up care, without cost to you, for side effects or injuries caused by being in this study. The costs for any other medical problems not caused by being in this study are your responsibility. Financial compensation for such things as lost wages, disability or discomfort due to injury is not available.

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Initials: _____
Date: _____

You **DO NOT** waive any of your legal rights by signing this form.

CLOSING STATEMENT

You have read the information which has been stated above and have received satisfactory answers to all of the questions which you have asked and you willingly sign and initial each page of this consent form. You will receive a copy of the signed informed consent. You hereby consent to be a participant in this study.

I volunteer to take part in this study of my own free will. I understand that I may withdraw my consent at any time.

SIGNATURES

Please read the following paragraph out loud to the person obtaining the consent.

I have read in a language that I understand well, the above information. The content and meaning of this information has been explained to me. **I have asked the staff any questions I may have and have had enough time to decide if I want to take part in this study.** I hereby voluntarily consent and offer to take part in this study and authorize the use and disclosure of my medical information.

_____	_____	_____
Date/Time	Print Participant Name	Participant Signature

COVANCE STAFF ONLY

Date/ Scientific Time	Name of Person Conducting Informed Consent Discussion	Signature of Person Conducting the Informed Consent Discussion

Copy of consent form given to subject on (date) _____ by (initials) _____

Independent Investigational Review Board, Inc.
Approved: 11/18/08; Revised: 12/30/08, 1/20/09, 3/16/09

APPROVED BY
Independent IRB
Signature 3/16/09 Date

Initials: _____
Date: _____

Sample Volunteer Information and Consent Form - Evansville (16 March 2009)

INFORMED CONSENT AUTHORIZATION TO PARTICIPATE IN A CLINICAL INVESTIGATION

Title: (Protocol #: SM 08-01) A Controlled Study of the Ability of a Traditional Swedish Smokeless Tobacco Product ("Snus") to Increase the Quit Rate Among Cigarette Smokers Who Wish to Stop Smoking

Principal Investigator: Randall R. Stoltz, MD
(Main Study Doctor)

Site of Investigation: Covance Clinical Research Unit, Inc
617 Oakley St.
Evansville, IN 47710

24 hour Telephone #: (812) 474-5000 or (800) 552-4434

Sponsor: Swedish Match AB

Participant's Name:_____

You are being asked to participate in a tobacco-switching research study because you currently smoke cigarettes and desire to stop smoking. Your decision to participate in this study is voluntary. If you decide to participate in the study and then change your mind, you can leave the study at any time. However, before you give your consent to be a volunteer, we want you to read the following and ask as many questions as necessary to be sure that you understand what your participation would involve.

Covance Clinical Research Unit Inc. is paid to test investigational products. The study doctors in this study work for Covance, but do not have a financial interest in the outcome of this study

NATURE AND PURPOSE OF THE STUDY

Snus is a smokeless tobacco product made from ground tobacco leaves, water, and food-allowed additives in a paper sachet (packet) that is placed under the upper lip. The placement of the Snus under the upper lip means that there is no need to spit as in other oral tobacco products. Snus is commonly used in Sweden as an alternative to smoking tobacco.

The purpose of this study is to examine if the use of Snus compared to placebo (inactive ingredients manufactured to appear the same as Snus) can increase the quit rate among cigarette smokers who wish to stop smoking. Withdrawal symptoms will be examined and tobacco dependence will be measured. The safety of Snus compared to placebo will be examined. Blood samples will be collected to study breakdown products of nicotine and biological indicators related to tobacco use. This study is not intended to eliminate your tobacco dependence.

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Signature 3/16/09 Date

Initials: _____
Date: _____

RESEARCH PARTICIPANT SELECTION

You have been offered an opportunity to participate in this research study because you are a male or female between the ages of 25 and 65 years of age, (inclusive) who has smoked at least 10 cigarettes a day for at least one year and desires to quit smoking. You must otherwise be healthy.

If you are a woman, you must not be pregnant or breast feeding. Women of childbearing potential must have been practicing one of the following methods of birth control for at least one month prior to the start of the study and agree to continue practicing it during the study: hormonal contraceptives, intrauterine device (IUD), spermicide and barrier (i.e., condom, diaphragm or cervical cap with spermicidal foam, gel, film or suppository), spouse/partner sterility; or is practicing abstinence and agrees to continue abstinence or to start an acceptable method of contraception from the above list if sexual activity starts.

It is important that you answer all of the screening questions completely. You must disclose all past and present diseases, allergies and all medications that you are taking, including prescription and non prescription drugs.

Approximately 250 volunteers will be enrolled in this multi site research study.

STUDY DURATION

The duration of your participation in this study is approximately 30 weeks including the screening visit. This study requires 6 outpatient clinic visits (screening, baseline, Weeks 6, 10, 16 and 28) and 8 telephone contacts (Weeks 1, 2, 3, 4, 8, 13, 20 and 24).

STUDY DESIGN

The study consists of four phases: Screening (up to 2 weeks), Study Product Test Period (4 weeks), Intervention Phase (approximately 12 weeks), and a Follow-up Phase (approximately 12 weeks). If you are interested, you will be invited to the clinic to attend an Information Session and Screening visit to determine if you are eligible to participate. During the Baseline visit, you will be randomly (by chance) assigned to receive either Snus or placebo. You will have an equal chance of receiving either Snus or placebo. You will not have a choice as to whether you receive Snus or placebo and neither you nor the study doctor will know which of the study products you are receiving, however, this information can be made available if medically necessary. Over the next 4 weeks, you will become familiar with the product and will try to refrain from cigarettes by using this product when you feel the urge to smoke. The Snus/placebo packet is to be placed under the upper lip and may be held for up to 60 minutes. You will be instructed to use the Snus/placebo when you feel the urge to smoke. If after 15 to 20 minutes of using this product you still feel the urge to smoke, you may do so provided that you remove the Snus/placebo from your mouth. You will be encouraged to gradually substitute as many cigarettes with Snus as possible and to refrain from all cigarettes at the latest by the first day of Week 5. You will use the study product for a total of 12 weeks (study product will be discontinued at the Week 16 visit). You will be asked to what extent you have replaced cigarettes with the study product and your breath will be analyzed for

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Signature 3/16/09 Date

Initials: _____
Date: _____

carbon monoxide (CO), a gas that is found in the breath of smokers. You will receive an educational booklet on the hazards of smoking and will be provided brief counseling at each visit. After the interventional phase, your progress will be followed for an additional 12 weeks.

The Snus/placebo products come in two sizes, a 1 gram size (typically replaces one cigarette) and a 0.5 gram size. You will be encouraged to use at least five 1 gram Snus/placebo sachets per day (or ten sachets if you chose the 0.5 gram sachet). The recommended maximum number of 1 gram sachets per day is 24. However, this number may be increased in heavy smokers (15-20 cigarettes per day) who try to replace all cigarettes with study product.

The Snus/placebo study product is for your use only and is not to be given to anyone else. The Snus/placebo study product should be kept refrigerated. The Snus/placebo study product must be kept out of the reach of children and those of limited mental capacity. Snus will not be provided to you as part of the trial after Week 16 of the Study.

SCREENING

The Screening Phase will consist of an Information Session and Screening Visit (which may be scheduled consecutively at one session at the study doctor's discretion). During the Information Session, you will receive information on the health risks associated with a range of nicotine products including: cigarettes, non-Snus smokeless tobacco, Snus, and nicotine replacement therapy. Possible alternatives to the use of Snus will be described. The effects of nicotine on the body and an account will be given of experience with Snus, including potential health risks associated with different smokeless tobacco products.

At the Screening Visit you will sign this informed consent form after all of your questions have been answered and if you are willing to participate in this study. A complete medical history will be recorded. This will include your history of smoking (i.e., at what age you started to smoke, average number of cigarettes smoked per day during the past year, history of quit attempts, your desire to quit smoking, history of nicotine replacement therapy and/or other drugs or aids used in attempts to quit smoking, history of previous smokeless tobacco use). A physical examination including the inside of your mouth, measurement of your vital signs (blood pressure, heart rate, breathing rate and temperature), and height and weight will be performed. An ECG will be performed. Blood and urine samples will be collected for routine laboratory tests including a screening for drugs of abuse. Women who are able to have children will have a pregnancy test. Women between the ages of 45 and 55 will have a Follicular Stimulating Hormone (FSH) test to verify post-menopausal status. You will receive educational materials on smoking cessation from the National Cancer Institute's "Cleaning the Air" booklet and brief counseling (approximately 10 minutes).

You will be permitted to participate in the study at the discretion of the study doctor if the results of the study screening laboratory tests and other assessments are satisfactory. Screening procedures may need to be repeated in order to qualify for this study. You

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3/16/09
Date

Initials: _____
Date: _____

will be advised of the study restrictions and when to report to the clinic to begin the study. You may be considered an alternate for this study until such time that you have received study product.

STUDY PROCEDURES

Study Product test Period (Week 1 through Week 4)

Baseline Visit

You will return to the study clinic within 2 weeks of the Screening Visit. At this visit your eligibility to participate in this study will be reviewed. You will exhale into a device that measures the amount of carbon monoxide (CO) in your breath (CO exhaled air test). Blood samples will be collected for analysis of nicotine metabolites and biomarkers of exposure and/or disease related to tobacco use. You will complete two questionnaires related to your nicotine dependence and symptoms of nicotine withdrawal. After a brief counseling session, you will receive a study diary and study product, either Snus or placebo. In the diary you will record the number and size of the study product that you used and the number of cigarettes that you smoked daily. You should gradually decrease the number of cigarettes that you smoke through the use of the study product.

Week 1 through 4

A study staff member will contact you weekly by phone to review your smoking status, use of the study product, and brief behavioral counseling. You will also be asked how you are feeling. You continue to complete your diary during this portion of the study.

Intervention Phase (Week 5 through Week 16)

Throughout the Intervention Phase you will complete clinic visits and telephone contacts. Telephone contacts will occur at Weeks 8 and 13 and will include a review of your smoking status, use of the study product, how you feel, and brief behavioral counseling.

Clinic Visits (Week 6 and Week 10)

At these visits the following procedures will be performed:

- Your vital signs and weight will be measured
- CO exhaled air test
- Blood samples will be collected for biomarker blood tests (Week 6 only)
- You will complete a questionnaire to evaluate any symptoms of nicotine withdrawal that you might have
- You will receive brief behavioral counseling
- You will receive more study product
- You will be asked how you are feeling
- You will be asked if you are still smoking
- Your diary will be reviewed and you will receive a new diary.

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Signature 3/16/09 Date

Initials: _____
Date: _____

Clinic Visit (Week 16)
At this visit the following procedures will be performed:

- Your vital signs and weight will be measured
- A physical examination will be performed
- An examination of your mouth will be performed
- CO exhaled air test
- You will complete a questionnaire to determine your nicotine dependence
- You will complete a questionnaire to evaluate any symptoms of nicotine withdrawal that you might have
- Blood samples will be collected for biomarker tests
- You will receive brief behavioral counseling
- You will be asked if you are still smoking
- You will be asked how you are feeling
- Your diary will be reviewed for information regarding study product use and compliance.

You will not receive any more study product after this study visit.

Upon completion of the trial, if you have been successful in quitting cigarette smoking, but still require nicotine replacement, it is preferred that you switch to another smokeless tobacco product or nicotine replacement product, such as Nicoderm or Nicorette, rather than begin cigarette smoking again.

If you choose to discontinue your participation in this study prior to Week 16, you will be asked to undergo the procedures outlined above.

Follow-up Phase (Week 17 through Week 28)
Telephone contacts will occur at Weeks 20 and 24 and will include a review of your smoking status and brief behavioral counseling. You will also be asked how you are feeling.

Final Clinic Visit (Week 28)
The following procedures will be performed at this visit:

- Physical examination
- Examination of your mouth
- Your vital signs and weight will be measured
- CO exhaled air test
- You will complete a questionnaire to determine your nicotine dependence
- You will complete a questionnaire to evaluate any symptoms of nicotine withdrawal that you might have
- Blood samples will be collected for biomarker tests
- You will receive brief behavioral counseling
- You will be asked if you are still smoking

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Independent IRB
Signature 3/16/09 Date

Initials: _____
Date: _____

- You will be asked how you are feeling to assess for adverse events
- You will be asked if you have used over-the counter nicotine replacement therapy, smoking cessation services, smokeless tobacco, or smoking products other than cigarettes since week 16.

If you discontinue your participation in this study after Week 16 but prior to Week 28, you will be asked to undergo the procedures outlined above.

If you should develop a visible side effect, such as a skin rash, we may need to take pictures of it for the study records.
The study doctor may require longer observation in the clinic or additional laboratory testing based on the effects of the study product or the results of the laboratory tests as necessary.

Withdrawal Procedures
If you withdraw early from the study, for any reason, you will be asked to complete the lab testing and discharge procedures outlined in the Week 16 or Week 28 sections listed above as applicable.

RESTRICTIONS

MAY I HAVE...?

- Tobacco or Nicotine-Containing Products: You may continue to use your usual brand of cigarettes according to the study design, however, you may not use any other tobacco or nicotine-containing products throughout the study including: pipes, cigarillos, snuff, and chewing tobacco. Over-the-counter nicotine replacement products are prohibited during the study.

- Drugs for smoking cessation: You must not have used any smoking cessation drugs (i.e., Wellbutrin®, Chantix®) for at least 3 months prior to the start of the study.

- Other Medications: You may use other medications with the knowledge and approval of the study doctor.

Blood Sampling
Blood samples will be taken approximately 5 times throughout the course of the study, (including screening and 6 outpatient clinic visits). Approximately 230 mL of blood, (somewhat less than 1 cup), will be drawn throughout the study. Additional blood samples may be required if any of your lab values are abnormal. It is possible that more than one attempt to obtain a blood sample may be necessary.

For comparison, a standard blood donation at a blood collection center, once in any 56-day period, is about 2 cups of blood. Additional blood samples may be drawn during the study if the study doctor considers it necessary for monitoring your health.

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Signature
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Research Participant Responsibilities
As a research participant you will be asked to complete the study procedures for this study, come to the study clinic for all of your scheduled visits, follow the instructions listed in this informed consent form, and notify the study doctor if any information regarding your health or availability to participate in this study changes.

STUDY DOCTOR AVAILABILITY
In the event of any type of medical emergency, the study doctor will be on call and available, throughout the study.

RISKS AND DISCOMFORTS
There may be risks to you if you participate in this study. According to the Surgeon General and other public health authorities, all tobacco products carry significant risks. There may also be social and/or personal adjustments to switching products or quitting.

Tobacco-burning cigarettes are required by law to carry one of four warning labels. The four warning labels for these products are:

•SURGEON GENERAL'S WARNING: Smoking Causes Lung Cancer, Heart Disease, Emphysema, and May Complicate Pregnancy.
•SURGEON GENERAL'S WARNING: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health.
•SURGEON GENERAL'S WARNING: Smoking by Pregnant Women May Result in Fetal Injury, Premature Birth, and Low Birth Weight.
•SURGEON GENERAL'S WARNING: Cigarette Smoke Contains Carbon Monoxide
.

Oral tobacco products: Snus is an oral tobacco product and is required to carry one of three warnings:
• WARNING: This product may cause mouth cancer.
• WARNING: This product may cause gum disease and tooth loss.
• WARNING: This product is not a safe alternative to cigarettes.

The use of Snus has been associated with oral lesions. The use fo Snus may increase your risk of cardiovascular disease including heart attack.

Nicotine Overdose
It is possible that you may experience symptoms of nicotine overdose with excessive use of the Snus particularly if you are still smoking. Typical symptoms include nausea, vomiting, diarrhea, stomach pain, cold sweat, problems with hearing or vision, rapid or uneven heartbeats, and chest pain. In its most severe form nicotine overdose can lead to seizures and death.

Effects of Quitting Smoking
Generally, any risks of smoking cessation are far outweighed by the benefits. Nevertheless, it is reasonable to prepare for the discomforts of stopping smoking:

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Independent IRB
Signature 3/16/09 Date

Initials: _____
Date: _____

- Symptoms of withdrawal are common as patients attempt to stop smoking. Withdrawal symptoms can include insomnia, irritability, frustration or anger, anxiety, difficulty concentrating, restlessness, a decreased heart rate and an intense craving for cigarettes.

- Some people who stop smoking experience depression; this can be severe enough that it requires counseling or antidepressant medication. Symptoms of sleeplessness, emotional irritability, sadness, inattention, or other signs of depression should be discussed with the Study Doctor or study staff.

- Weight gain can occur with smoking cessation because people tend to eat more after quitting. The average weight gain is eight to 10 pounds. An exercise program and dieting can minimize weight gain. The benefits of quitting smoking are much greater than the risk of gaining weight.

Study Procedure Risk

During the collection of blood samples, you may experience pain and/or bruising at the insertion site of the needle. Although rare, localized clot formation and infections may occur. Lightheadedness and/or fainting may also occur during or shortly after the blood draw.

UNKNOWN/UNFORESEEABLE RISKS

In addition to the risks listed above, there may be some unknown or infrequent and unforeseeable risks associated with the use of this study product, including allergic reaction or interaction with medications. You will be informed in a timely manner both verbally and in writing of any new information, findings or changes to the way the research will be performed that might influence your willingness to continue your participation in this study.

RISKS TO THE UNBORN

Pregnancy/Fetal Risks: The Surgeon General's warnings for cigarette smoking state that smoking by pregnant women may complicate pregnancy and may result in fetal injury, premature birth, low birth weight, and therefore **may be hazardous.** The use of Snus was associated with increased risk of preterm delivery and preeclampsia (a dangerous and potentially fatal complication of pregnancy).

If you think that you have become pregnant during the study it is important that you inform the study doctor immediately. If you become pregnant or think that you may be pregnant, you will be removed from the study and the study doctor will refer you to seek obstetric care, the cost of which will be your responsibility. The study doctor may request to track your pregnancy and will report the pregnancy and outcome to the Sponsor and the IRB.

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Signature 3/16/09 Date

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Date: _____

BIRTH CONTROL REQUIREMENTS

Female: Women of childbearing potential must have been practicing one of the following methods of birth control for at least one month prior to the start of the study and agree to continue practicing it during the study: hormonal contraceptives, intrauterine device (IUD), spermicide and barrier (i.e., condom, diaphragm or cervical cap with spermicidal foam, gel, film or suppository), spouse/partner sterility; or is practicing abstinence and agrees to continue abstinence or to start an acceptable method of contraception from the above list if sexual activity starts.

Women that smoke and use hormonal contraceptives (pills, patches, etc.) are at increased risk of blood clots.

BENEFITS

Your participation in this study may help to stop smoking but there is no guarantee that it will decrease your dependence on nicotine.

Participation in this study is purely for research purposes, and participation in this study will not improve your health or treat any medical problem you may have.

You may benefit by having physical examinations. The results of laboratory tests done at the screening visit will be made available to you. However, if you test positive for any unauthorized drugs or alcohol, all the tests may not be completed.

COST

There is no cost for participating in this research study. The study sponsor pays all the study costs.

PAYMENT FOR BEING IN THE STUDY

You will be paid for taking part in this study as outlined below. This is to compensate you for your time and travel. Each portion of the study has a monetary value assigned to it, which accumulates as you participate in this study.

Payment Schedule

Screening Visit	$0.00 Site to assign per their discretion
Outpatient Clinic Visits $125.00 x 5 visits	$625.00
Telephone contacts $50.00 x 8 contacts	$400.00
TOTAL	$1,025.00

Total compensation for study completion will be $1,025.00. If you choose to withdraw from the study, you will receive payment only for the days that you have completed as outlined above. If it is necessary for you to return to the clinic for additional safety follow up visits, you will be paid $150.00 for each completed visit.

All research participants will be paid within 10 business days of the completion of their participation in the study depending on the number of visits they completed.

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Independent IRB
Signature 3/16/09 Date

Initials: _____
Date: _____

In agreeing to participate in this study, you will be acting as an independent contractor, not as an employee of Covance Clinical Research Unit, Inc. Because payments made to you for participating in this study will be reported to the IRS as income, you are required to provide your social security number as required by law. No deductions for any state or federal withholding or any other similar taxes will be made. It is the responsibility of the participant to report this compensation on state and federal tax returns and for the payment of any taxes that are due on this compensation.

The Internal Revenue Service (IRS) requires Covance to deduct 30% from the final payment when participants are foreign nationals who do not have a Social Security or Tax identification number.

TREATMENT ALTERNATIVE

You do not have to participate in this study in order to quit smoking. There are several FDA approved over-the-counter and prescription medications that assist people to quit smoking. Some of these medications include: Nicotine Replacement Therapy (i.e., nicotine gum, lozenges and patches) which can be obtained over-the-counter and prescription medications like Wellbutrin® and Chantix®.

RIGHT TO WITHDRAW OR REMOVAL FROM STUDY

You are free to withdraw from this study at any time, and you agree to inform the study doctor immediately if you intend to withdraw for any reason. To terminate your participation in this study, you must contact the study doctor at the contact information listed on page one of this informed consent form. You may be asked to come to the study clinic or doctor's office to complete some end of study procedures which are listed in the Withdrawal Procedures section of this document. Your decision to participate in this study or to withdraw from this study will not influence the availability of your future medical care and will involve no penalty or loss of benefits to which you are otherwise entitled. You may withdraw from this study at any time.

You agree that the study doctor in charge of the study can remove you from this study without your consent for any reason, including, but not limited to:

a. His/her judgment that any condition or circumstance may jeopardize your welfare such as increased risk, change in potential benefit, or the integrity of the study.
b. Your failure to follow the instructions of the study doctor(s).
c. If the study is stopped by the sponsor and/or doctors participating in the study prior to completion.

OFFER TO ANSWER ANY QUESTIONS ABOUT THIS STUDY

If you have any questions, concerns, or complaints during this study, or if you think you may have experienced a research-related injury, you should contact Randall R. Stoltz, MD at (812) 474-5000 or (800) 552-4434.

APPROVED BY
Independent IRB
Signature
3/16/09
Date

Initials: _____
Date: _____

If you have any questions regarding your rights as a research participant, please contact Kim Lerner, Chair of the Independent Investigational Review Board, Inc. at toll free 1-(877) 888-iirb (4472) during regular working hours. You can also contact the Independent Investigational Review Board, Inc. if you would like to report problems in a research study, express concerns, ask questions, request information, or provide input. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of participants in a research study. For more information about your rights and role as a research participant you can visit the Research Participant section of the IIRB, Inc. website at www.iirb.com.

CONFIDENTIALITY/MEDICAL RECORDS

If you agree to take part in the research, information about your health and your participation will be collected and recorded by the study doctor. This information will contain your full name and address, and may contain other information about you such as your initials and date of birth. Your name will not be disclosed outside the clinic unless required by law.

Sponsor, representatives of the Sponsor, US Food and Drug Administration (FDA), health authorities and the Independent IRB may inspect your medical records which may include your name, address and other personal information that identifies you. If necessary, some or all of your medical records may be copied during these inspections. The purpose of these inspections is to make sure that the study is carried out correctly. We may also have to disclose records when legally required by state law and local agencies (i.e. reportable diseeases).

The results of this research may be presented at meetings or in publications. However, you will not be personally identified in any presentations or publications.

Because of the need to use information as noted above, absolute confidentiality cannot be guaranteed.

BUSINESS CONFIDENTIALITY

The information and any materials or items that you are given about or during the study - such as information identifying the research unit, the sponsor, any study drug(s), and/or the type of study being performed - should be considered confidential business information of Covance and the study sponsor. You are of course free to discuss such information under confidence with your doctor or with your friends and family while considering whether to participate in this study or at any time when discussing your present or future healthcare. However, distributing confidential business information as described above to the media or posting it on the internet is prohibited.

IN CASE OF INJURY

Your safety is the major concern of every member of the staff. Please contact the study staff as soon as possible if you have side effects or injuries. The phone number for Covance is (812) 474-5000 or (800) 552-4434.

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Initials: _____
Date: _____

Covance will provide immediate medical treatment and follow-up care, without cost to you, for side effects or injuries caused by being in this study. The costs for any other medical problems not caused by being in this study are your responsibility. Financial compensation for such things as lost wages, disability or discomfort due to injury is not available.

You **DO NOT** waive any of your legal rights by signing this form.

CLOSING STATEMENT

You have read the information which has been stated above and have received satisfactory answers to all of the questions which you have asked and you willingly sign and initial each page of this consent form. You will receive a copy of the signed informed consent. You hereby consent to be a participant in this study.

I volunteer to take part in this study of my own free will. I understand that I may withdraw my consent at any time.

SIGNATURES

Please read the following paragraph out loud to the person obtaining the consent.

I have read in a language that I understand well, the above information. The content and meaning of this information has been explained to me. **I have asked the staff any questions I may have and have had enough time to decide if I want to take part in this study.** I hereby voluntarily consent and offer to take part in this study and authorize the use and disclosure of my medical information.

_____	_____	_____
Date/Time	Print Participant Name	Participant Signature

COVANCE STAFF ONLY

Date/ Scientific Time	Name of Person Conducting Informed Consent Discussion	Signature of Person Conducting the Informed Consent Discussion

Copy of consent form given to subject on (date) _____ by (initials) _____

Independent Investigational Review Board, Inc.
Approved: 11/18/08; Revised: 12/30/08, 1/20/09, 3/16/09

APPROVED BY
Independent IRB
Signature 3/16/09 Date

Initials: _____
Date: _____

Sample Volunteer Information and Consent Form - Dallas (14 July 2009)

INFORMED CONSENT AUTHORIZATION TO PARTICIPATE IN A CLINICAL INVESTIGATION

Title: (Protocol #: SM 08-01) A Controlled Study of the Ability of a Traditional Swedish Smokeless Tobacco Product ("Snus") to Increase the Quit Rate Among Cigarette Smokers Who Wish to Stop Smoking

Principal Investigator: William W. Lewis, MD
(Main Study Doctor)

Site of Investigation: Covance CRU, Inc.
1341 West Mockingbird Lane, Suite 300E and 400 E
Dallas, TX 75247

Telephone #: (214) 920-9053

24 hour Telephone #: (972) 955-5373

Sponsor: Swedish Match AB

Participant's Name:_____

You are being asked to participate in a tobacco-switching research study because you currently smoke cigarettes and desire to stop smoking. Your decision to participate in this study is voluntary. If you decide to participate in the study and then change your mind, you can leave the study at any time. However, before you give your consent to be a volunteer, we want you to read the following and ask as many questions as necessary to be sure that you understand what your participation would involve.

Covance Clinical Research Unit Inc. is paid to test investigational products. The study doctors in this study work for Covance, but do not have a financial interest in the outcome of this study

NATURE AND PURPOSE OF THE STUDY

Snus is a smokeless tobacco product made from ground tobacco leaves, water, and food-allowed additives in a paper sachet (packet) that is placed under the upper lip. The placement of the Snus under the upper lip means that there is no need to spit as in other oral tobacco products. Snus is commonly used in Sweden as an alternative to smoking tobacco.

The purpose of this study is to examine if the use of Snus compared to placebo (inactive ingredients manufactured to appear the same as Snus) can increase the quit rate among cigarette smokers who wish to stop smoking. Withdrawal symptoms will be examined and tobacco dependence will be measured. The safety of Snus compared to placebo will be examined. Blood samples will be collected to study breakdown products

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of nicotine and biological indicators related to tobacco use. This study is not intended to eliminate your tobacco dependence.

RESEARCH PARTICIPANT SELECTION

You have been offered an opportunity to participate in this research study because you are a male or female between the ages of 25 and 65 years of age, (inclusive) who has smoked at least 10 cigarettes a day for at least one year and desires to quit smoking. You must otherwise be healthy.

If you are a woman, you must not be pregnant or breast feeding. Women of childbearing potential must have been practicing one of the following methods of birth control for at least one month prior to the start of the study and agree to continue practicing it during the study: hormonal contraceptives, intrauterine device (IUD), spermicide and barrier (i.e., condom, diaphragm or cervical cap with spermicidal foam, gel, film or suppository), spouse/partner sterility; or is practicing abstinence and agrees to continue abstinence or to start an acceptable method of contraception from the above list if sexual activity starts.

It is important that you answer all of the screening questions completely. You must disclose all past and present diseases, allergies and all medications that you are taking, including prescription and non prescription drugs.

Approximately 250 volunteers will be enrolled in this multi site research study.

STUDY DURATION

The duration of your participation in this study is approximately 30 weeks including the screening visit. This study requires 6 outpatient clinic visits (screening, baseline, Weeks 6, 10, 16 and 28) and 8 telephone contacts (Weeks 1, 2, 3, 4, 8, 13, 20 and 24).

STUDY DESIGN

The study consists of four phases: Screening (up to 2 weeks), Study Product Test Period (4 weeks), Intervention Phase (approximately 12 weeks), and a Follow-up Phase (approximately 12 weeks). If you are interested, you will be invited to the clinic to attend an Information Session and Screening visit to determine if you are eligible to participate. During the Baseline visit, you will be randomly (by chance) assigned to receive either Snus or placebo. You will have an equal chance of receiving either Snus or placebo. You will not have a choice as to whether you receive Snus or placebo and neither you nor the study doctor will know which of the study products you are receiving, however, this information can be made available if medically necessary. Over the next 4 weeks, you will become familiar with the product and will try to refrain from cigarettes by using this product when you feel the urge to smoke. The Snus/placebo packet is to be placed under the upper lip and may be held for up to 60 minutes. You will be instructed to use the Snus/placebo when you feel the urge to smoke. If after 15 to 20 minutes of using this product you still feel the urge to smoke, you may do so provided that you remove the Snus/placebo from your mouth. You will be encouraged to gradually substitute as many cigarettes with Snus as possible and to refrain from all cigarettes at the latest by

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Signature
7/14/09
Date

the first day of Week 5. You will use the study product for a total of 12 weeks (study product will be discontinued at the Week 16 visit). You will be asked to what extent you have replaced cigarettes with the study product and your breath will be analyzed for carbon monoxide (CO), a gas that is found in the breath of smokers. You will receive an educational booklet on the hazards of smoking and will be provided brief counseling at each visit. After the interventional phase, your progress will be followed for an additional 12 weeks.

The Snus/placebo products come in two sizes, a 1 gram size (typically replaces one cigarette) and a 0.5 gram size. You will be encouraged to use at least five 1 gram Snus/placebo sachets per day (or ten sachets if you chose the 0.5 gram sachet). The recommended maximum number of 1 gram sachets per day is 24. However, this number may be increased in heavy smokers (15-20 cigarettes per day) who try to replace all cigarettes with study product.

The Snus/placebo study product is for your use only and is not to be given to anyone else. The Snus/placebo study product should be kept refrigerated. The Snus/placebo study product must be kept out of the reach of children and those of limited mental capacity. Snus will not be provided to you as part of the trial after Week 16 of the Study.

SCREENING

The Screening Phase will consist of an Information Session and Screening Visit (which may be scheduled consecutively at one session at the study doctor's discretion). During the Information Session, you will receive information on the health risks associated with a range of nicotine products including: cigarettes, non-Snus smokeless tobacco, Snus, and nicotine replacement therapy. Possible alternatives to the use of Snus will be described. The effects of nicotine on the body and an account will be given of experience with Snus, including potential health risks associated with different smokeless tobacco products.

At the Screening Visit you will sign this informed consent form after all of your questions have been answered and if you are willing to participate in this study. A complete medical history will be recorded. This will include your history of smoking (i.e., at what age you started to smoke, average number of cigarettes smoked per day during the past year, history of quit attempts, your desire to quit smoking, history of nicotine replacement therapy and/or other drugs or aids used in attempts to quit smoking, history of previous smokeless tobacco use). A physical examination including the inside of your mouth, measurement of your vital signs (blood pressure, heart rate, breathing rate and temperature), and height and weight will be performed. An ECG will be performed. Blood and urine samples will be collected for routine laboratory tests including a screening for drugs of abuse, HIV and hepatitis. Women who are able to have children will have a pregnancy test. Women between the ages of 45 and 55 will have a Follicular Stimulating Hormone (FSH) test to verify post-menopausal status. You will receive educational materials on smoking cessation from the National Cancer Institute's "Cleaning the Air" booklet and brief counseling (approximately 10 minutes).

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Signature
7/14/09
Date

Positive results for hepatitis and HIV must be reported to a local health agency. This is the legal obligation of health professionals in this state. Based on state law or research unit policy, you may be asked to sign a separate HIV consent form. If you are disqualified for study participation by other screening procedures or if you do not complete the screening visit, it is possible that this testing will not be completed.

You will be permitted to participate in the study at the discretion of the study doctor if the results of the study screening laboratory tests and other assessments are satisfactory. Screening procedures may need to be repeated in order to qualify for this study. You will be advised of the study restrictions and when to report to the clinic to begin the study. You may be considered an alternate for this study until such time that you have received study product.

STUDY PROCEDURES

Study Product test Period (Week 1 through Week 4)

Baseline Visit

You will return to the study clinic within 2 weeks of the Screening Visit. At this visit your eligibility to participate in this study will be reviewed. You will exhale into a device that measures the amount of carbon monoxide (CO) in your breath (CO exhaled air test). Blood samples will be collected for analysis of nicotine metabolites and biomarkers of exposure and/or disease related to tobacco use. You will complete two questionnaires related to your nicotine dependence and symptoms of nicotine withdrawal. After a brief counseling session, you will receive a study diary and study product, either Snus or placebo. In the diary you will record the number and size of the study product that you used and the number of cigarettes that you smoked daily. You should gradually decrease the number of cigarettes that you smoke through the use of the study product.

Week 1 through 4

A study staff member will contact you weekly by phone to review your smoking status, use of the study product, and brief behavioral counseling. You will also be asked how you are feeling. You continue to complete your diary during this portion of the study.

Intervention Phase (Week 5 through Week 16)

Throughout the Intervention Phase you will complete clinic visits and telephone contacts. Telephone contacts will occur at Weeks 8 and 13 and will include a review of your smoking status, use of the study product, how you feel, and brief behavioral counseling.

Clinic Visits (Week 6 and Week 10)

At these visits the following procedures will be performed:

- Your vital signs and weight will be measured
- CO exhaled air test
- Blood samples will be collected for biomarker blood tests (Week 6 only)
- You will complete a questionnaire to evaluate any symptoms of nicotine withdrawal that you might have

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Independent IRB
Signature 7/14/09 Date

- You will receive brief behavioral counseling
- You will receive more study product
- You will be asked how you are feeling
- You will be asked if you are still smoking
- Your diary will be reviewed and you will receive a new diary.

Clinic Visit (Week 16)
At this visit the following procedures will be performed:

- Your vital signs and weight will be measured
- A physical examination will be performed
- An examination of your mouth will be performed
- CO exhaled air test
- You will complete a questionnaire to determine your nicotine dependence
- You will complete a questionnaire to evaluate any symptoms of nicotine withdrawal that you might have
- Blood samples will be collected for biomarker tests
- You will receive brief behavioral counseling
- You will be asked if you are still smoking
- You will be asked how you are feeling
- Your diary will be reviewed for information regarding study product use and compliance.

You will not receive any more study product after this study visit.

Upon completion of the trial, if you have been successful in quitting cigarette smoking, but still require nicotine replacement, it is preferred that you switch to another smokeless tobacco product or nicotine replacement product, such as Nicoderm or Nicorette, rather than begin cigarette smoking again.

If you choose to discontinue your participation in this study prior to Week 16, you will be asked to undergo the procedures outlined above.

Follow-up Phase (Week 17 through Week 28)
Telephone contacts will occur at Weeks 20 and 24 and will include a review of your smoking status and brief behavioral counseling. You will also be asked how you are feeling.

Final Clinic Visit (Week 28)
The following procedures will be performed at this visit:

- Physical examination
- Examination of your mouth
- Your vital signs and weight will be measured
- CO exhaled air test

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Signature 7/14/09 Date

- You will complete a questionnaire to determine your nicotine dependence
- You will complete a questionnaire to evaluate any symptoms of nicotine withdrawal that you might have
- Blood samples will be collected for biomarker tests
- You will receive brief behavioral counseling
- You will be asked if you are still smoking
- You will be asked how you are feeling to assess for adverse events
- You will be asked if you have used over-the counter nicotine replacement therapy, smoking cessation services, smokeless tobacco, or smoking products other than cigarettes since week 16.

If you discontinue your participation in this study after Week 16 but prior to Week 28, you will be asked to undergo the procedures outlined above.

If you should develop a visible side effect, such as a skin rash, we may need to take pictures of it for the study records.

The study doctor may require longer observation in the clinic or additional laboratory testing based on the effects of the study product or the results of the laboratory tests as necessary.

Withdrawal Procedures

If you withdraw early from the study, for any reason, you will be asked to complete the lab testing and discharge procedures outlined in the Week 16 or Week 28 sections listed above as applicable.

RESTRICTIONS

MAY I HAVE...?

- Tobacco or Nicotine-Containing Products: You may continue to use your usual brand of cigarettes according to the study design, however, you may not use any other tobacco or nicotine-containing products throughout the study including: pipes, cigarillos, snuff, and chewing tobacco. Over-the-counter nicotine replacement products are prohibited during the study.

- Drugs for smoking cessation: You must not have used any smoking cessation drugs (i.e., Wellbutrin®, Chantix®) for at least 3 months prior to the start of the study.

- Other Medications: You may use other medications with the knowledge and approval of the study doctor.

Blood Sampling

Blood samples will be taken approximately 5 times throughout the course of the study, (including screening and 6 outpatient clinic visits). Approximately 230 mL of blood, (somewhat less than 1 cup), will be drawn throughout the study. Additional blood

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samples may be required if any of your lab values are abnormal. It is possible that more than one attempt to obtain a blood sample may be necessary.

For comparison, a standard blood donation at a blood collection center, once in any 56-day period, is about 2 cups of blood. Additional blood samples may be drawn during the study if the study doctor considers it necessary for monitoring your health.

Research Participant Responsibilities
As a research participant you will be asked to complete the study procedures for this study, come to the study clinic for all of your scheduled visits, follow the instructions listed in this informed consent form, and notify the study doctor if any information regarding your health or availability to participate in this study changes.

STUDY DOCTOR AVAILABILITY
In the event of any type of medical emergency, the study doctor will be on call and available, throughout the study.

RISKS AND DISCOMFORTS
There may be risks to you if you participate in this study. According to the Surgeon General and other public health authorities, all tobacco products carry significant risks. There may also be social and/or personal adjustments to switching products or quitting.

Tobacco-burning cigarettes are required by law to carry one of four warning labels. The four warning labels for these products are:

•SURGEON GENERAL'S WARNING: Smoking Causes Lung Cancer, Heart Disease, Emphysema, and May Complicate Pregnancy.
•SURGEON GENERAL'S WARNING: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health.
•SURGEON GENERAL'S WARNING: Smoking by Pregnant Women May Result in Fetal Injury, Premature Birth, and Low Birth Weight.
•SURGEON GENERAL'S WARNING: Cigarette Smoke Contains Carbon Monoxide

Oral tobacco products: Snus is an oral tobacco product and is required to carry one of three warnings:
• WARNING: This product may cause mouth cancer.
• WARNING: This product may cause gum disease and tooth loss.
• WARNING: This product is not a safe alternative to cigarettes.

The use of Snus has been associated with oral lesions. The use of Snus may increase your risk of cardiovascular disease including heart attack.

Nicotine Overdose
It is possible that you may experience symptoms of nicotine overdose with excessive use of the Snus particularly if you are still smoking. Typical symptoms include nausea, vomiting, diarrhea, stomach pain, cold sweat, problems with hearing or vision, rapid or

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uneven heartbeats, and chest pain. In its most severe form nicotine overdose can lead to seizures and death.

Effects of Quitting Smoking

Generally, any risks of smoking cessation are far outweighed by the benefits. Nevertheless, it is reasonable to prepare for the discomforts of stopping smoking:

- Symptoms of withdrawal are common as patients attempt to stop smoking. Withdrawal symptoms can include insomnia, irritability, frustration or anger, anxiety, difficulty concentrating, restlessness, a decreased heart rate and an intense craving for cigarettes.

- Some people who stop smoking experience depression; this can be severe enough that it requires counseling or antidepressant medication. Symptoms of sleeplessness, emotional irritability, sadness, inattention, or other signs of depression should be discussed with the Study Doctor or study staff.

- Weight gain can occur with smoking cessation because people tend to eat more after quitting. The average weight gain is eight to 10 pounds. An exercise program and dieting can minimize weight gain. The benefits of quitting smoking are much greater than the risk of gaining weight.

Study Procedure Risk

During the collection of blood samples, you may experience pain and/or bruising at the insertion site of the needle. Although rare, localized clot formation and infections may occur. Lightheadedness and/or fainting may also occur during or shortly after the blood draw.

UNKNOWN/UNFORESEEABLE RISKS

In addition to the risks listed above, there may be some unknown or infrequent and unforeseeable risks associated with the use of this study product, including allergic reaction or interaction with medications. You will be informed in a timely manner both verbally and in writing of any new information, findings or changes to the way the research will be performed that might influence your willingness to continue your participation in this study.

RISKS TO THE UNBORN

Pregnancy/Fetal Risks: The Surgeon General's warnings for cigarette smoking state that smoking by pregnant women may complicate pregnancy and may result in fetal injury, premature birth, low birth weight, and therefore **may be hazardous.** The use of Snus was associated with increased risk of preterm delivery and preeclampsia (a dangerous and potentially fatal complication of pregnancy).

If you think that you have become pregnant during the study it is important that you inform the study doctor immediately. If you become pregnant or think that you may be pregnant, you will be removed from the study and the study doctor

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will refer you to seek obstetric care, the cost of which will be your responsibility. The study doctor may request to track your pregnancy and will report the pregnancy and outcome to the Sponsor and the IRB.

BIRTH CONTROL REQUIREMENTS

Female: Women of childbearing potential must have been practicing one of the following methods of birth control for at least one month prior to the start of the study and agree to continue practicing it during the study: hormonal contraceptives, intrauterine device (IUD), spermicide and barrier (i.e., condom, diaphragm or cervical cap with spermicidal foam, gel, film or suppository), spouse/partner sterility; or is practicing abstinence and agrees to continue abstinence or to start an acceptable method of contraception from the above list if sexual activity starts.

Women that smoke and use hormonal contraceptives (pills, patches, etc.) are at increased risk of blood clots.

BENEFITS

Your participation in this study may help to stop smoking but there is no guarantee that it will decrease your dependence on nicotine.

Participation in this study is purely for research purposes, and participation in this study will not improve your health or treat any medical problem you may have.

You may benefit by having physical examinations. The results of laboratory tests done at the screening visit will be made available to you. However, if you test positive for any unauthorized drugs or alcohol, all the tests may not be completed.

COST

There is no cost for participating in this research study. The study sponsor pays all the study costs.

PAYMENT FOR BEING IN THE STUDY

You will be paid for taking part in this study as outlined below. This is to compensate you for your time and travel. Each portion of the study has a monetary value assigned to it, which accumulates as you participate in this study.

Payment Schedule

Screening Visit	$0.00
Outpatient Clinic Visits $125.00 x 5 visits	$625.00
Telephone contacts $50.00 x 8 contacts	$400.00
TOTAL	$1,025.00

Total compensation for study completion will be $1,025.00. If you choose to withdraw from the study, you will receive payment only for the days that you have completed as outlined above. If it is necessary for you to return to the clinic for additional safety follow up visits, you will be paid $150.00 for each completed visit.

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All research participants will be paid within 14 business days of the completion of their participation in the study depending on the number of visits they completed.

In agreeing to participate in this study, you will be acting as an independent contractor, not as an employee of Covance Clinical Research Unit, Inc. Because payments made to you for participating in this study will be reported to the IRS as income, you are required to provide your social security number as required by law. No deductions for any state or federal withholding or any other similar taxes will be made. It is the responsibility of the participant to report this compensation on state and federal tax returns and for the payment of any taxes that are due on this compensation.

The Internal Revenue Service (IRS) requires Covance to deduct 30% from the final payment when participants are foreign nationals who do not have a Social Security or Tax identification number.

TREATMENT ALTERNATIVE

You do not have to participate in this study in order to quit smoking. There are several FDA approved over-the-counter and prescription medications that assist people to quit smoking. Some of these medications include: Nicotine Replacement Therapy (i.e., nicotine gum, lozenges and patches) which can be obtained over-the-counter and prescription medications like Wellbutrin® and Chantix®.

RIGHT TO WITHDRAW OR REMOVAL FROM STUDY

You are free to withdraw from this study at any time, and you agree to inform the study doctor immediately if you intend to withdraw for any reason. To terminate your participation in this study, you must contact the study doctor at the contact information listed on page one of this informed consent form. You may be asked to come to the study clinic or doctor's office to complete some end of study procedures which are listed in the Withdrawal Procedures section of this document. Your decision to participate in this study or to withdraw from this study will not influence the availability of your future medical care and will involve no penalty or loss of benefits to which you are otherwise entitled. You may withdraw from this study at any time.

You agree that the study doctor in charge of the study can remove you from this study without your consent for any reason, including, but not limited to:

a. His/her judgment that any condition or circumstance may jeopardize your welfare such as increased risk, change in potential benefit, or the integrity of the study.
b. Your failure to follow the instructions of the study doctor(s).
c. If the study is stopped by the sponsor and/or doctors participating in the study prior to completion.

OFFER TO ANSWER ANY QUESTIONS ABOUT THIS STUDY

If you have any questions, concerns, or complaints during this study, or if you think you may have experienced a research-related injury, you should contact William W. Lewis, MD at (972) 955-5373.

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If you have any questions regarding your rights as a research participant, please contact Kim Lerner, Chair of the Independent Investigational Review Board, Inc. at toll free 1-(877) 888-iirb (4472) during regular working hours. You can also contact the Independent Investigational Review Board, Inc. if you would like to report problems in a research study, express concerns, ask questions, request information, or provide input. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of participants in a research study. For more information about your rights and role as a research participant you can visit the Research Participant section of the IIRB, Inc. website at www.iirb.com.

CONFIDENTIALITY/MEDICAL RECORDS

If you agree to take part in the research, information about your health and your participation will be collected and recorded by the study doctor. This information will contain your full name and address, and may contain other information about you such as your initials and date of birth. Your name will not be disclosed outside the clinic unless required by law.

Sponsor, representatives of the Sponsor, US Food and Drug Administration (FDA), health authorities and the Independent IRB may inspect your medical records which may include your name, address and other personal information that identifies you. If necessary, some or all of your medical records may be copied during these inspections. The purpose of these inspections is to make sure that the study is carried out correctly. We may also have to disclose records when legally required by state law and local agencies (i.e. reportable diseases).

The results of this research may be presented at meetings or in publications. However, you will not be personally identified in any presentations or publications.

Because of the need to use information as noted above, absolute confidentiality cannot be guaranteed.

BUSINESS CONFIDENTIALITY

The information and any materials or items that you are given about or during the study - such as information identifying the research unit, the sponsor, any study drug(s), and/or the type of study being performed - should be considered confidential business information of Covance and the study sponsor. You are of course free to discuss such information under confidence with your doctor or with your friends and family while considering whether to participate in this study or at any time when discussing your present or future healthcare. However, distributing confidential business information as described above to the media or posting it on the internet is prohibited.

IN CASE OF INJURY

Your safety is the major concern of every member of the staff. Please contact the study staff as soon as possible if you have side effects or injuries. The phone number for Covance is (972) 955-5373.

APPROVED BY
Independent IRB

Signature | 7/14/09 Date

Covance will provide immediate medical treatment and follow-up care, without cost to you, for side effects or injuries caused by being in this study. The costs for any other medical problems not caused by being in this study are your responsibility. Financial compensation for such things as lost wages, disability or discomfort due to injury is not available.

You **DO NOT** waive any of your legal rights by signing this form.

CLOSING STATEMENT

You have read the information which has been stated above and have received satisfactory answers to all of the questions which you have asked and you willingly sign and initial each page of this consent form. You will receive a copy of the signed informed consent. You hereby consent to be a participant in this study.

I volunteer to take part in this study of my own free will. I understand that I may withdraw my consent at any time.

SIGNATURES

Please read the following paragraph out loud to the person obtaining the consent.

I have read in a language that I understand well, the above information. The content and meaning of this information has been explained to me. **I have asked the staff any questions I may have and have had enough time to decide if I want to take part in this study.** I hereby voluntarily consent and offer to take part in this study and authorize the use and disclosure of my medical information.

_____	_____	_____
Date/Time	Print Participant Name	Participant Signature

COVANCE STAFF ONLY

Date/ Scientific Time	Name of Person Conducting Informed Consent Discussion	Signature of Person Conducting the Informed Consent Discussion

Copy of consent form given to subject on (date) _____ by (initials) _____

Independent Investigational Review Board, Inc.
Approved: 6/9/09 Revised: 6/16/09, 7/14/09

APPROVED BY
Independent IRB
Signature 7/14/09
Date