

AMMSYS Research Inc.

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JUN 28 2000

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AMMSYS Research Inc.**

**Process Group — 10 Minutes
2:15 PM — Wednesday, June 28th**

00N-1256

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Rx-to-OTC Switch Considerations

Gerald F. Dunaway, Ph.D.

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A Clinical Research Organization

Rx-to-OTC Switch Considerations

Convey Importance of:

Consumer Behavior Research – Observed
and Recorded in “Actual Use Studies” – to
Switch Decisions

Consumer Understanding

- Consumer Behavior Research
 - Attitude, comprehension and observational research
- Rx-to-OTC Switch
 - Consumer driven process
- Understanding Consumer Behavior
 - Observed and recorded in actual use studies
 - Essential to Rx-to-OTC decision process
 - Evaluated by label comprehension studies
- Rx-to-OTC Use Studies
 - Research tool for observing and documenting consumer behavior

Case for Consumer Behavior Research in “Actual Use Studies”

- A 20-year review of Rx-to-OTC switches documents a progressive need for a better understanding of consumer behavior related to switch studies and switch decisions.

Case for Consumer Behavior Research in “Actual Use Studies”

- Early Phase Switches

- Antihistamines, decongestants provided symptomatic relief
- Limited public health impact
- Consumer behavior not a defining issue

Case for Consumer Behavior Research in “Actual Use Studies”

- Intermediate Phase Switches
 - Easily self-recognizable conditions (heartburn, diarrhea, baldness)
 - Greater public health impact than earlier switches
 - Decreased health care costs
 - Doctor visit not needed
 - Consumer behavior important but not essential to switch decision

Case for Consumer Behavior Research in “Actual Use Studies”

■ Current Phase Switches

- Not as easily self-recognizable (osteoporosis, high cholesterol)
- May require a simple test
- Major public health impact
- Consumer behavior essential to switch decisions

Summary

- Consumer behavior observed and documented in “actual use studies” is essential to current and future switch decisions.
- Studies should be conducted in a “real life” retail environment.
- Most effective tool is the “Actual Use Study.”

Actual Use Study

An Effective Research Tool for:

- Measuring efficacy and safety
- Documenting & demonstrating consumer understanding
- Understanding how consumers interact products
- Determining what the consumer can and will do
- Conducted studies in a 'virtual' retail environment

Actual Use Study

Traditional Static Model

- Often double-blinded/placebo
- Restrictive recruiting
- Non-retail setting
- Cumbersome measurements
- Consumer has little flexibility
- Limited self-selection opportunity
- Limited consumer behavior research
- May not detect unexpected/rare AEs

Actual Use Study Evolving Dynamic Model

- Designed to answer specific safety or efficacy concerns
- Progressive recruiting – “All comers”
- OTC ‘real life’ retail environment
- Unrestrictive measurements
- Lets consumer be consumer
- Self-selection environment
- Maximum consumer flexibility
- Consumers respond to retail environment

Nicotrol® Patch Study

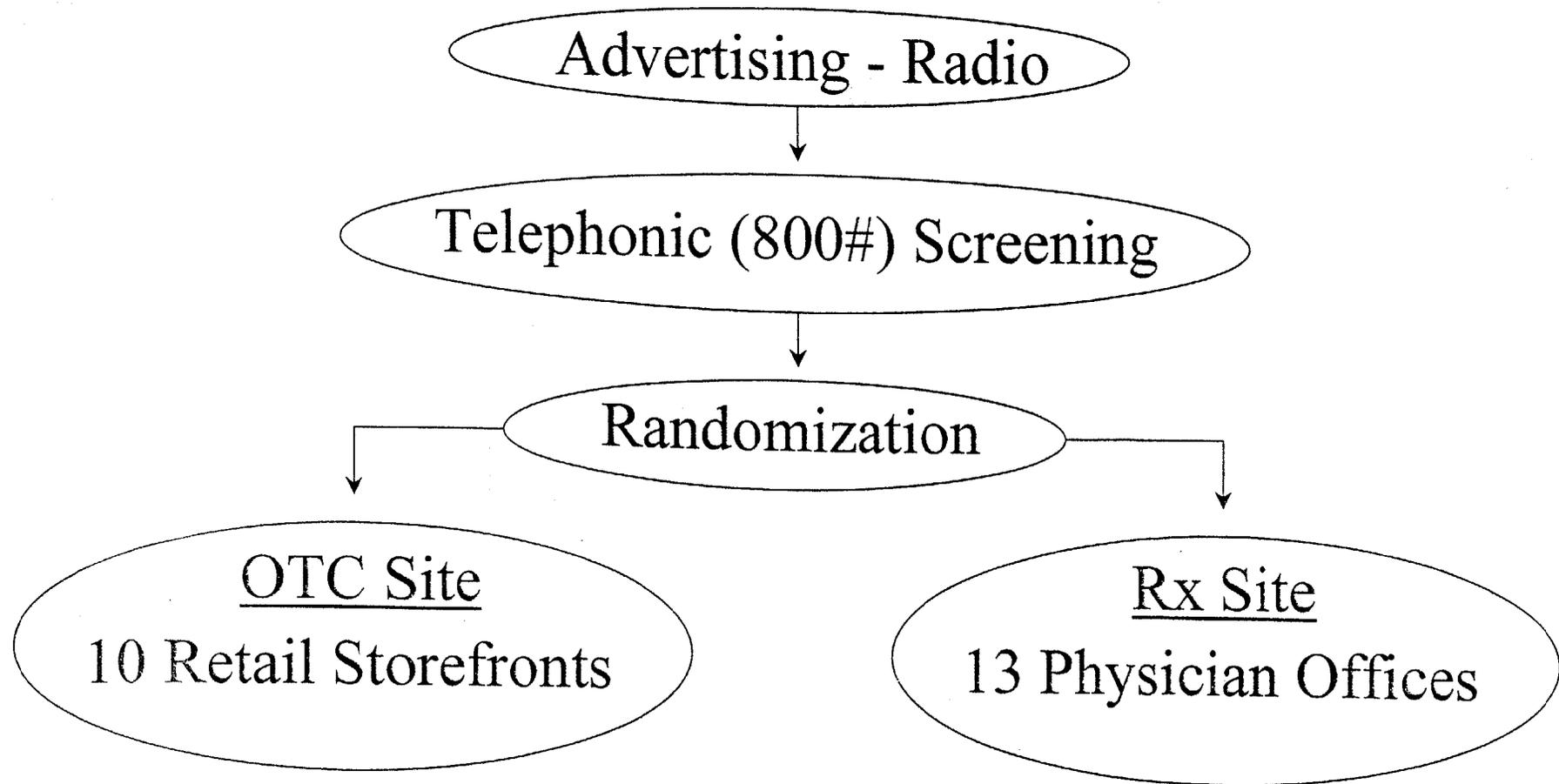
Study Objectives

- Achieve comparable efficacy in OTC and Rx arms
- Create “virtual” OTC retail environment
- Permit patients to self-select

Subsidiary Objectives

- Locate OTC sites in shopping centers/learning points
- Measure consumer response toward behavior modification material/learning points
- Measure consumer attitude toward purchasing study product/learning points
- Measure consumer response to advertising/learning points

Nicotrol® Use Study Flow Chart – 23 Sites



Nicotrol® Market Geographics

A Major U.S. Population Center

■ Area population	5.9 million
■ Smokers	1.2 million
■ Motivated smokers	120,000
■ Sample size	2,500

Nicotrol® - Summary of Enrollment

Total calls received	14,809
Total subjects enrolled*	3,385
Subjects who failed to initiate treatment	150
	(OTC=32 Rx=118)
Total subjects treated	3,235

* Completed enrollment in 4 weeks

Rx-to-OTC Conclusions

- No need for radical change in the Rx-to-OTC process.
- The Rx-to-OTC switch process should be considered on a case-by-case basis.
- Categories of products should not be presumptively excluded from OTC consideration. Research should drive these decisions.

Rx-to-OTC Conclusions

- Rx-to-OTC should be viewed as a consumer driven process. FDA should accept principles of behavioral science as valid research tools.
- FDA should frame questions that concern the agency and charge industry with the responsibility of finding answers.
- “Use studies” with appropriate design features can answer virtually all questions related to what the consumer will do – specifically, self-selection and label compliance issues.

Rx-to-OTC Switch Considerations

Gerald F. Dunaway, Ph.D.
President
AMMSYS Research Inc.
Annapolis, Maryland

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Good Afternoon,

My name is Gerry Dunaway. I am President of AMMSYS Research Inc., a contract research organization headquartered in Annapolis, Maryland. Prior to founding this company, I spent 30+ years with the Procter & Gamble Company in research and marketing management. In this hearing, I represent myself. I do not represent others. I am not being compensated for this presentation.

I want to thank the agency for scheduling these hearings. This is a positive step for both the agency and industry in achieving a better understanding of the Rx-to-OTC process.

My company specializes in designing and conducting large Rx-to-OTC switch studies. We have designed and conducted large multi-site OTC studies for H₂ blockers, NRT, and cholesterol lowering drugs with enrollment ranging from a low of 650 subjects to 3585 subjects.

In the last 36 months, we have conducted 7 large multi-site OTC studies with a total combined enrollment of 14,932 subjects.

The studies we conduct always adhere to the scientific and regulatory 'rigor' of FDA guidelines. However, with the concurrence of the contracting company, we modify the traditional Rx-to-OTC use study methodology to: 1) create a real life retail environment for the OTC arm of the study and 2) observe and document consumer behavior data – self-recognizable conditions, self-selection and label compliance issues.

My comments are directed to the section of the agenda headed "Consumer Understanding." I will address the question: "How can FDA be assured of consumer understanding of the benefits and risks of specific drug products and the ability of consumers to use products safely and effectively were the product to be marketed OTC?"

My response to that questions is: through carefully crafted research questions integrated into actual use studies that are conducted in a "real life" retail environment.

The reason I am here today is to convey the importance of consumer behavior research -- observed and recorded in an actual OTC use study -- to current switch decisions.

(Slide 2 on screen)

Rx-to-OTC Switch Considerations

Convey Importance of:

Consumer Behavior Research – Observed
and Recorded in “Actual Use Studies” – to
Switch Decisions

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Consumer Understanding

- **Consumer Behavior Research**
 - Attitude, comprehension and observational research
- **Rx-to-OTC Switch**
 - Consumer driven process
- **Understanding Consumer Behavior**
 - Observed and recorded in actual use studies
 - Essential to Rx-to-OTC decision process
 - Evaluated by label comprehension studies
- **Rx-to-OTC Use Studies**
 - Research tool for observing and documenting consumer behavior

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A functional definition for consumer behavior related to Rx-to-OTC clinical research is the study of how consumers make decisions about what they can and will do in relation to the study drug and the environment in which it is acquired.

Rx-to-OTC switch should be viewed as a consumer driven process. The consumer is the primary consideration in each step of the decision process: safety, dosing, labeling, self-recognition, self-selection, medical monitoring and health benefits.

Understanding consumer behavior is essential to current switch decisions especially related to self-recognizable and self-selection issues, i.e., What can the consumer do? What will the consumer do?

Consumer behavior research -- conducted as a part of an actual use study -- supplements the label comprehension study. The label comprehension study tells us what the consumer understands. Consumer behavior tells us what the consumer will do. Both are essential to OTC decisions.

The best way to observe and record consumer behavior is through an actual "use study."

(Slide 4 on screen)

Case for Consumer Behavior Research in “Actual Use Studies”

- A 20-year review of Rx-to-OTC switches documents a progressive need for a better understanding of consumer behavior related to switch studies and switch decisions.

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Over the past 20 years, we have been through three phases of Rx-to-OTC switches: early, intermediate and current. We looked at each phase to determine the impact of consumer behavior on switch decisions. Here is what we found.

(Slide 5 on screen)

Case for Consumer Behavior Research in “Actual Use Studies”

- Early Phase Switches
 - Antihistamines, decongestants provided symptomatic relief
 - Limited public health impact
 - Consumer behavior not a defining issue

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Early phase switches included antihistamines, decongestants, etc. These products were not curative in nature, but provided symptomatic relief for the consumer.

The risk factors were low and they had limited public health impact.

Self-recognizable and self-selection issues were not major considerations. Consequently, consumer behavior in relation to the study drug was not a defining issue.

(Slide 6 on screen)

Case for Consumer Behavior Research in “Actual Use Studies”

- Intermediate Phase Switches
 - Easily self-recognizable conditions (heartburn, diarrhea, baldness)
 - Greater public health impact than earlier switches
 - Decreased health care costs
 - Doctor visit not needed
 - Consumer behavior important but not essential to switch decision

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Intermediate phase switches involved easily self-recognizable conditions such as: heartburn, diarrhea and baldness. These products had a greater public health impact than earlier switches.

Consumer behavior in terms of self-recognition and self-selection was important but not essential elements in switch decisions. Consequently, there was no pressing need to design “use studies” to investigate what the consumer would do in using these products.

(Slide 7 on screen)

Case for Consumer Behavior Research in “Actual Use Studies”

■ Current Phase Switches

- Not as easily self-recognizable (osteoporosis, high cholesterol)
- May require a simple test
- Major public health impact
- Consumer behavior essential to switch decisions

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Current phase switches with indications such as osteoporosis and hypercholesterolemia present a new set of questions concerning self-recognizable conditions, self-selection, and consumer compliance that make consumer behavior an integral part of the decision process. These questions in current and future switch decisions can only be answered through consumer research, i.e., “What will the consumer do?”

In some current and future switches, approval will depend almost entirely on answers to the questions “How will the consumer react?” and “What will the consumer do?” These products can have a major positive health impact and that positive impact may very well hang in the balance of how these questions are researched and answered.

(Slide 8 on screen)

Summary

- Consumer behavior observed and documented in “actual use studies” is essential to current and future switch decisions.
- Studies should be conducted in a “real life” retail environment.
- Most effective tool is the “Actual Use Study.”

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Consumer research is essential in current switch decisions. Answers to complex questions surrounding current phase and future switches can and should be discovered through well-crafted research questions and designs that investigate consumer behavior. These questions should be agreed upon by the sponsor and FDA in open collaborative discussions on a case-by-case basis. Research methodologies are available to answer all of these consumer related questions.

To fully understand what the consumer will do, consumer behavior should be observed in a ‘real life’ virtual retail environment.

There are a number of methodologies available. However, to answer self-recognizable and self-selection questions, i.e., What will the consumer do?, requires a ‘real life’ design that can best be implemented as part of an “actual use study.”

(Slide 9 on screen)

Actual Use Study

An Effective Research Tool for:

- Measuring efficacy and safety
- Documenting & demonstrating consumer understanding
- Understanding how consumers interact products
- Determining what the consumer can and will do
- Conducted studies in a 'virtual' retail environment

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And now a few brief comments on how the "actual use study" can be designed to be a very effective research tool in answering the agency's "What will the consumer do?" and "How can we be assured?" questions.

The primary purpose of the use study is to collect and evaluate efficacy and safety data. Beyond this, an appropriately designed use study can measure and document consumer understanding, describe how consumers use products and investigate what the consumer knows and will do under given conditions. With appropriate design features, the use study can produce valid answers to virtually all questions related to product usage and consumer behavior.

The Evolving “Actual Use Study”

The traditional use study is an evolving tool that can be adapted to consumer research data – specifically, self-recognizable and self-selection questions.

The Rx-to-OTC use study is evolving from a static model that tends to restrict and control the study population into a dynamic model that can, with appropriate design features, develop answers for virtually all consumer related questions.

(Slide 10 on screen)

Actual Use Study Traditional Static Model

- Often double-blinded/placebo
- Restrictive recruiting
- Non-retail setting
- Cumbersome measurements
- Consumer has little flexibility
- Limited self-selection opportunity
- Limited consumer behavior research
- May not detect unexpected/rare AEs

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The traditional ‘use study’ model continues to be influenced by the design of phase III use studies. It may be double blind with placebo. The study sample may not represent the universe. The design of the study rigidly controls the participants’ activities and decisions. There is limited consumer input and limited opportunity to observe consumer behavior. The OTC site may be located in a medical environment and the study design may not detect unexpected and/or rare AEs.

The evolving use study model can be designed with features that observe and document consumer behavior.

(Slide 11 on screen)

Actual Use Study Evolving Dynamic Model

- Designed to answer specific safety or efficacy concerns
- Progressive recruiting – “All comers”
- OTC ‘real life’ retail environment
- Unrestrictive measurements
- Lets consumer be consumer
- Self-selection environment
- Maximum consumer flexibility
- Consumers respond to retail environment

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The evolving OTC model is usually open label and less restrictive in recruiting. The study sample is more representative of the universe with a ‘naturalistic’ or ‘all comers’ approach to recruiting. OTC sites are located in a ‘real life’ retail environment and the design of the study requires the participant to actually make self-selection and label compliance decisions. Consumers like this environment. They make better ‘real life’ decisions about the study product in this kind of environment.

The evolving OTC use study model with appropriate designs features, can answer virtually any consumer research question while maintaining the scientific and regulatory rigor required by FDA.

Our company has used this adaptive design for several years. OTC sites in all studies conducted in the last five years have been located in leased storefronts in large active shopping centers. We have also built in design features, as required by the contracting company, to observe and document consumer behavior. Specifically, the consumer's response to self-recognizable and self-selection questions.

An example of the evolving Rx-to-OTC model is the Nicotrol® transdermal nicotine patch study that we did the McNeil Consumer Healthcare Company on the Patch. This was the pivotal study supporting the application to switch Nicotrol®.

(Slide 12 on screen)

This is a quick overview of the Nicotrol® study and results..

Nicotrol® Patch Study Study Objectives

- Achieve comparable efficacy in OTC and Rx arms
- Create “virtual” OTC retail environment
- Permit patients to self-select

Subsidiary Objectives

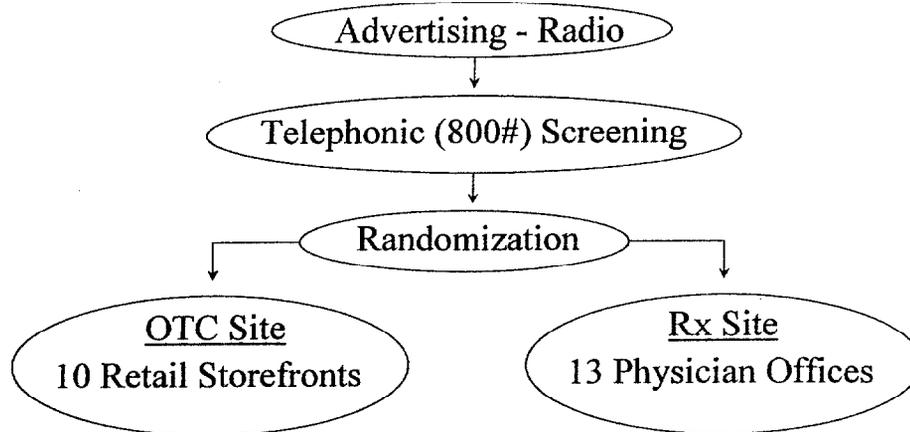
- Locate OTC sites in shopping centers/learning points
- Measure consumer response toward behavior modification material/learning points
- Measure consumer attitude toward purchasing study product/learning points
- Measure consumer response to advertising/learning points

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The objectives of the study were: achieve comparable efficacy in the two arms of the study – OTC and traditional Rx sites; create a “real life” retail environment for OTC sites; charge study participants for the product (comparable to retail price); and permit study subjects to self-select. There were several additional subsidiary questions that addressed consumer behavior and marketing issues.

(Slide 13 on screen)

Nicotrol® Use Study Flow Chart – 23 Sites

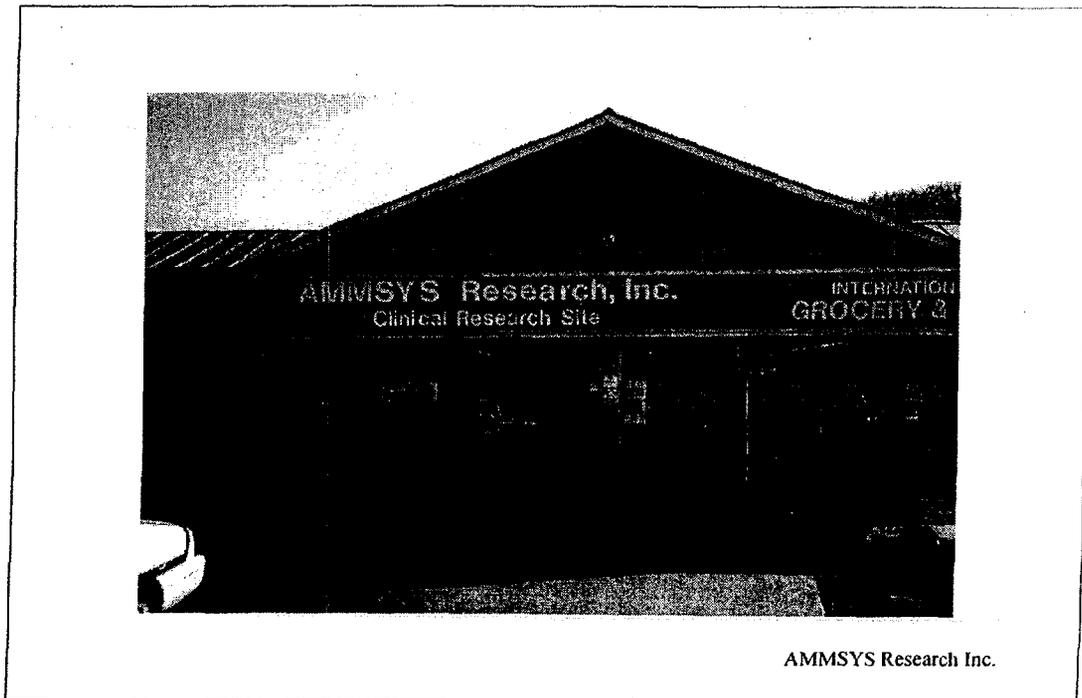


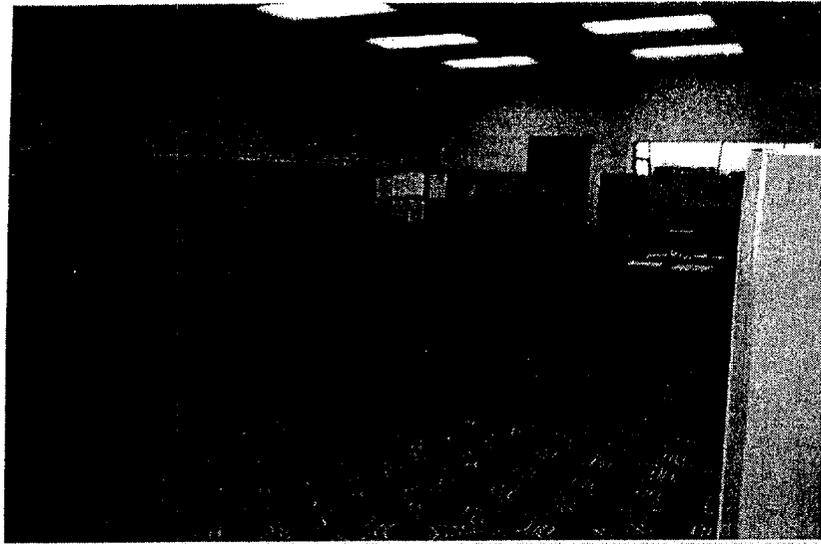
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This is the model of the study. It was a two arm, parallel, open label study with 23 sites. The 10 OTC sites were storefronts located in large, active shopping centers and the 13 Rx sites were physicians offices. The OTC storefronts are stores we lease in shopping centers and equip and staff as OTC sites. Consumers responded in an enthusiastic and positive manner to participating in an OTC trial where the site is a “real life” retail store located in a shopping center. Our experience tells us that this is the best way to get a true measurement of the OTC-Rx relationship for a product. Sites were staffed with trained research nurses who functioned as study coordinators.

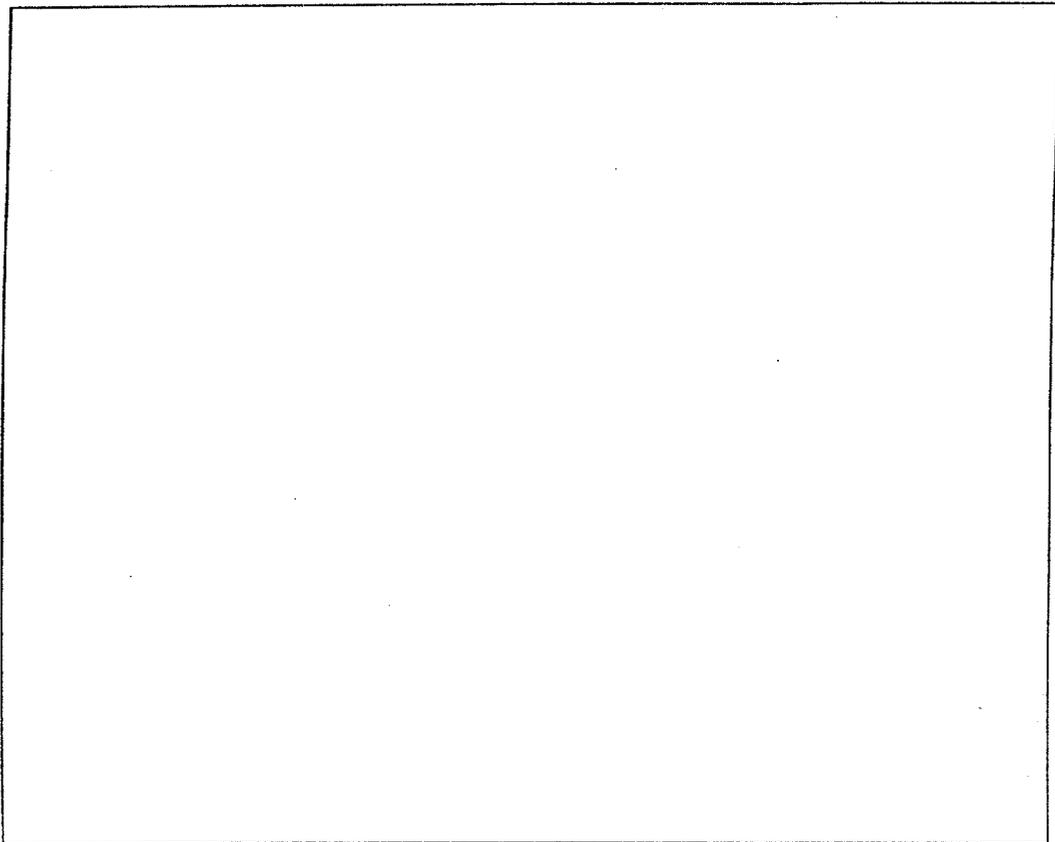
These are representative pictures of outside and inside views of the 10 OTC storefront sites.

(Slides 14 & 15)





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Nicotrol® Market Geographics

A Major U.S. Population Center

▪ Area population	5.9 million
▪ Smokers	1.2 million
▪ Motivated smokers	120,000
▪ Sample size	2,500

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(Slide 16 on screen)

These are the market geographics. Since geographic dispersion was not a key consideration, we concentrated the 23 sites in one large metropolitan market.

This is considerably more cost effective in centralizing, recruiting and screening than the traditional widely dispersed 40 to 50 sites for a study of this size.

Nicotrol® - Summary of Enrollment

Total calls received	14,809
Total subjects enrolled*	3,385
Subjects who failed to initiate treatment	150
	(OTC=32 Rx=118)
Total subjects treated	3,235

* Completed enrollment in 4 weeks

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These are the results. The radio advertising built around morning and afternoon drive time generated 14,809 calls to our call center. 3385 subjects were enrolled in the study. Enrollment was completed in 4 weeks. 150 subjects enrolled but failed to initiate treatment. 3235 subjects received treatment.

(Slide 17 on screen)

Rx-to-OTC Conclusions

- No need for radical change in the Rx-to-OTC process.
- The Rx-to-OTC switch process should be considered on a case-by-case basis.
- Categories of products should not be presumptively excluded from OTC consideration. Research should drive these decisions.

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There is no need for radical change in the Rx-to-OTC process.

We urge the agency to consider Rx-to-OTC switches on a case-by-case data driven basis. Categories of products should not be presumptively excluded from OTC consideration. Research tools are available to answer all consumer related issues on all products considered for switch.

Rx-to-OTC should be viewed as a consumer driven process. Consumer behavioral research should be accepted as a valid tool in researching consumer attitudes, actions and decisions.

In open collaborative discussions with the sponsor, FDA should frame questions to be researched and charge industry with the responsibility of discovering the answers.

The "actual use study," with appropriate design features, can answer virtually every question related to consumer behavior and product usage.

Rx-to-OTC Conclusions

- Rx-to-OTC should be viewed as a consumer driven process. FDA should accept principles of behavioral science as valid research tools.
- FDA should frame questions that concern the agency and charge industry with the responsibility of finding answers.
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