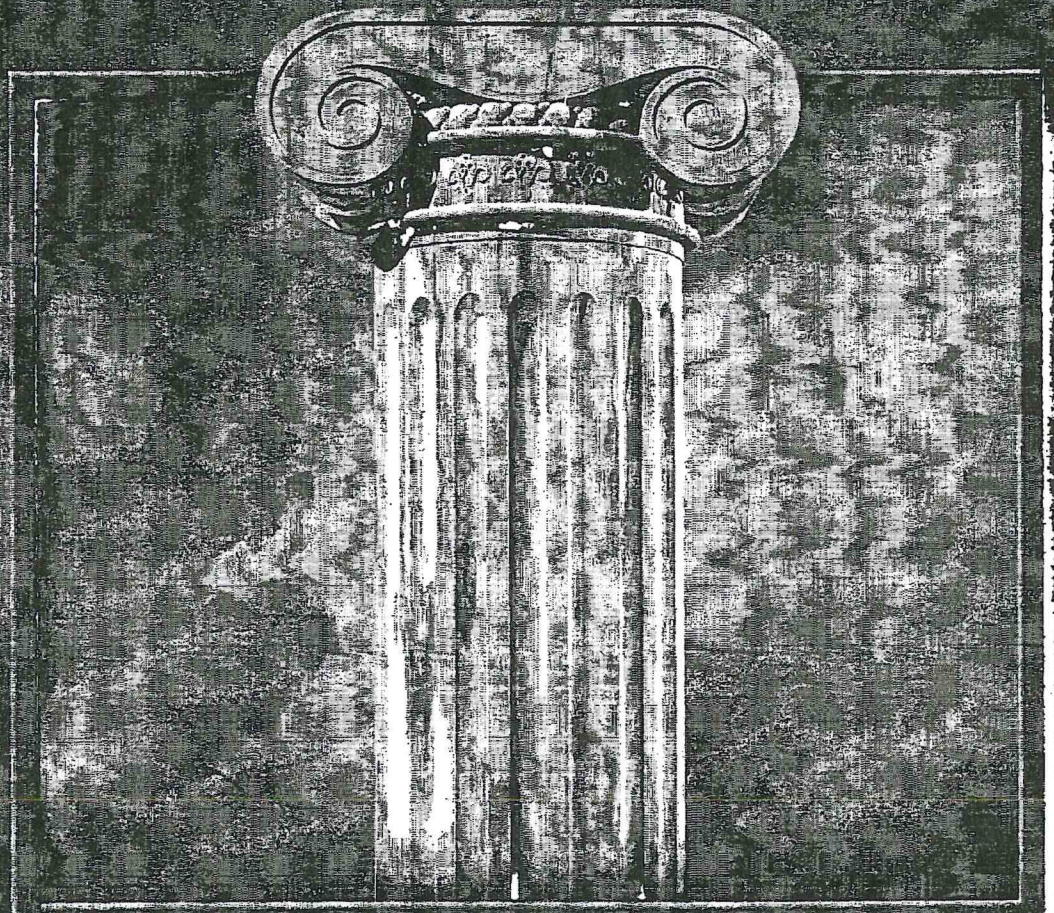
SALES TRAINING



MANAGEMENT • SALES • MARKETING

TRAINING & DEVELOPMENT

CNS

PLAINTIFF'S EXHIBIT 47

Introduction

Introduction

Critical Success Factors

- Professionalism
- Accountability
- Versatility/Flexibility
- Responsibility
- Communication
- Trust
- Respect
- Honesty
- Participation
- Commitment

Janssen Pharmaceutica

An Overview of the Company's History, Growth and Opportunity

Johnson & Johnson

Janssen Pharmaceutica

A Johnson & Johnson Family Company

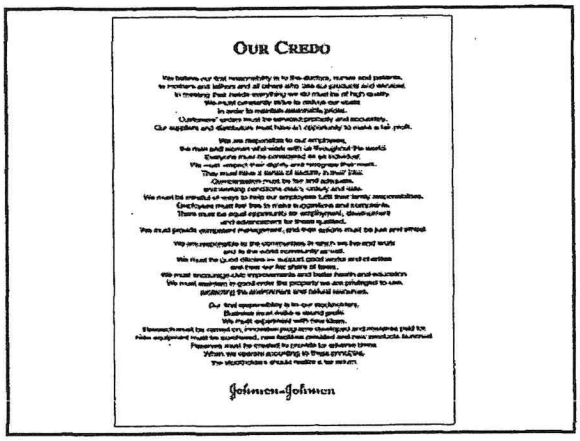
Janssen seeks individuals with a proven track record of success, exceptional interpersonal skills, and the ability to demonstrate leadership and teamwork.

Johnson & Johnson

Credo

Written by Robert Wood Johnson more than 50 years ago, the Credo guides our thinking and shapes our commitment to good business practices, while serving the people whose lives we impact through our products and services.

- Customers
- Employees
- Community
- Stockholders



OUR CREDO

Johnson-Johnson

Johnson & Johnson

Most comprehensive health-care company in the world

- Family of 197 companies in diverse health-care businesses
- 101,800 employees worldwide
- Three worldwide segments of business:
  - Pharmaceutical
  - Professional
  - Consumer
- Markets over 100 prescription drugs around the world
- Products marketed in more than 175 countries

Johnson & Johnson

Financial Highlights

- As of 2001, sales increased each year for the past 69 years
- Stock split 2 for 1 on May 22, 2001 (6th split since 1970)
- 2001 was company's 39th consecutive year of dividend increases
- 2001 sales of $33.0 billion
- Nearly $3.6 billion invested in R&D in 2001, driving innovation
  - 16% increase over prior year
- 2000 year-end close for common stock was $105.06
- Listed on the New York Stock Exchange - symbol JNJ

Janssen Pharmaceutica

Mission

Janssen's mission is to meet customer needs for high-quality, cost-effective health care by developing, producing and marketing differentiated pharmaceutical products and services that improve health outcomes.

Janssen Pharmaceutica

History

- Founded in 1953 in Beerse, Belgium, by Dr. Paul Janssen, a physician and researcher
- Joined J&J Family of Companies in 1961
- First U.S. presence was in New Brunswick in 1972 with two full time employees, Roger Aspeling and Dave Mallegol.

Janssen Pharmaceutica

History

- Developed and brought to market more than 80 compounds
- Janssen has launched a record 61 new medicines in the past 34 years.
- Introduced 231 products internationally between 1970 and 1980 - more than any other pharmaceutical company.
- Most profitable subsidiary of J&J

Janssen Pharmaceutica

Firsts

- First transdermal patch for chronic pain - **Duragesic®**
- First prescription shampoo for dandruff - **Nizoral Shampoo®**
- First oral broad-spectrum antifungal - **Nizoral Tabs®**
- First QD non-sedating antihistamine - **Hismanal®**
- First Rx drug to be advertised on television- **Imodium®**
- First in-house physician communications group - **Customer Action Center (CAC)**
- First oral antifungal approved in 30 years for onychomycosis - **Sporanox®**
- First, first-line Serotonin-Dopamine Antagonist (SDA) - **Risperdal®**

Janssen Pharmaceutica

Janssen People

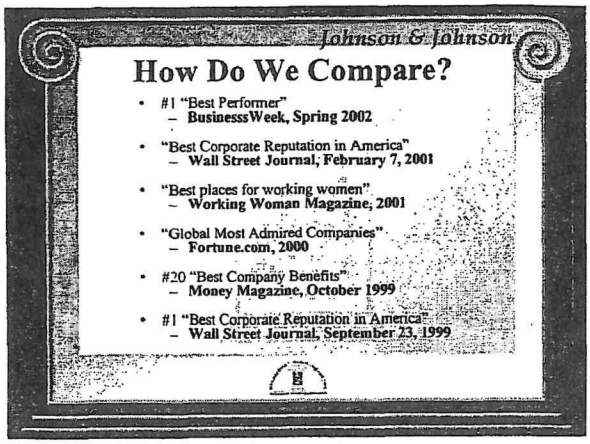
- Responsibility and Judgment
- Interpersonal Skills
- Communication Skills
- Intellectual Ability
- Assertiveness & Enthusiasm
- Organizational Skills

Janssen Pharmaceutica

Commitment to Diversity

For eight years, Janssen has been recognized by Johnson and Johnson for demonstrating continuing excellence in Equal Opportunity and Affirmative Action.

"The Continued Excellence Award"



Training Center Guidelines

Janssen Training And Development Center Guidelines & Responsibilities

Roles & Responsibilities

- Be considerate about noise. This includes the Training Center, break areas, and any locations that may be used by classes and others.
- Be courteous when entering a classroom. Avoid interruptions that may distract fellow participants.
- Turn off the ringer on your cell phones and pagers.
- You are responsible for keeping your work area clean and organized.

Roles & Responsibilities

- You are responsible for bringing your name badge to class *everyday* and badges must be worn at all times.
- Return all equipment, accessories, etc. issued during training classes (wireless card, security badges, etc.) to the Training Center Coordinator.
- Smoking is allowed only in one designated area.

Food

- Meals and breaks will be located in the designated area of the cafeteria – All food is to be consumed in this area only. All food trays should be placed on conveyor belts as you leave the cafeteria area
- No food or candy is permitted in the Training Center classrooms. *Beverages are allowed.* Recycling and garbage containers are provided in credenzas at the back of each room
- Breakfast is available from 7AM – 8AM
- Break intervals occur at 9:30AM-10:30AM and 2:30PM-3:30PM
- Wednesday afternoon designated for Break with the Board (3:00-3:30PM)
- One hour lunches are staggered: 11:30 (Room B/C) or 12:30 (all others) - Sales Training Manager to direct

Break with the Board

Each Wednesday afternoon from 3:00 – 3:30

- Located in the cafeteria break area
- One or more members of the Janssen board
- All classes in the Training Center will meet together during this break
- While informal, attendance is mandatory
- Board member will introduce themselves, discuss their position and answer any questions of the attendees

Fitness Center

- Forms are reviewed by Health and Wellness staff and approved list sent to coordinator
- Coordinator distributes Health Center badges (pm 1st day) for use Monday – Friday, 5PM to 6:45PM
- Depending on capacity, two groups (A&B) will be designated for staggered use of facility
- Badge must be returned at end of training
- Additional forms available through coordinator

Health, Accidents & Injuries

- Emergency and first aid medical services are available onsite (dial 'Hotline' from any in-house phone). Non-emergency medical needs should be directed to the Sales Training Manager. The Janssen Medical Department can assist with personal needs and can dispense limited over-the-counter medications.
- All workplace (Occupational) injuries/illnesses of any nature must be reported to the Janssen Occupational Nurse @ Ext. 2035. This is required by Federal Law.
- Call 3333 if no response- Janssen emergency number

Transportation

- Group transportation to/from the Training Center will be provided on a daily basis. It is each participant's responsibility to use transportation provided, no special arrangements will be made
  - A1 Limousine
  - 1 drop-off, 2 pick-ups
    - 7:00 a.m. Hotel departure
    - 5:15/6:45 p.m. Home Office departure
- No vehicles, other than those specifically denoted by Sales Training, will be allowed to commute to the home office
- Advisors will coordinate
- Should you miss the bus, in either direction, you will be responsible for obtaining and paying for your own transportation

Security

- Security staffed at entrance 7:00am-7:00pm
- Enter/exit the Training Center through the dedicated entrance
- Participants to sign in at Security desk each day
- *Badges must be worn at all times*, anyone not having a badge will be issued a visitor badge
- Badges will be provided to those participants who have been cleared to use the fitness center.
- For security and safety reasons, it is important for class participants to remain in the Training Center or with the class.
- If there is a need to meet with a Janssen employee outside of the Training Center, please coordinate it through the Sales Training Manager.
- Keep personal items with you at all times. Space will be provided for coats and luggage.

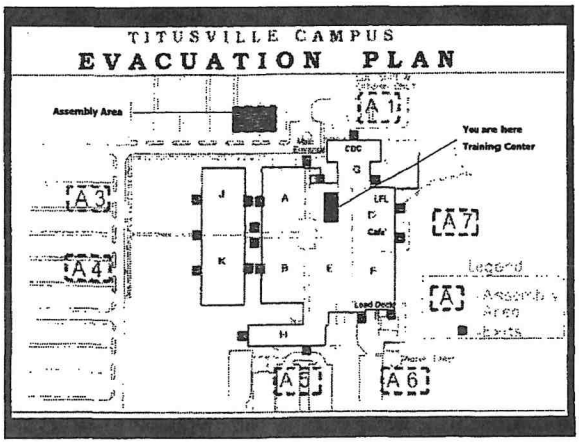
Computer Connectivity

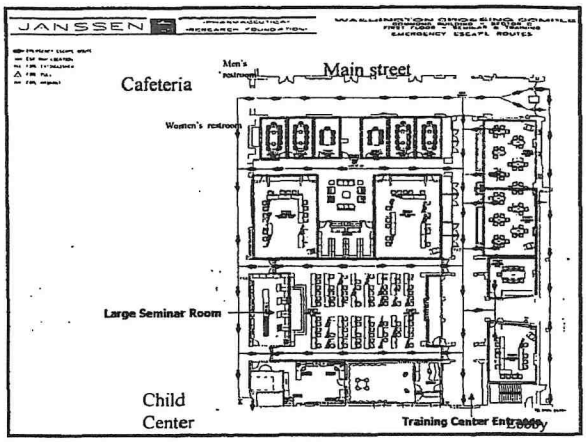
- Wireless Access
  - Use of your company issued laptop may be required for training purposes. It is each participant's responsibility to have the necessary materials/items (laptops, power cords, binders, sales aids, etc.) needed for class each day.
  - Wireless LAN cards will be issued to each participant and instructor on the 1st day of class and collected on the last day of class at Janssen. This will allow you wireless access to the J&J computer network while you are in the training center.

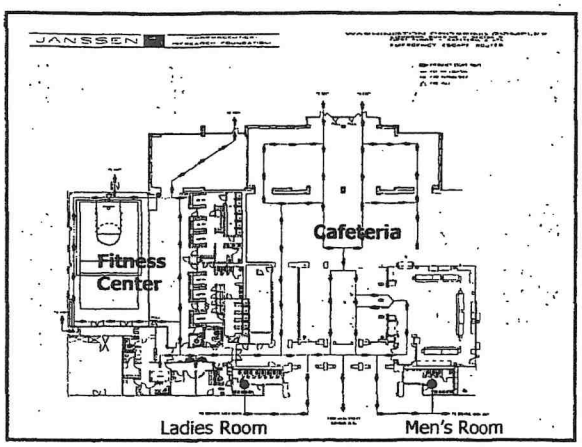
Fire & Emergency Evacuation

- Know your groups designated escape route
- Know the pre-determined emergency meeting place for your group
- Janssen Emergency Number is 3333

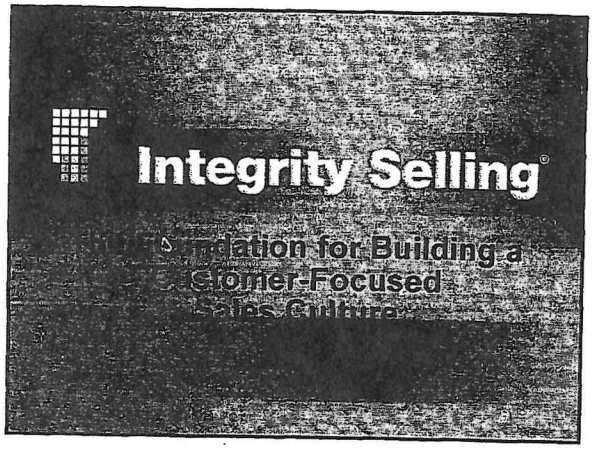
Refer to diagrams that follow







Integrity Selling



Changes and Challenges

- What changes or challenges have occurred in the pharmaceutical business?
- What challenges have these changes created?

Skills to Improve

- What selling skills would you like to improve through participating in the Integrity Selling® course?

Selling Defined

- To exchange goods or services for money or its equivalent

Integrity Defines Selling as:

- Identifying physician and patients needs,
- Helping to fill those needs, and
- Creating value for them.

Formula for Sales Power

Product Knowledge
+ Sales Know-How
+ Persuasive Ability
X Achievement Drive
= SALES POWER

Formula for Sales Power
Tenured Rep vs. New Rep.

Product Knowledge	9	5
+ Sales Know-How	8	5
+ Persuasive Ability	8	6
X Achievement Drive	2	9
= Sales Power	50	145

4 Traits of Successful Pharmaceutical Representatives

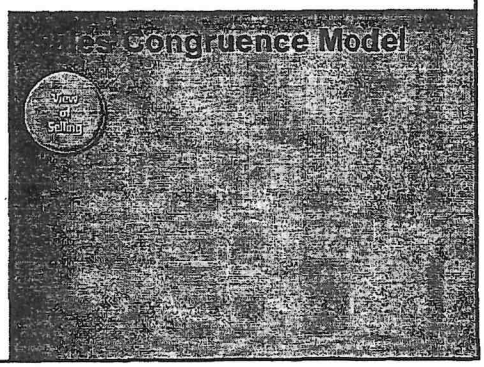
- ▶Strong Goal Clarity
- ▶High Achievement Drive
- ▶Healthy Emotional Intelligence
- ▶Excellent Social Skills

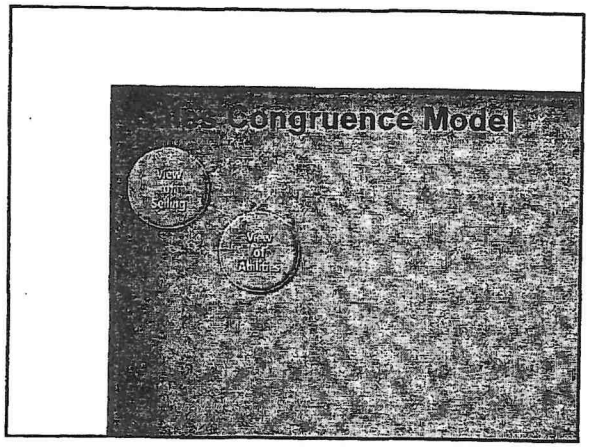
What's Different?

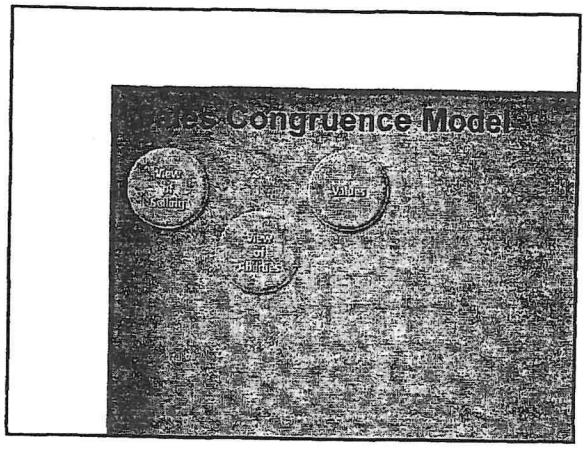
- ▶Structured Follow-Up
  - a) DM will facilitate
  - b) Weekly conference calls (3 weeks)
  - c) Will occur 2 weeks after IPT graduation

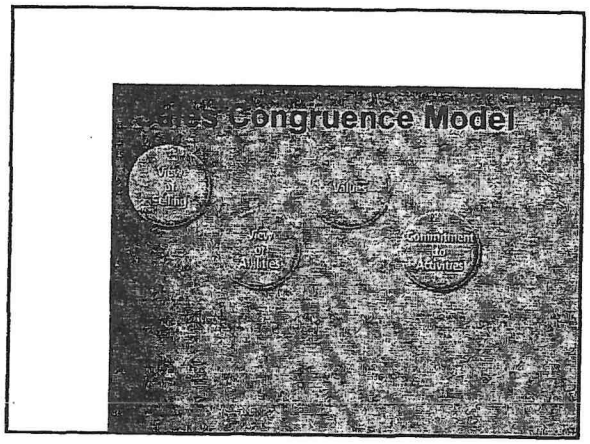
Janssen Success Traits

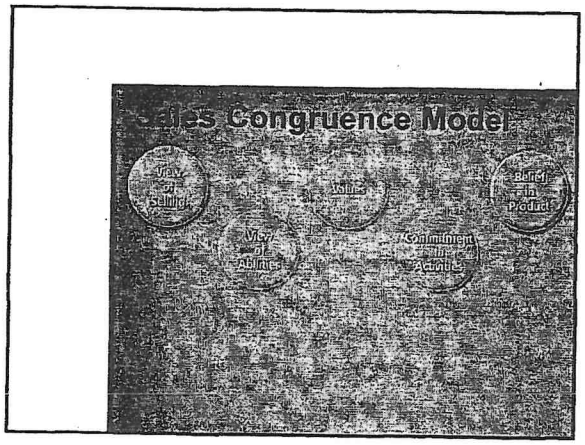
Sales Congruence Model

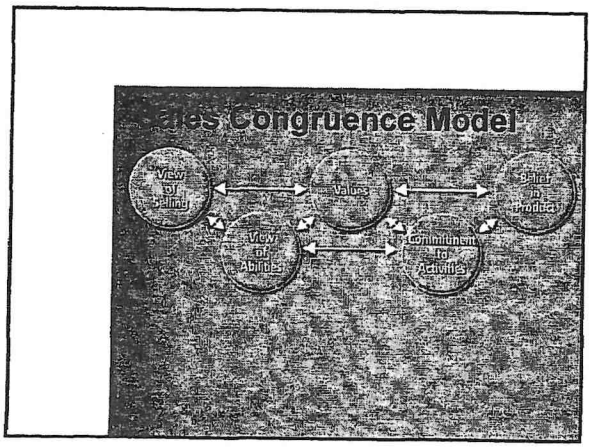


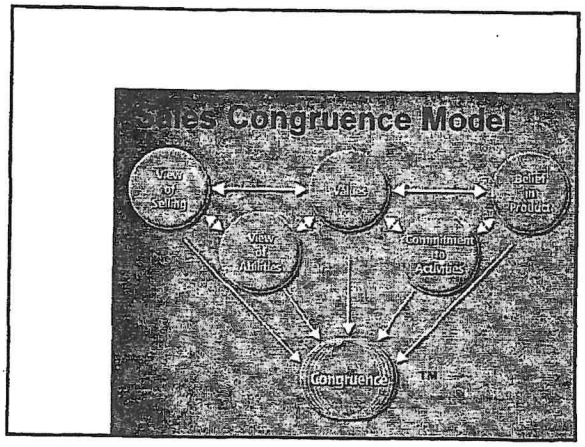


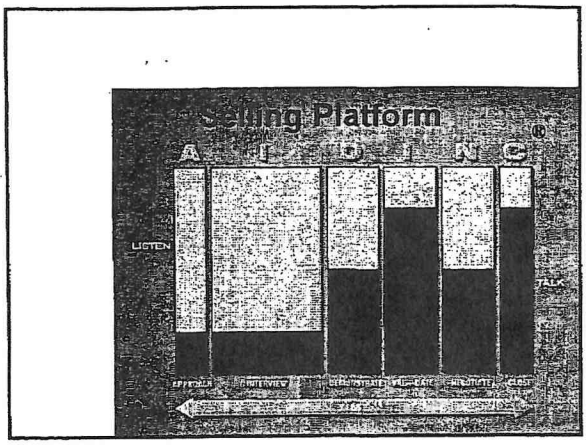










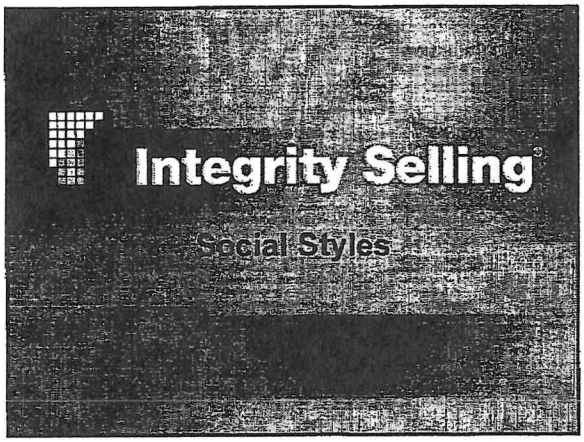


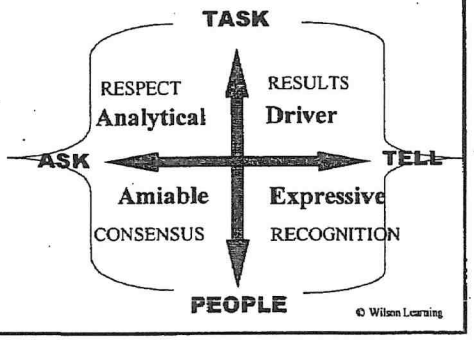
3 Dimensions of Behavior

Intellectual

Emotional

Creative/ Unconscious





Social Styles Activity

- How your style likes to be sold
- Selling tendencies of your style
- Challenges selling to the opposite style
- Bumper sticker and theme song

VIDEO

Approach Action Guides™

1. Tune the world out and people in.
2. Put them at ease and make them feel important.
3. Get them talking about their patients or their practice.
4. Hold eye contact and listen to how they feel.

VIDEO

Interview Action Guides™

1. *Ask* open-ended, indirect questions that draw out wants or needs.
2. *Listen* to and paraphrase all points
3. *Identify* dominant wants or needs and get agreement.
4. *Assure* physicians that you want to help them enjoy the most value.

VIDEO

Demonstration/Validate Action Guides™

DEMONSTRATE	*VALIDATE*
▶ Discuss drug features in terms or end-result benefits for the disease state or patient type.	▶ Translate drug features into clinician or patient benefits.
▶ Offer proof and evidence	▶ Reassure and reinforce physicians to neutralize their fear or prescribing.
▶ Ask for their reactions or opinions (check-in).	▶ Communicate the six magic words "What this means to you is..."

Managed Markets

Translate "Cost" into VALUE

How does the physician define value?

VIDEO

Validation Action Guides **Combining with Demonstrate**™

1. Translate drug features into clinician or patient benefits.
2. Justify price and formulary status and emphasize value.
3. Offer proof and evidence.
4. Reassure and reinforce physicians to neutralize their fear or prescribing.

VIDEO

Negotiation Action Guides™

1. Find out what concerns or questions remain.
2. Welcome and understand objections.
3. Identify and isolate specific objections.
4. Discuss possible solutions – ask their opinions for best solutions.

Check-In Closing Question

1. Ask for an opinion.
2. Get a positive response.

VIDEO

Close Action Guides™

1. Ask check-in closing questions to get opinions and response.
2. Listen to and reinforce each response.
3. Restate how the drug benefits will address the challenges in treating a particular disease state.
4. Ask for a actionable next step
5. Hold the physicians accountable

Ways To Gain Commitment

1. Ask for Prescriptions.

   Example: "Will you prescribe (my product) instead of the competition?"
2. Ask for Trial Patients.

   Example: "How many new patients will you trail on my product?"
3. Ask for Action.

   Example: "Will you tell recommend (my product) to your colleagues?"
4. Tell the Physician

   Example: "Based on the benefits we discussed for (my product), prescribe Aciphex for your next heartburn patient?"

Benefits you Will Receive from Integrity Selling

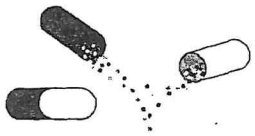
- ▶Greater self-confidence
- ▶Increased productivity
- ▶More achievement drive
- ▶Increased job satisfaction
- ▶Improved physicians relationships

Clinical Pharmacology

Department of Medical Services

An Introduction to Clinical Pharmacology

Medical Services
Janssen Pharmaceutica



Topics of Discussion

- Pharmacodynamics
- Pharmacokinetics
- Drug Interactions
- Adverse Drug Effects
- Drug Delivery Systems
- The Package Insert

Pharmacodynamics

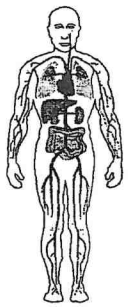
Pharmacodynamics

- Clinical effect
  - Therapeutic and non-therapeutic effects
- Mechanism of action
  - Drug receptors
- Measurement of clinical effect
  - Onset of action
  - Duration of action
  - Efficacy and Potency

Pharmacokinetics

Pharmacokinetics

- ADME
  - absorption
  - distribution
  - metabolism
  - excretion



Pharmacokinetics- Absorption

- Bioavailability
- Factors affecting absorption
  - Acidity of stomach / intestine
  - Gastric emptying
  - Presence of food in stomach
  - Drug formulation

Pharmacokinetics- Distribution

- Affecting factors
  - Blood flow to tissues
  - Lipid solubility of drug
    - Blood brain barrier
    - Placenta barrier
- Volume of distribution (Vd)
- Plasma protein binding

Pharmacokinetics- Metabolism

- Parent drug
- Organs responsible for metabolism
  - Liver
  - Kidney
- Metabolite(s)
  - Active
  - Inactive
- Cytochrome P450 Enzyme System

Pharmacokinetics- Metabolism

- Cytochrome P450 Enzyme System
  - Cytochrome P450 (CYP450) is the collective term for a group of related enzymes located in the human liver and other tissues
  - CYP450 enzymes exist in many forms
    - e.g. 1A2, 3A4, 2D6
  - Responsible for the metabolism and detoxification of many substances
    - exogenous compounds
    - endogenous compounds

The Cytochrome P450 Enzyme System

- 3 Roles of the Drug at the Enzyme Level
  - Substrate
    - Binds at the enzyme for metabolism
    - No augmentation of co-administered drugs
  - Inhibitor
  - Inducer

The Cytochrome P450 Enzyme System

- Inhibitor
  - Decreases activity of P450 Enzymes
    - An enzyme inhibitor can decrease the metabolism of co-administered drugs
    - Can lead to a increase in therapeutic efficacy of the co-administered drug
    - Dosage of a co-administered drug may have to be decreased

The Cytochrome P450 Enzyme System

- Enzyme Induction
  - Increased synthesis of more CYP450 enzymes
    - An enzyme inducer can increase the metabolism of co-administered drugs
    - Can lead to a decrease in therapeutic efficacy of the co-administered drug
    - Dosage of a co-administered drug may have to be increased

The Cytochrome P450 Enzyme System

- Clinical Significance - <u>What factors determine a clinically significant drug interaction?</u>
  - Drugs
    - Enzyme(s) involved
    - Affinities for enzyme receptor sites
    - Concentration of drugs (drug dose)
    - Therapeutic windows (index)
  - Other factors
    - Genetics, disease states, age, environment, etc.

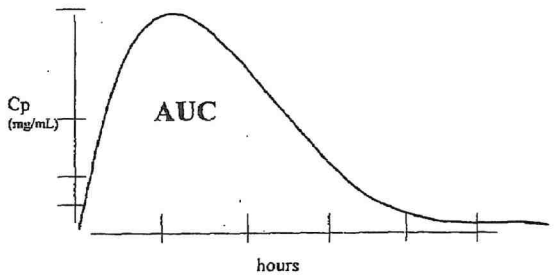
Pharmacokinetics- Excretion

- Organs
  - Kidney
  - Others (skin, lungs, breast, liver)
- Renal impairment
- Liver impairment

Pharmacokinetics- Drug Levels In the Blood

- **Peak drug concentration**
- **Area under the curve (AUC)**
- Therapeutic range
- Steady-state
  - Loading dose
  - Maintenance dose
- Half-life ($t_{1/2}$)

Serum Concentration vs. Time Curve



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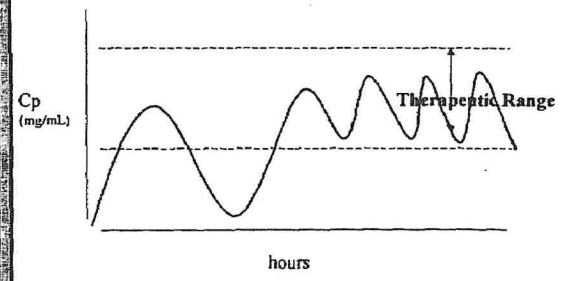
Serum Concentration vs. Time Curve



Pharmacokinetics- Half -Life

- One half-life ($t_{1/2}$) = time required for one-half of the concentration of drug in the blood to be eliminated

Drug Interactions

Drug Interactions

- Chemical
- Pharmacokinetic
  - Absorption
  - Distribution
  - Metabolism
  - Excretion
- Pharmacodynamic
  - Antagonism
  - Additive effect

Adverse Drug Effects

Adverse Drug Effects

- Toxicity
- Therapeutic Index
  - Narrow
  - Wide
- Dose-related and non-dose-related

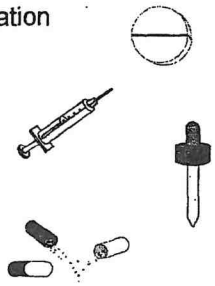
Drug Delivery Systems

Drug Delivery Systems

- Drug form
  - Tablet / caplet, capsule
  - Suspension, elixir, syrup
  - Ointment, cream, lotion, powder
  - Aerosol, suppositories
- Formulation

Drug Delivery Systems, continued

- Route of Administration
  - Oral (PO)
  - Sublingual (SL)
  - Intravenous (IV)
  - Intramuscular (IM)
  - Inhalation
  - Rectal
  - Topical
  - Transdermal



Package Insert

Package Insert

- Importance
- Major components: description, clinical pharmacology, indications, contraindications, warnings, precautions, adverse reactions, drug abuse and dependence, overdose, dosage and administration, how supplied
- Updates

REDACTED

ADHD Overview

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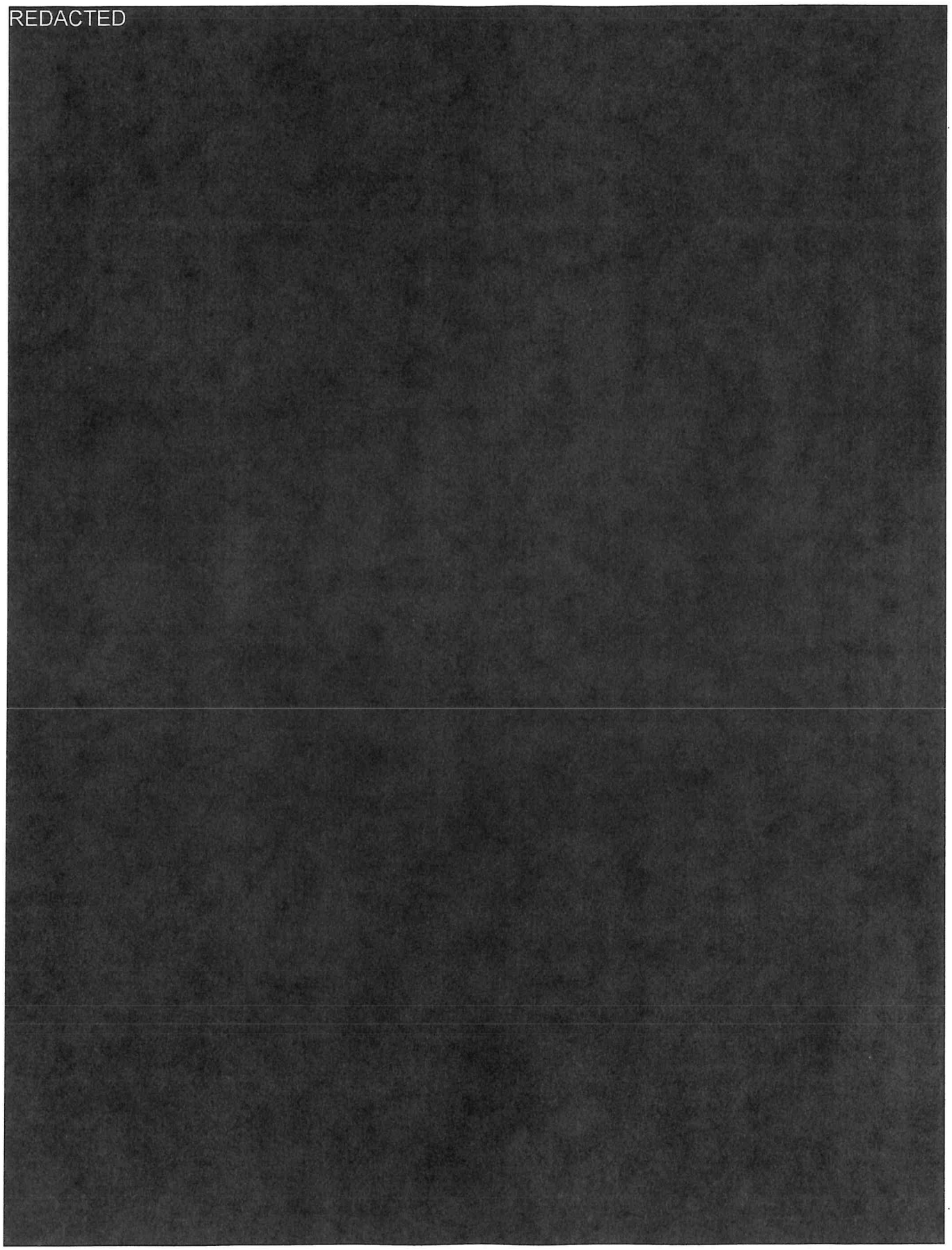

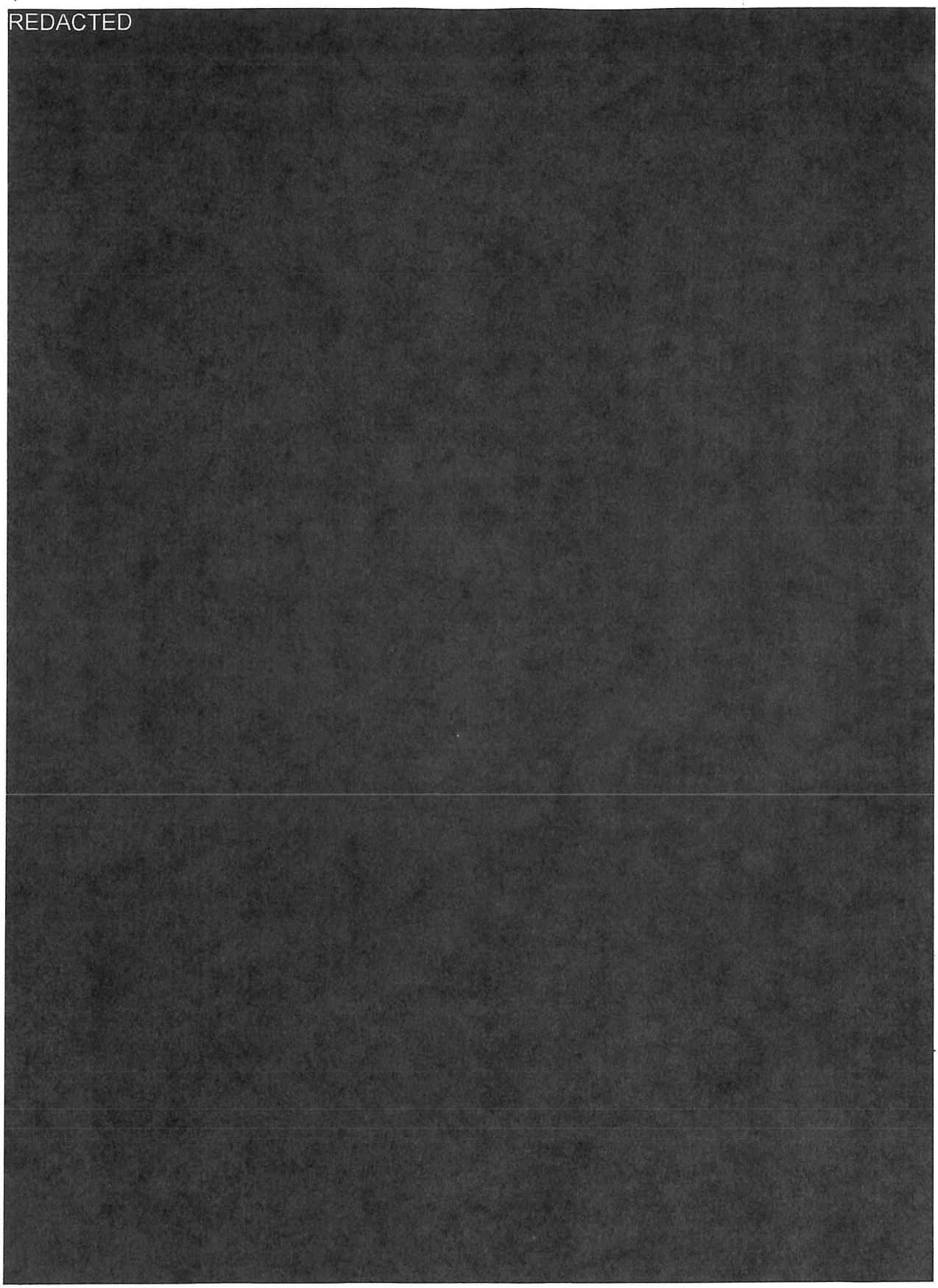
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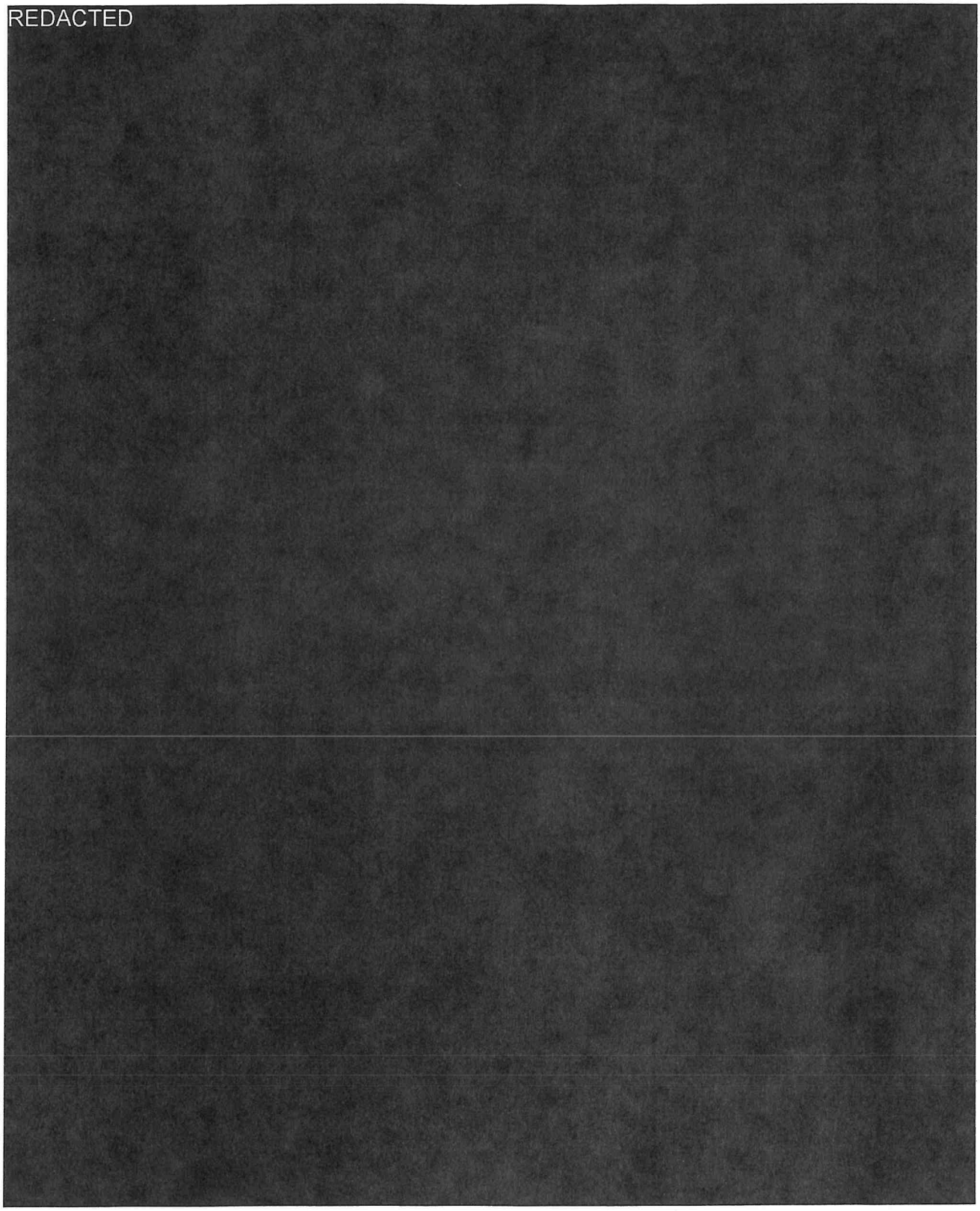

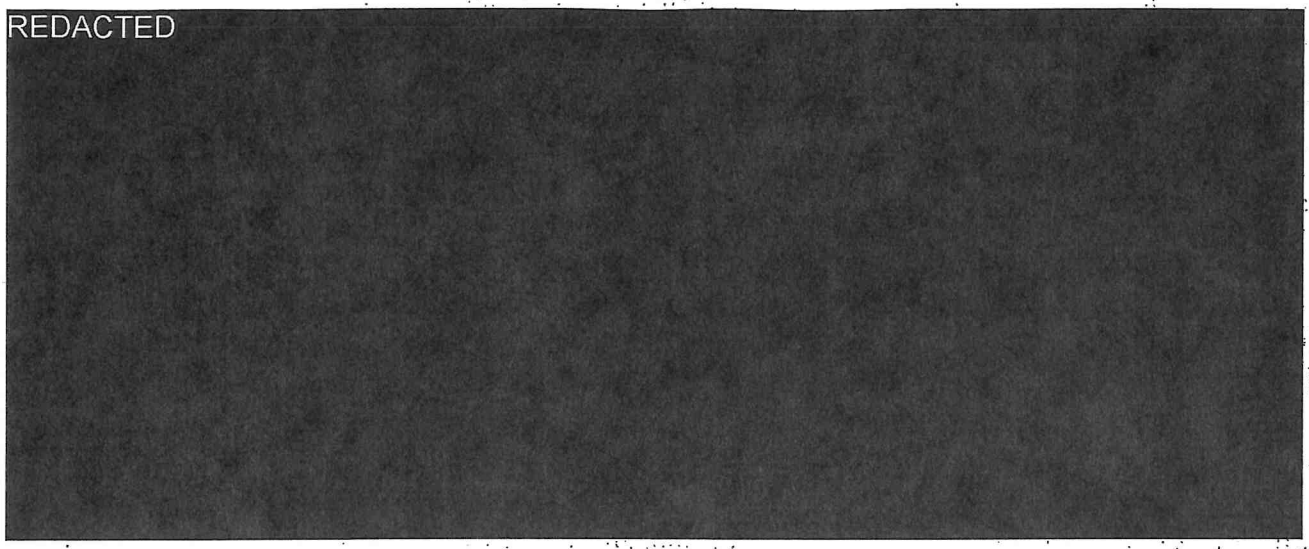
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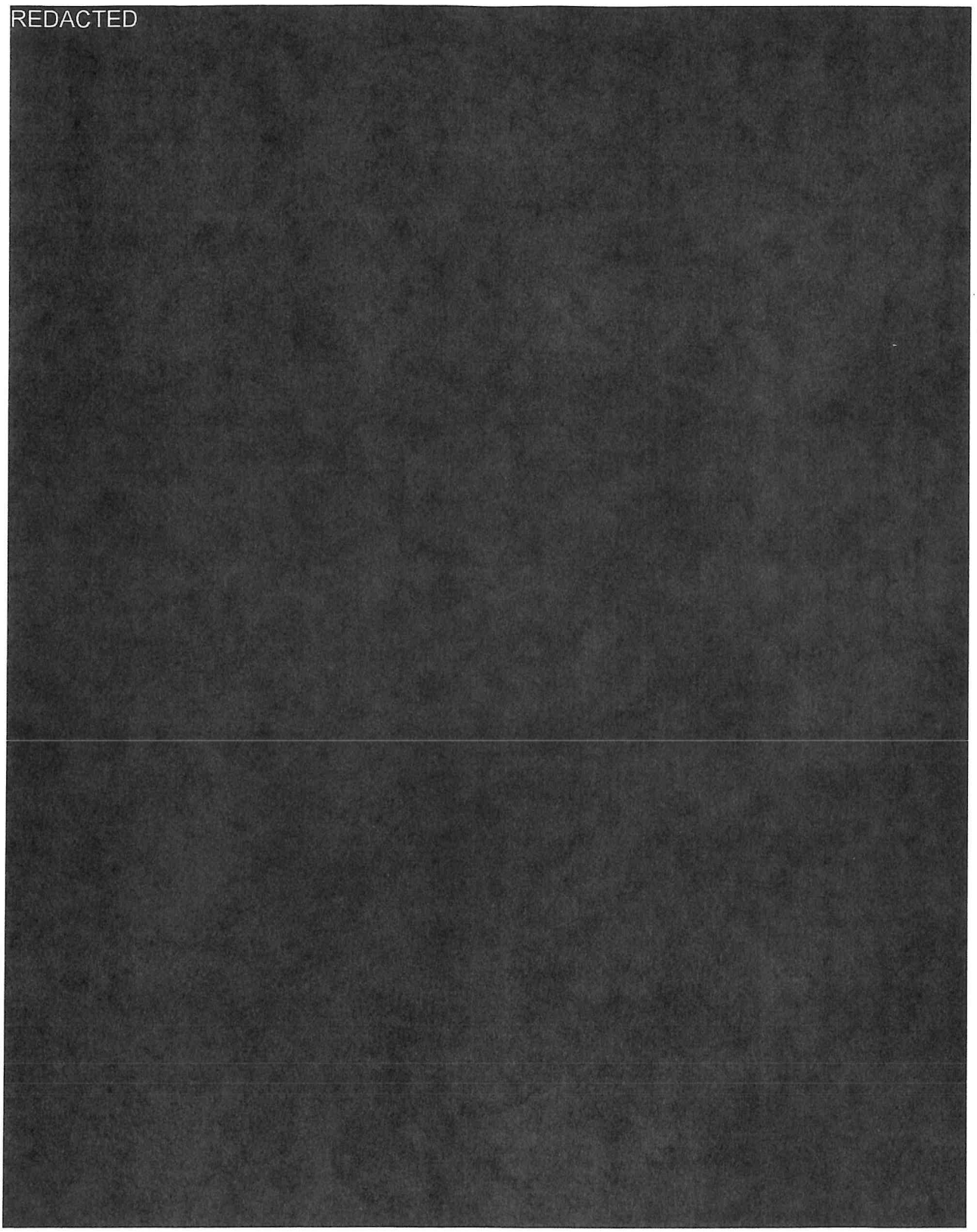
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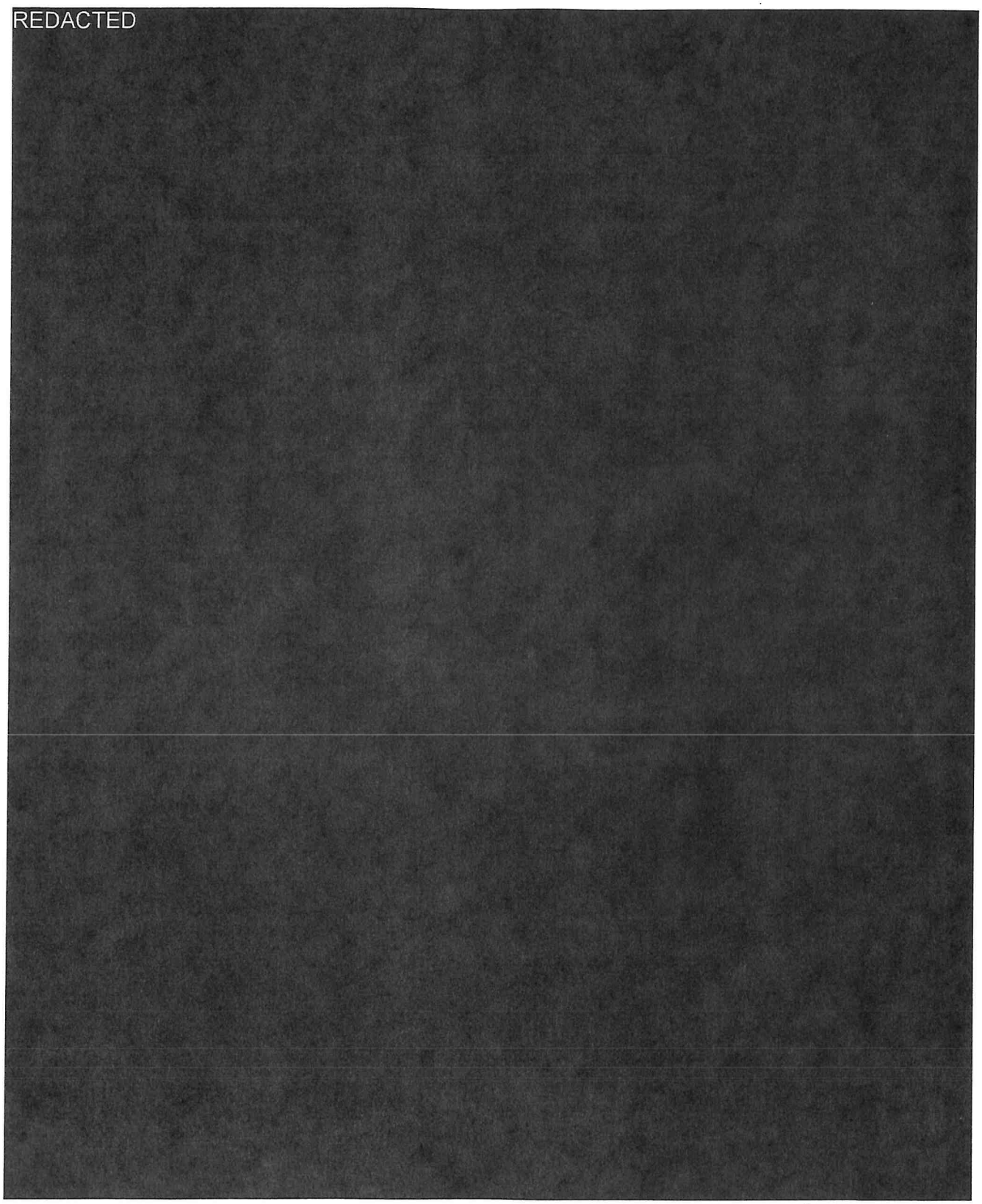
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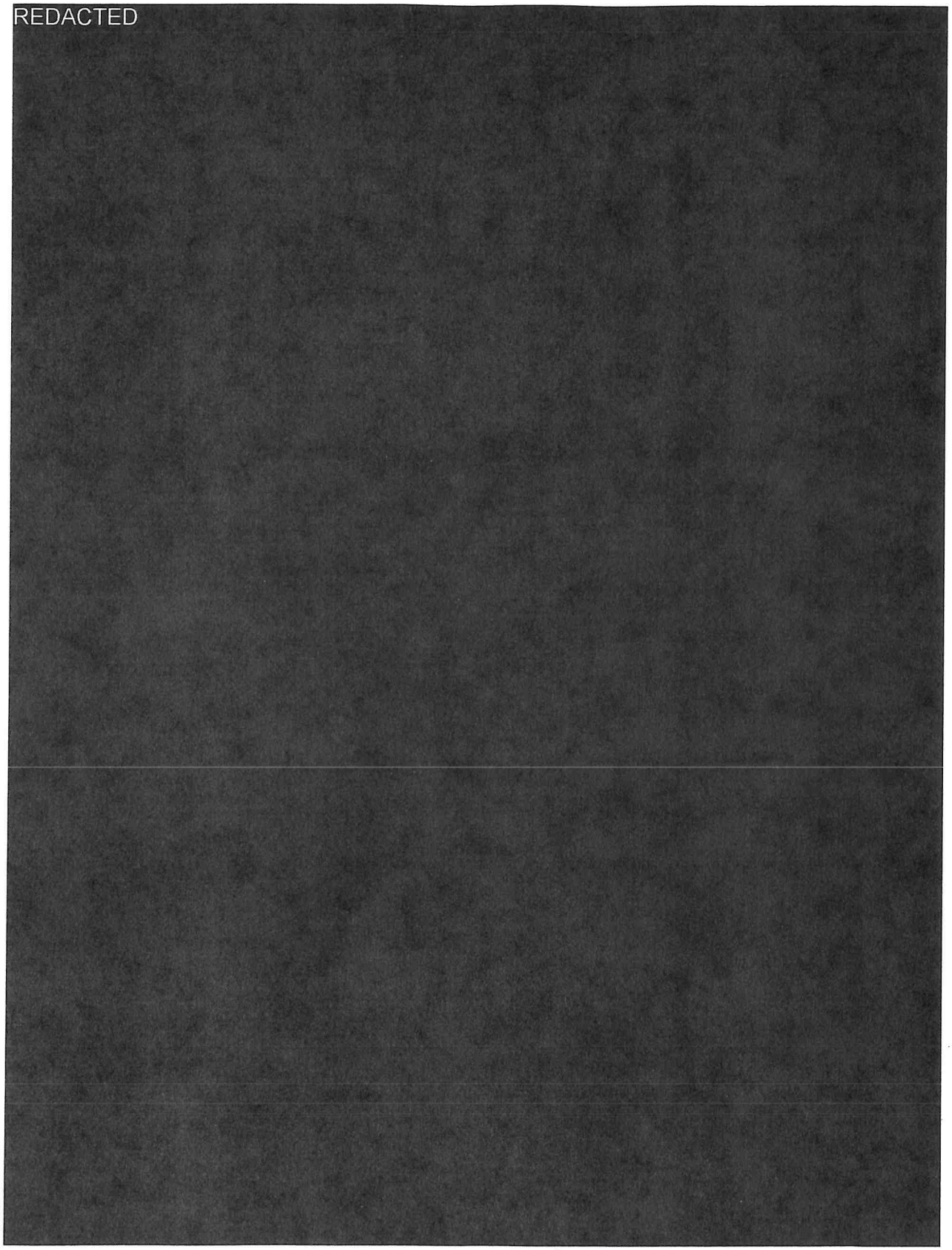

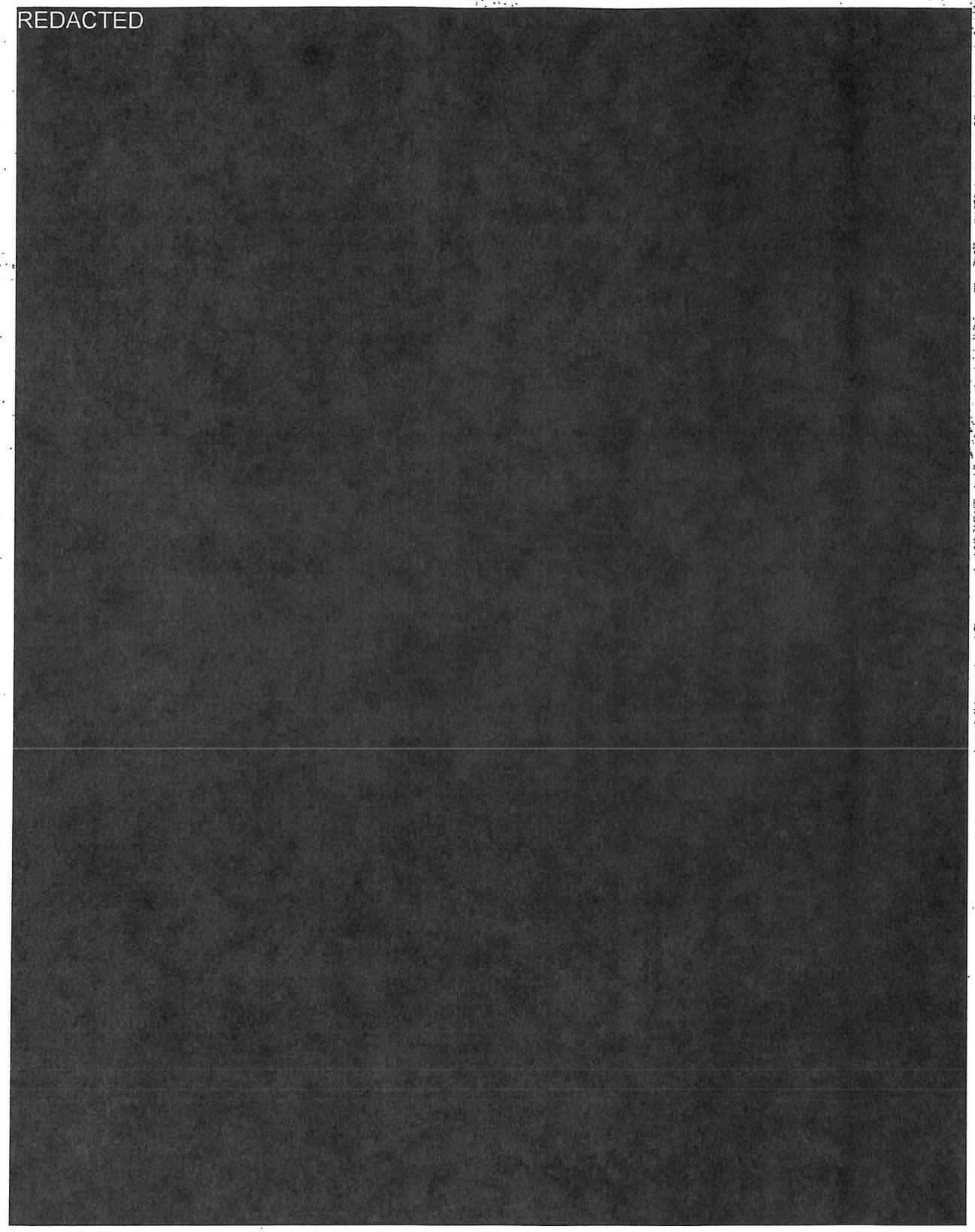
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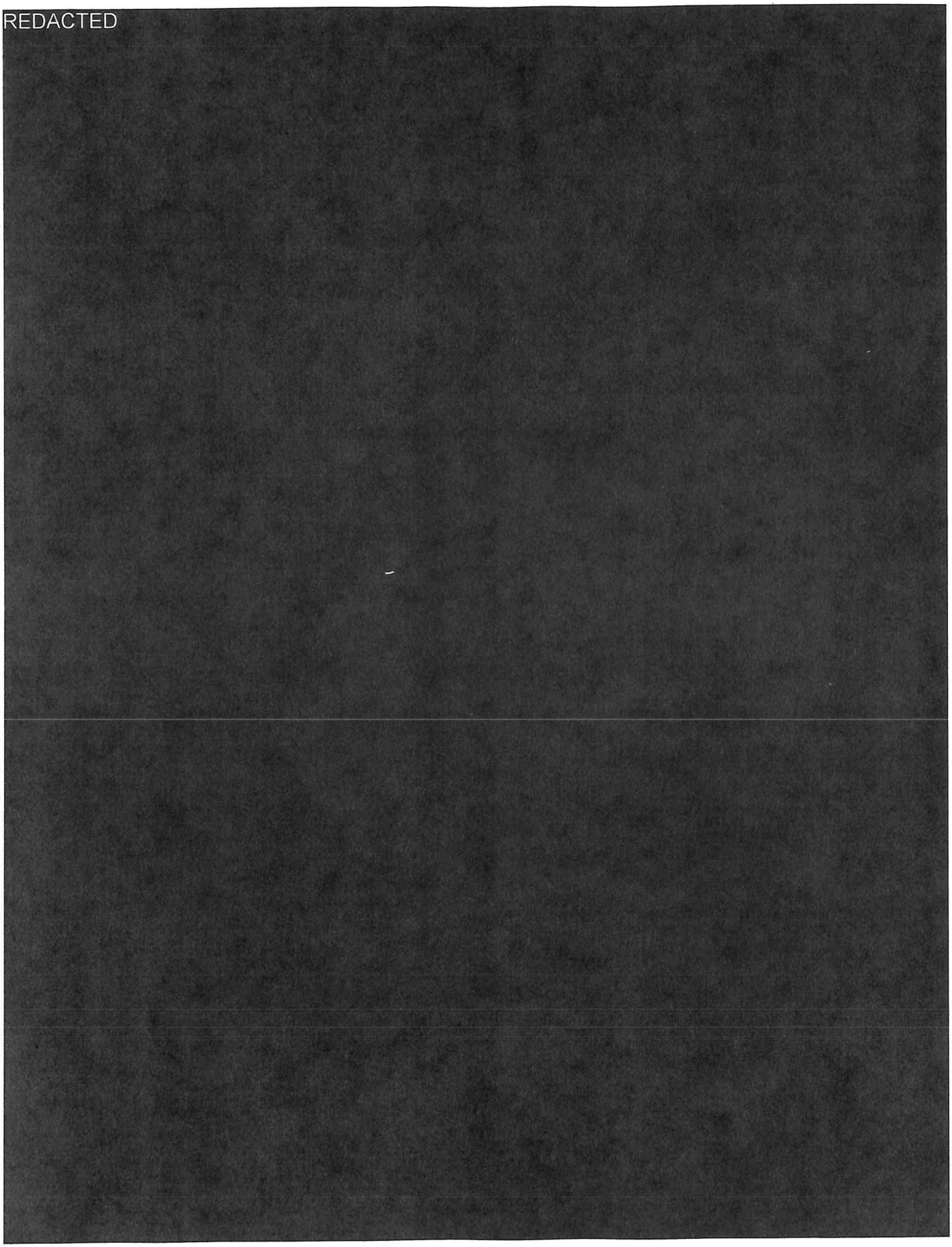

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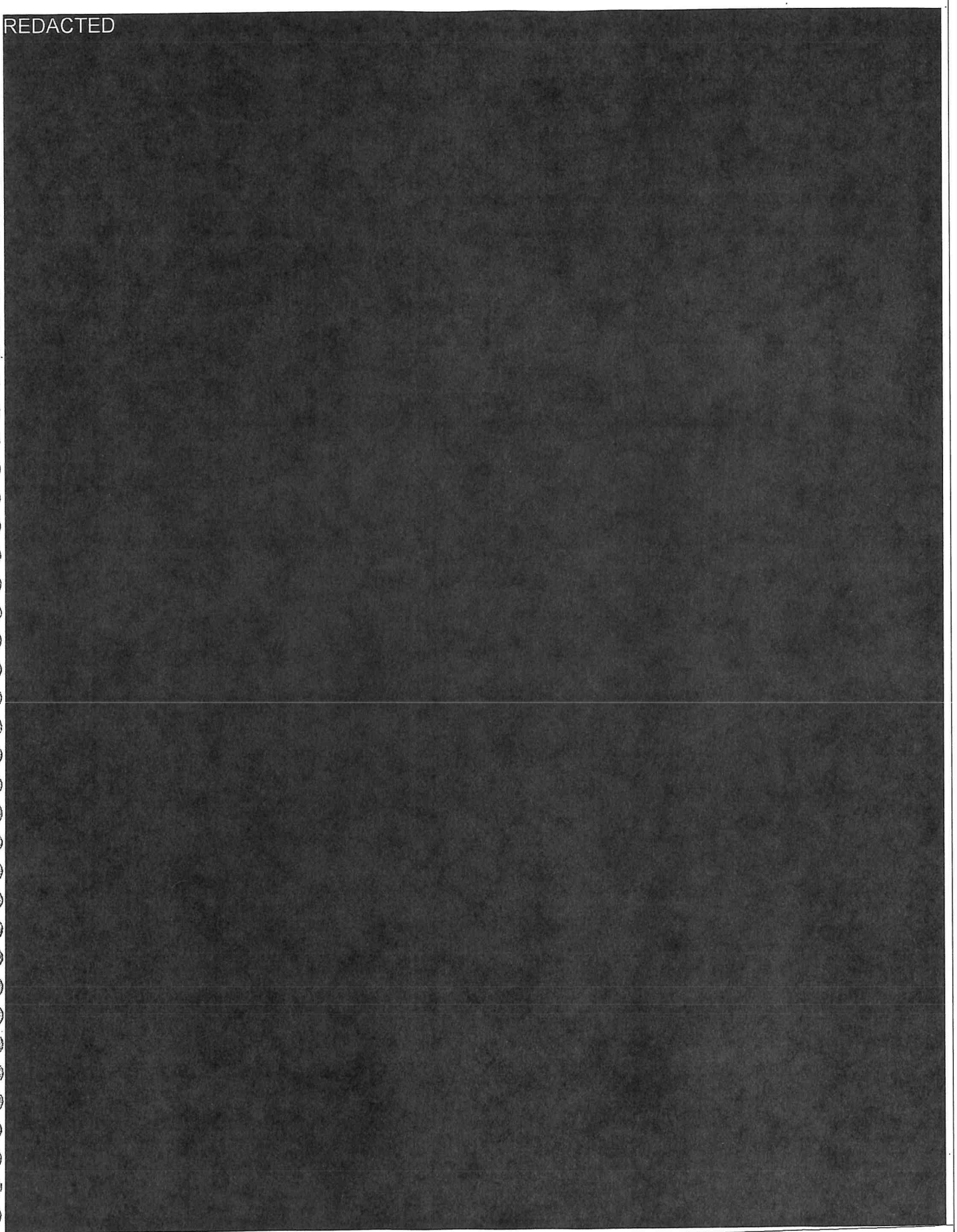

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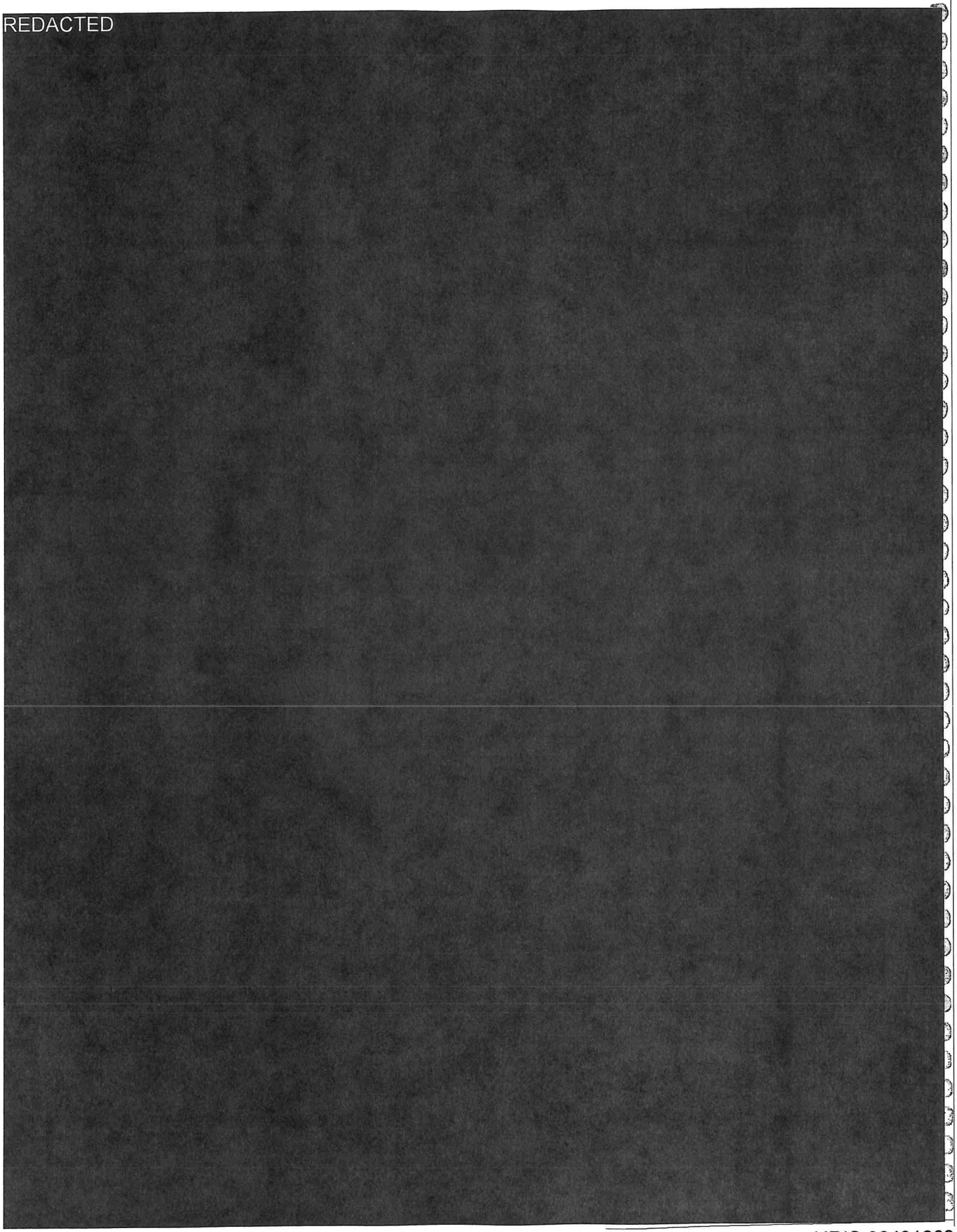

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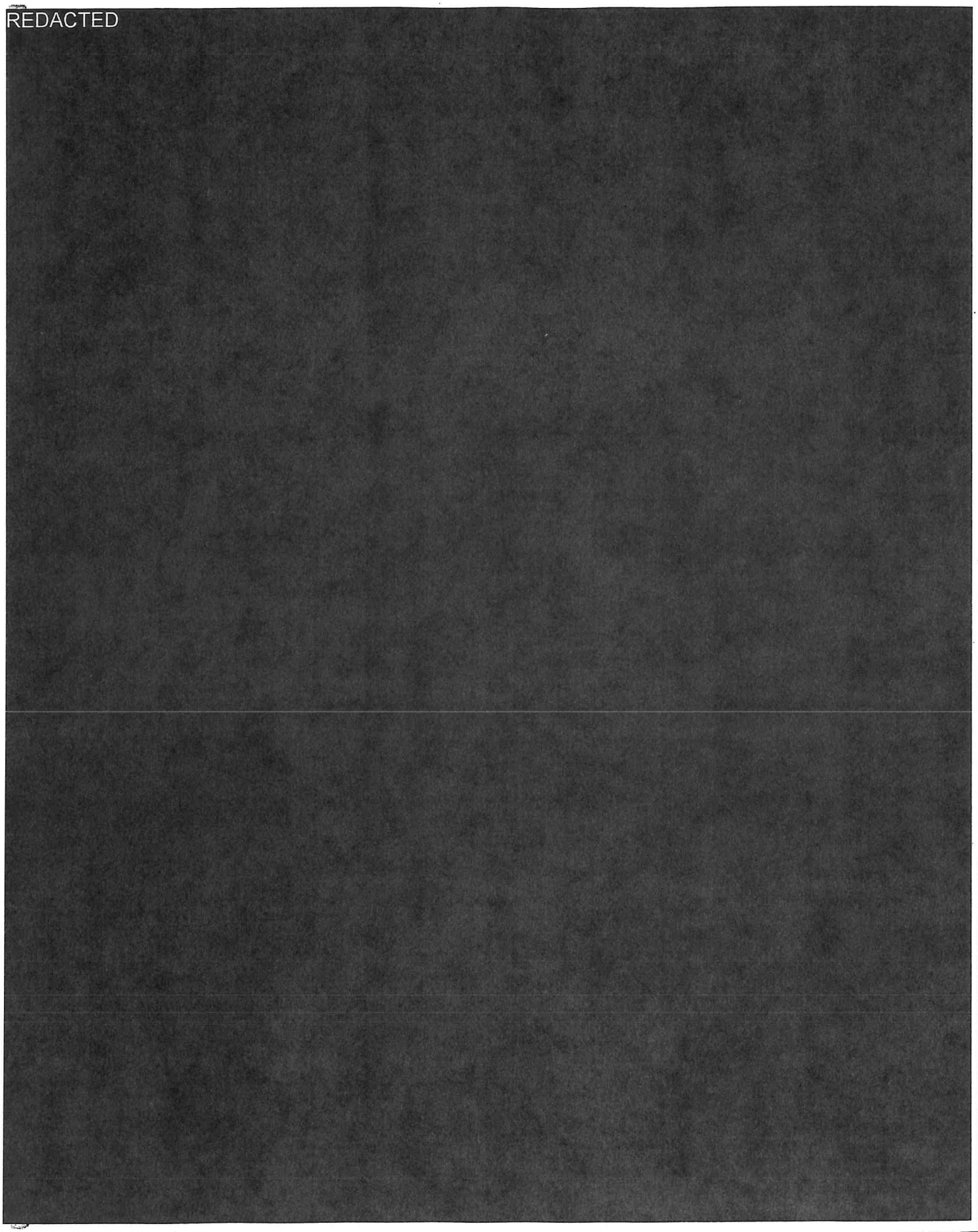

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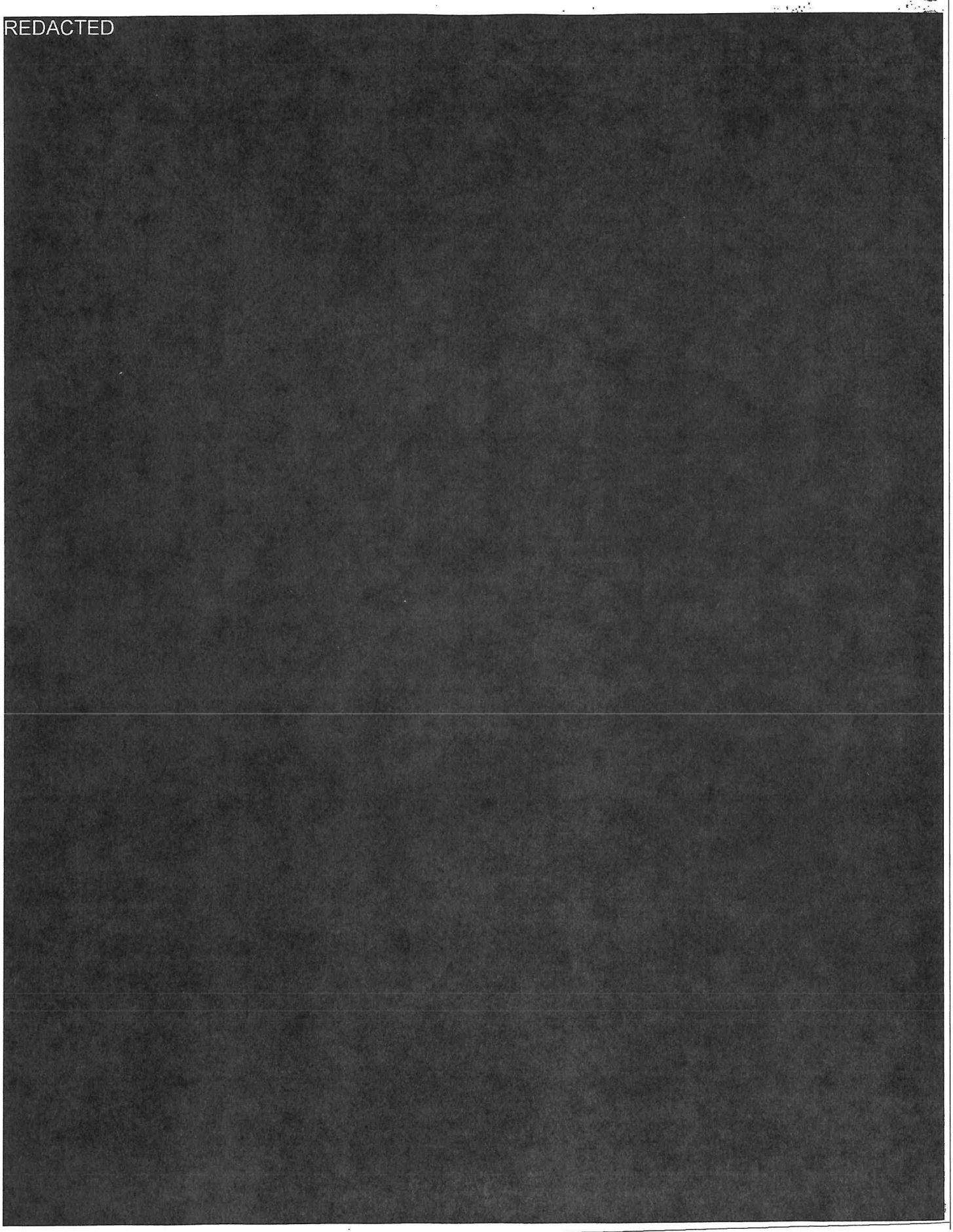


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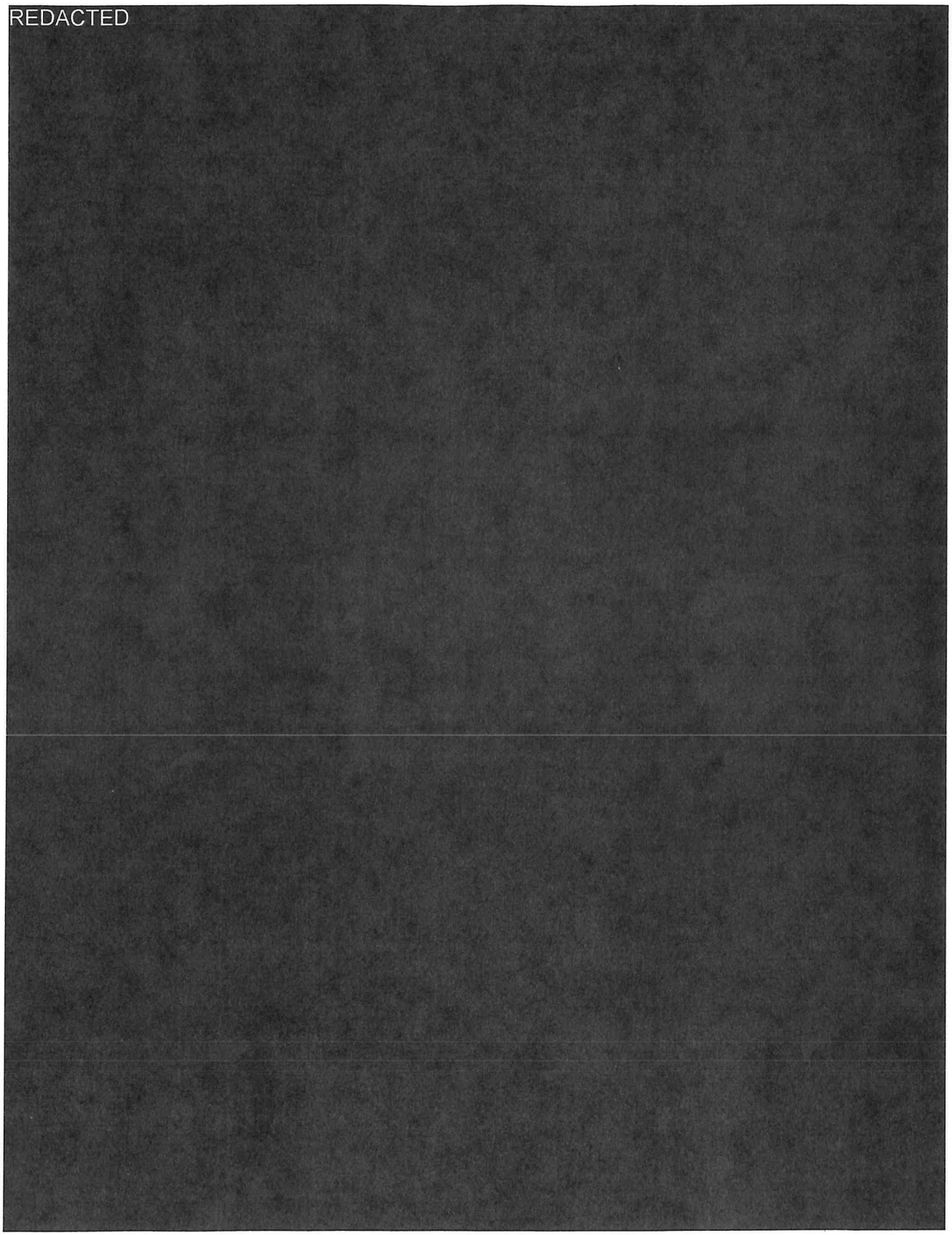
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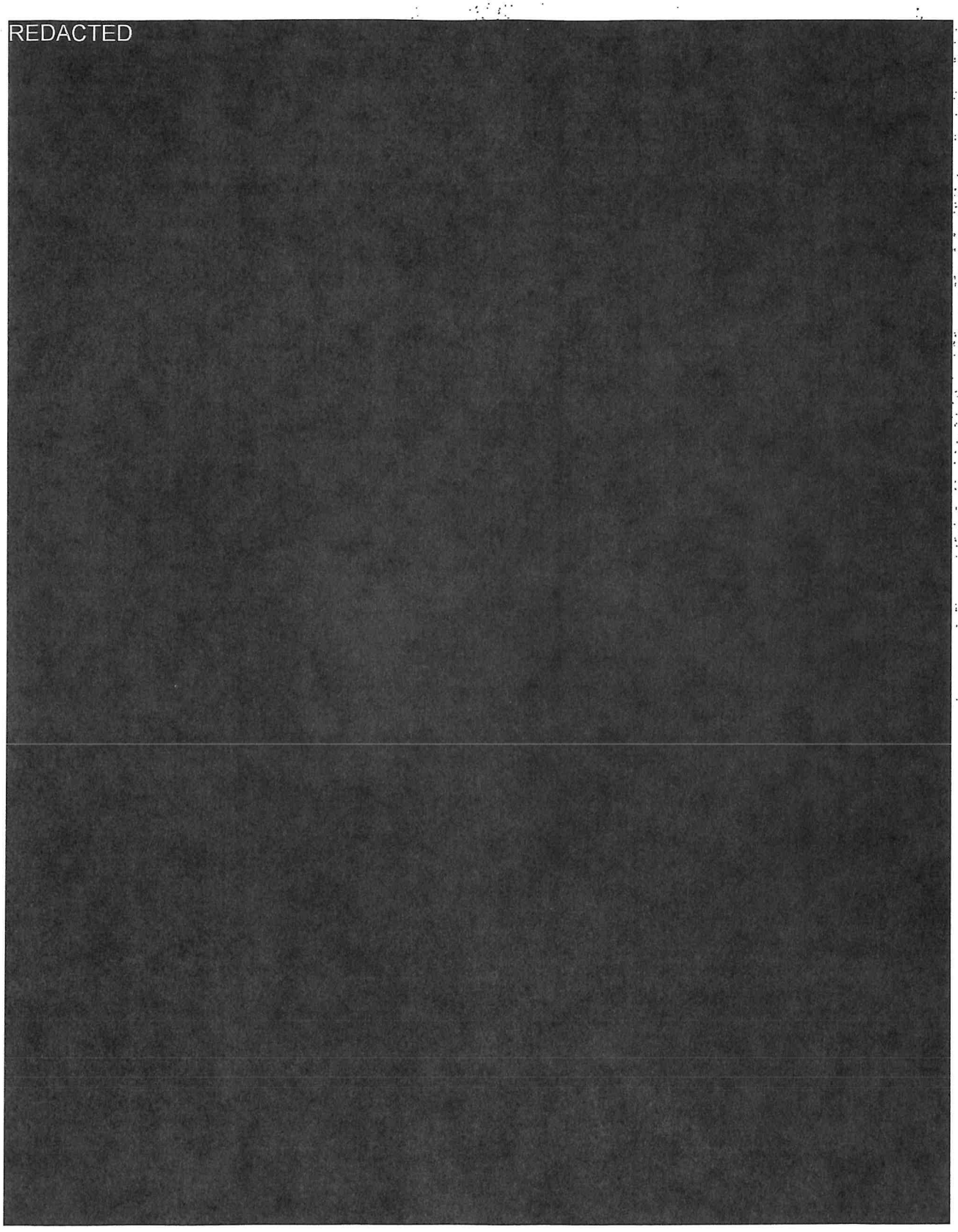


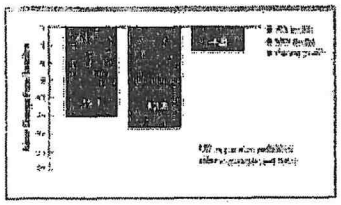
Strattera XR
Flashcard

Strattera Flashcard

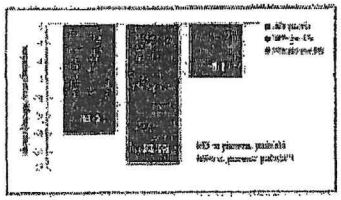
WHAT SHOULD YOU QUESTION WHEN CONSIDERING ATOMOXETINE FOR TREATING ADHD?

EFFICACY VERSUS METHYLPHENIDATE BID

How does the efficacy of atomoxetine and BID methylphenidate compare to placebo?



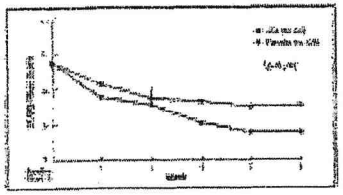
- Atomoxetine was compared to a BID regimen of methylphenidate.[1]
- There is no published data comparing atomoxetine to methylphenidate TID.



- In a second study, symptom reduction with atomoxetine failed to separate statistically from placebo.[1]

EFFICACY VERSUS PLACEBO

Did atomoxetine statistically separate from placebo at all three points?



- In adults, symptom reduction with atomoxetine was not statistically different from that of placebo at week 8.[1]
- Additionally, the effect sizes in the two adult studies were 0.39 and 0.40, respectively.[1]

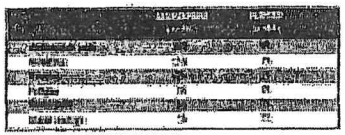
WHAT SHOULD YOU QUESTION WHEN CONSIDERING ATOMOXETINE FOR TREATING ADHD?

MECHANISM OF ACTION

- Imbalances of both dopamine and norepinephrine have been implicated in the pathology of ADHD.[2]
- Methylphenidate affects both dopamine and norepinephrine.[3]
- Atomoxetine inhibits reuptake of norepinephrine only.[1]

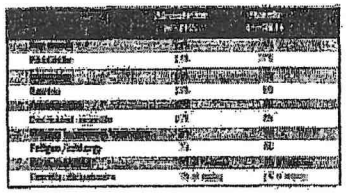
TOLERABILITY IN CHILDREN

Did patients treated with atomoxetine report a high incidence of gastrointestinal, sleep-related, and other side effects?



- Atomoxetine BID was associated with a higher incidence of stomach and sleep problems versus placebo in children.[1]

TOLERABILITY IN ADULTS



- Atomoxetine BID was associated with a higher incidence of gastrointestinal disorders, fatigue, and sexual dysfunction versus placebo in adults.[1]

1. Strattera [package insert]. Indianapolis, IN: Lilly USA, LLC; 2009.
2. Arnsten AFT. Stimulants: therapeutic actions in ADHD. Neuropsychopharmacology. 2006;31(11):2376-2383.
3. Concerta [package insert]. Titusville, NJ: McNeil Pediatrics; 2009.

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Subject to Legal & Regulatory Review

Adderall XR
Flashcard

CNS IPT

Adderall XR™ Flashcard Workshop

Workshop 2A Agenda

- Opening remarks/ Agenda overview 5 min
- Guided tour of flashcard 25 min
- Partner practice 45 min
- Wrap-up 15 min

Workshop Objectives

At the conclusion of this workshop you will…

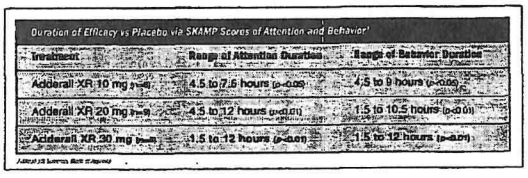
- Understand the rationale behind elements of the flashcard.
- Be able to identify opportunities and pitfalls in working with the Adderall XR™ flashcard.
- Be able to verbalize key elements of the flashcard.
- Be able to demonstrate appropriate use of the flashcard in sales calls.

Adderall XR™ Flashcard - Key Themes

- Begin every sales call by using your core Sales Aid
  - As always, selling efficacy is the main priority.
- Use the Adderall XR™ Flashcard to sell against your high prescribing XR physicians.
  - The objective of this flashcard is to initiate discussion around the downsides of AXR therapy.
- After using the flashcard, drive safety, dosing and closing components of the call.

Duration of Effect

Data shows that only the highest dose of Adderall XR™ demonstrated improved attention and behavior for up to 12 hours.

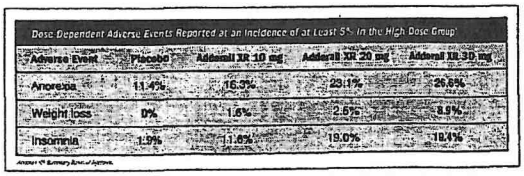


Duration of Efficacy vs Placebo via SKAMP Scores of Attention and Behavior[1]

Treatment	Range of Attention Duration	Range of Behavior Duration
Adderall XR 10 mg	4.5 to 7.5 hours	4.5 to 9 hours
Adderall XR 20 mg	4.5 to 12 hours	1.5 to 10.5 hours
Adderall XR 30 mg	1.5 to 12 hours	1.5 to 12 hours

Adverse Events

The incidence of some adverse events appears to increase with the dose of Adderall XR™.



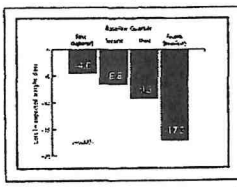
Dose Dependent Adverse Events Reported at an Incidence of at Least 5% in the High Dose Group[1]

Adverse Event	Placebo	Adderall XR 10 mg	Adderall XR 20 mg	Adderall XR 30 mg
Anorexia	11.4%	16.3%	23.1%	26.8%
Weight loss	0%	1.6%	2.6%	8.9%
Insomnia	1.9%	11.6%	19.0%	18.1%

Of the 553 children exposed to Adderall XR during clinical trials, 195 were exposed to the highest dose (30mg/day). Only 87 of these patients received 30mg/day for more than a week.

Long-Term Effect on Growth

Administration of Adderall XR™ demonstrated a decrease in growth rate over the course of 2 years.[2]



Mean Decrease in Expected Weight Over 2 Years[2]

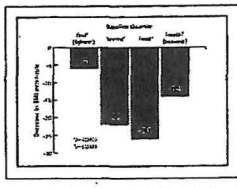
- Patients experienced up to a 17 lb decrease in expected weight over 2 years.[2]
- The percentage of patients in the 5th percentile or lower increased significantly (3.8% at baseline versus 12.9% at endpoint).[2]

References: 1. Center for Drug Evaluation and Research, Food and Drug Administration. Review and Evaluation of Clinical Data. NDA 21-303 Adderall XR™. Summary Basis of Approval. 2001. 2. Biederman J, Spencer TJ, Furman DV, on behalf of the Adderall XR Study Group. Extended-release mixed amphetamine salts in ADHD, growth parameter analysis. Poster presented at 156th Annual Meeting of the American Psychiatric Association, May 17-22, 2003, San Francisco, Calif.

CONCERTA® is a registered trademark of the ALZA Corporation. Adderall XR™ is a trademark, and Adderall® is a registered trademark of Shire US Inc. Please see accompanying full prescribing information for CONCERTA.

Long-Term Effect on Growth *(cont'd)*

Administration of Adderall XR™ demonstrated a decrease in growth rate over the course of 2 years.[2]



Mean Decrease in BMI Percentile Over 2 Years[2]

- Mean body mass index (BMI) decreased from the 66th percentile at baseline to the 43rd percentile at the end of 2 years.[2]

References: 1. Center for Drug Evaluation and Research, Food and Drug Administration. Review and Evaluation of Clinical Data. NDA 21-303 Adderall XR™. Summary Basis of Approval. 2001. 2. Biederman J, Spencer TJ, Furman DV, on behalf of the Adderall XR Study Group. Extended-release mixed amphetamine salts in ADHD, growth parameter analysis. Poster presented at 156th Annual Meeting of the American Psychiatric Association, May 17-22, 2003, San Francisco, Calif.

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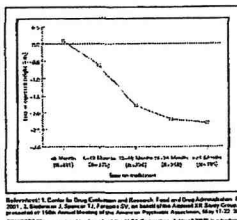

Mean Height Deficit in Centimeters Over 2 Years[2]

- Patients treated for more than 12 months showed a significantly greater deficit in height than those treated for less than 6 months.[2]

References: 1. Center for Drug Evaluation and Research, Food and Drug Administration. Review and Evaluation of Clinical Data. NDA 21-303 Adderall XR™. Summary Basis of Approval. 2001. 2. Biederman J, Spencer TJ, Furman DV, on behalf of the Adderall XR Study Group. Extended-release mixed amphetamine salts in ADHD, growth parameter analysis. Poster presented at 156th Annual Meeting of the American Psychiatric Association, May 17-22 2003, San Francisco, Calif.

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Key Communication Points

- Only the highest dose of Adderall XR™ demonstrates improved attention and behavior for up to 12 hours
- At the highest dose, clinicians must sacrifice tolerability
  - 27% anorexia (vs 11% for placebo)
  - 9% loss of weight (vs 0% for placebo)
  - 20% insomnia (vs 2% for placebo)
- After two years of Adderall XR™ therapy, significant losses were found in both height and weight.
  - patients lost up to 7.8 kg in expected weight. ($p \leq .0001$)
  - body mass index decreased by up to 26 percentiles (for example 50th to 24th percentile)
  - patients lost an average of 2.5 cm in expected height.($p \leq .0001$)


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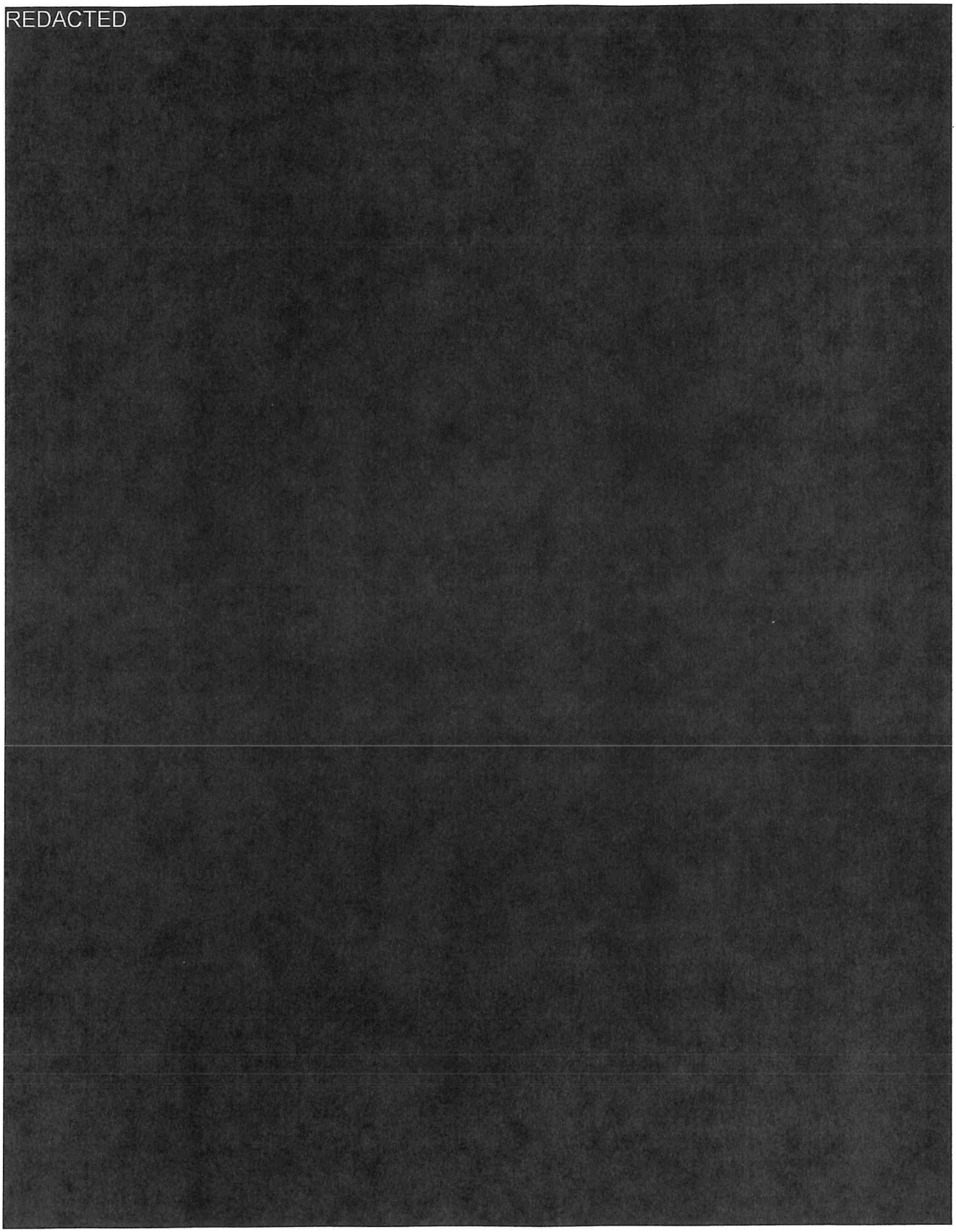

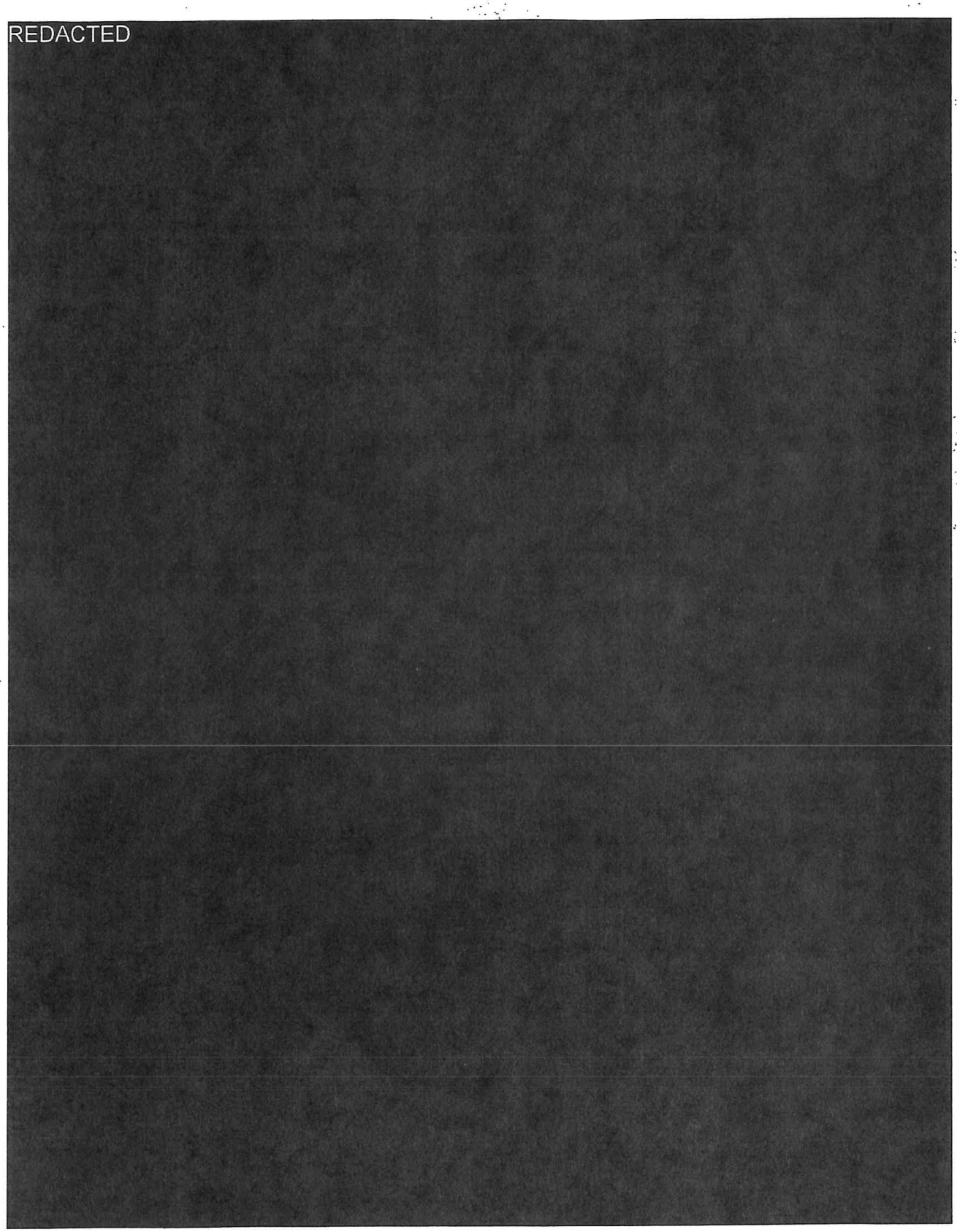
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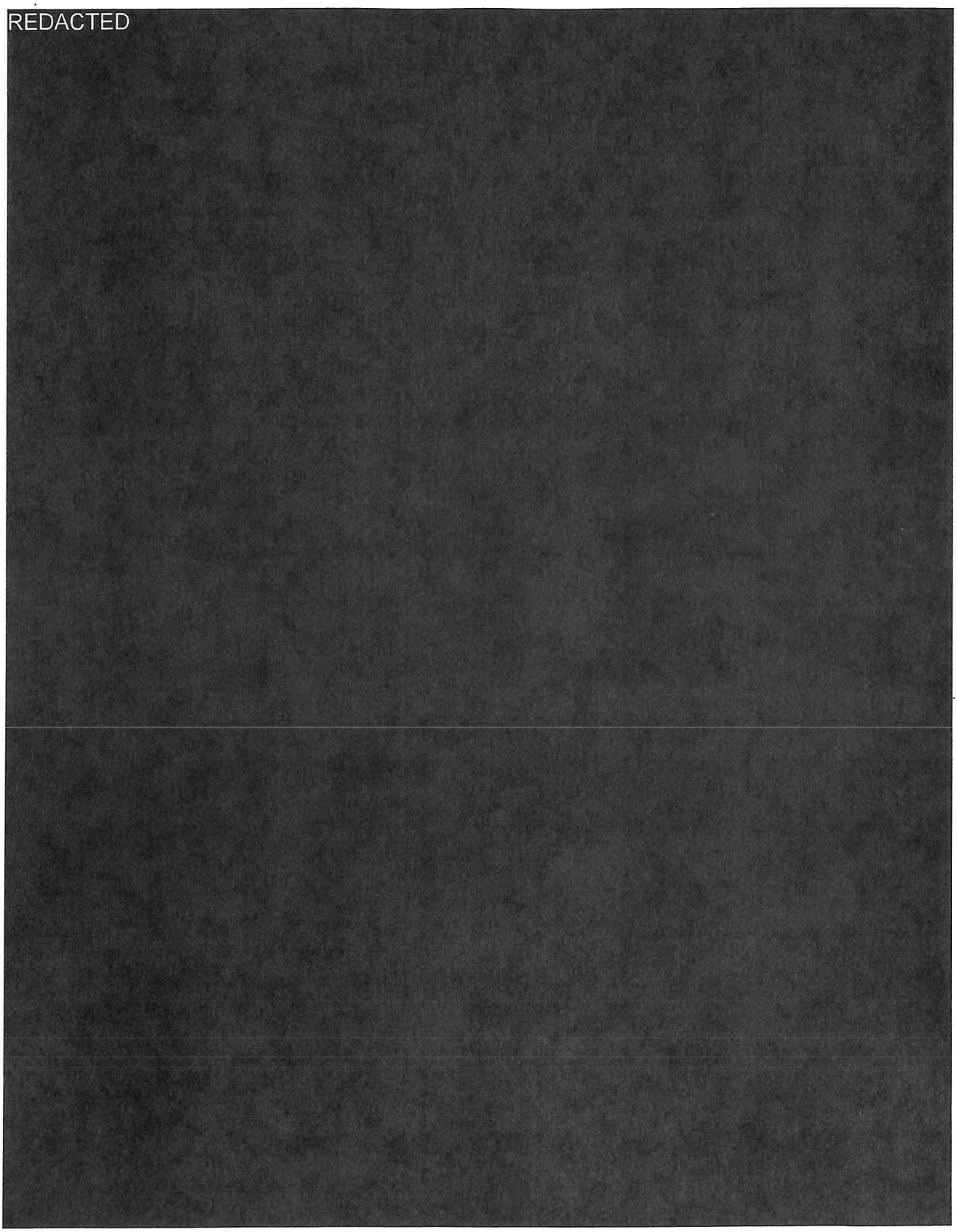

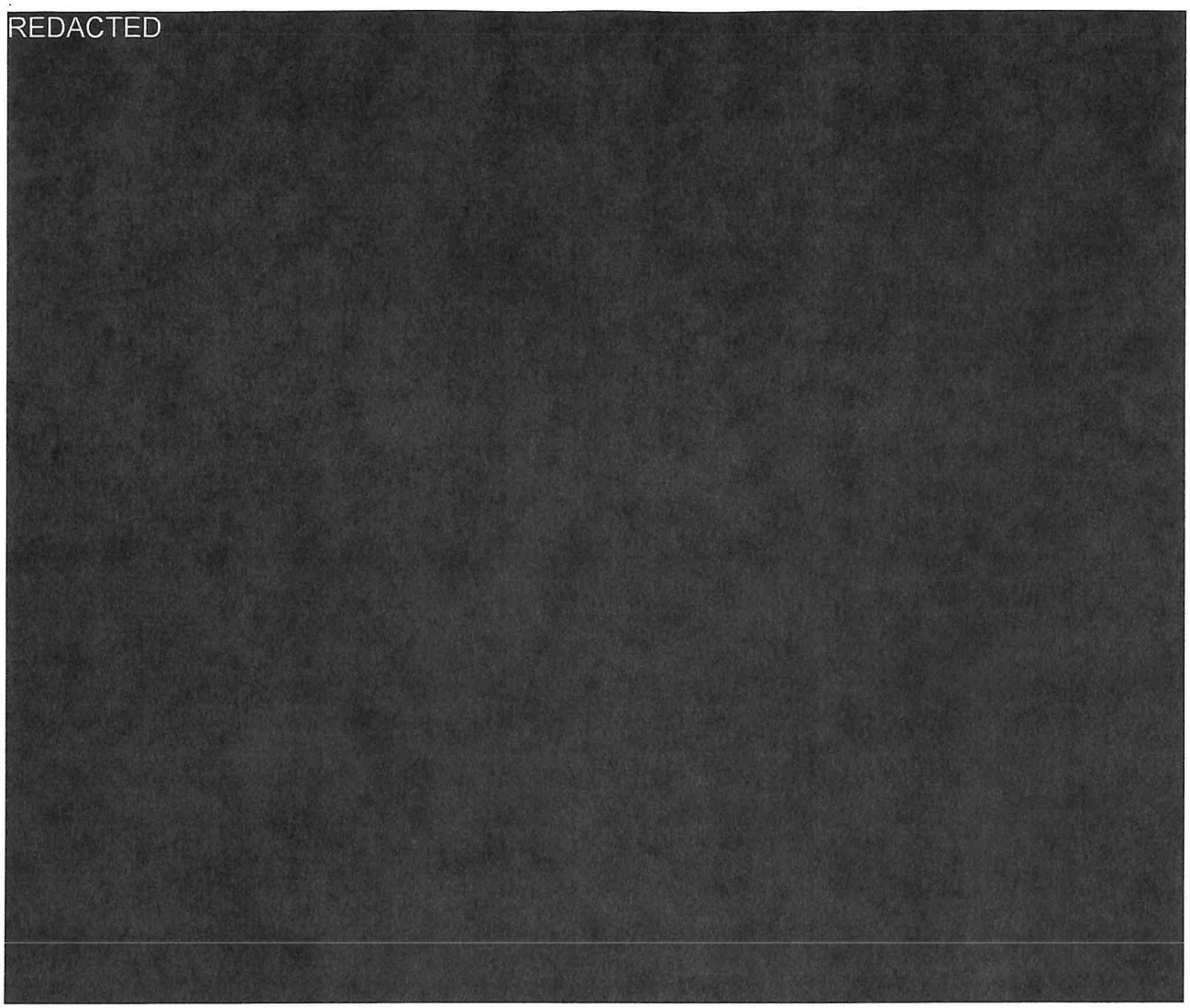
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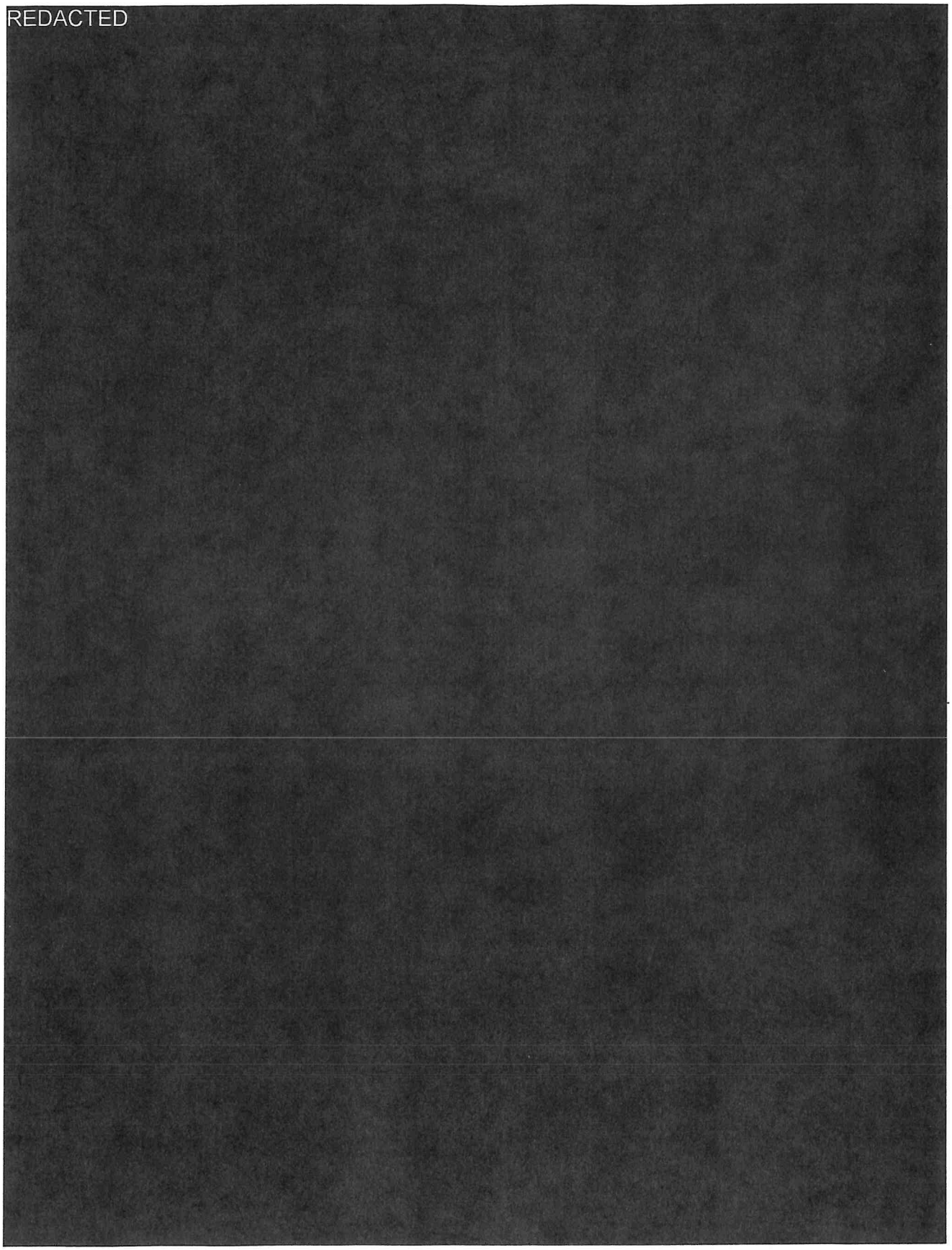

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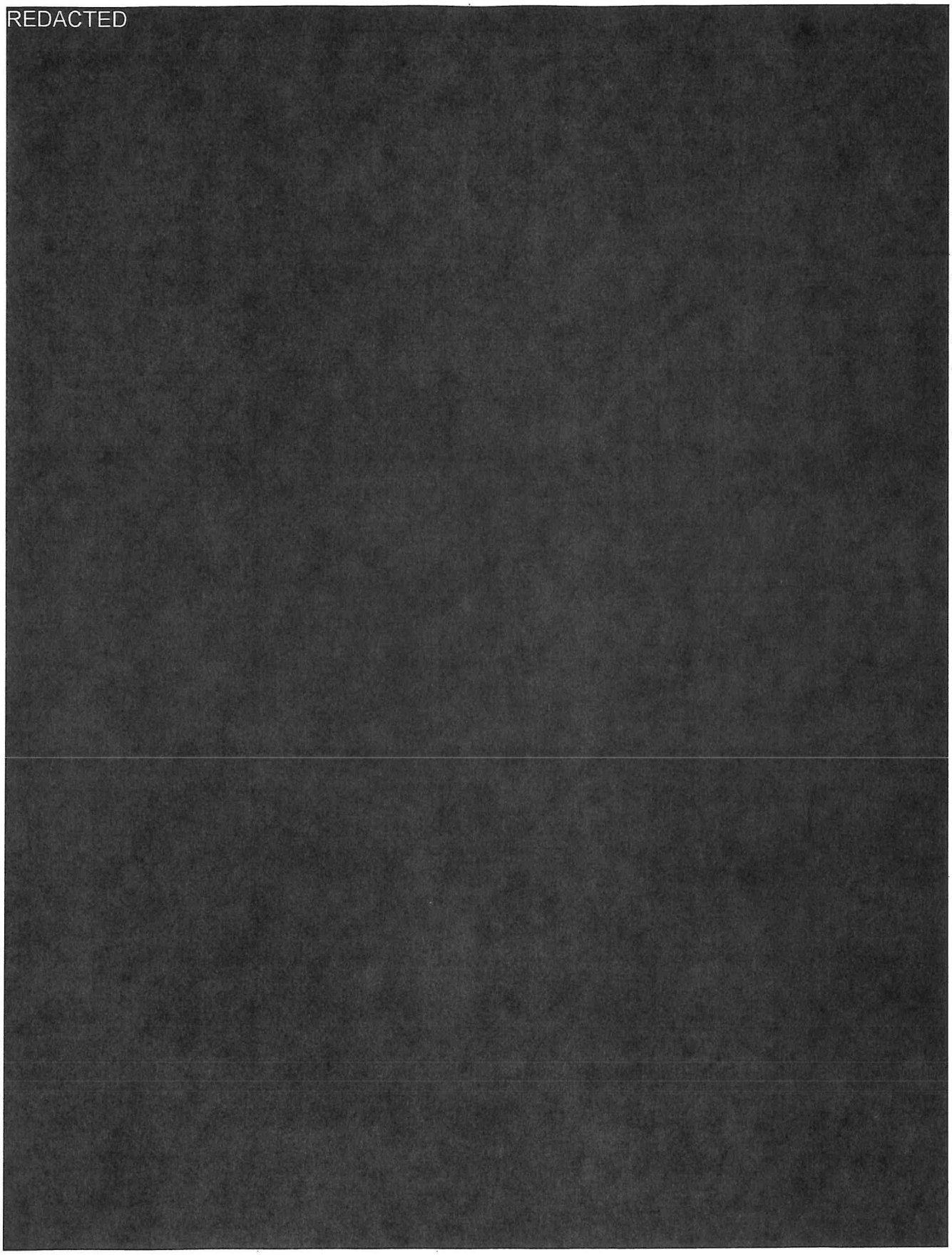

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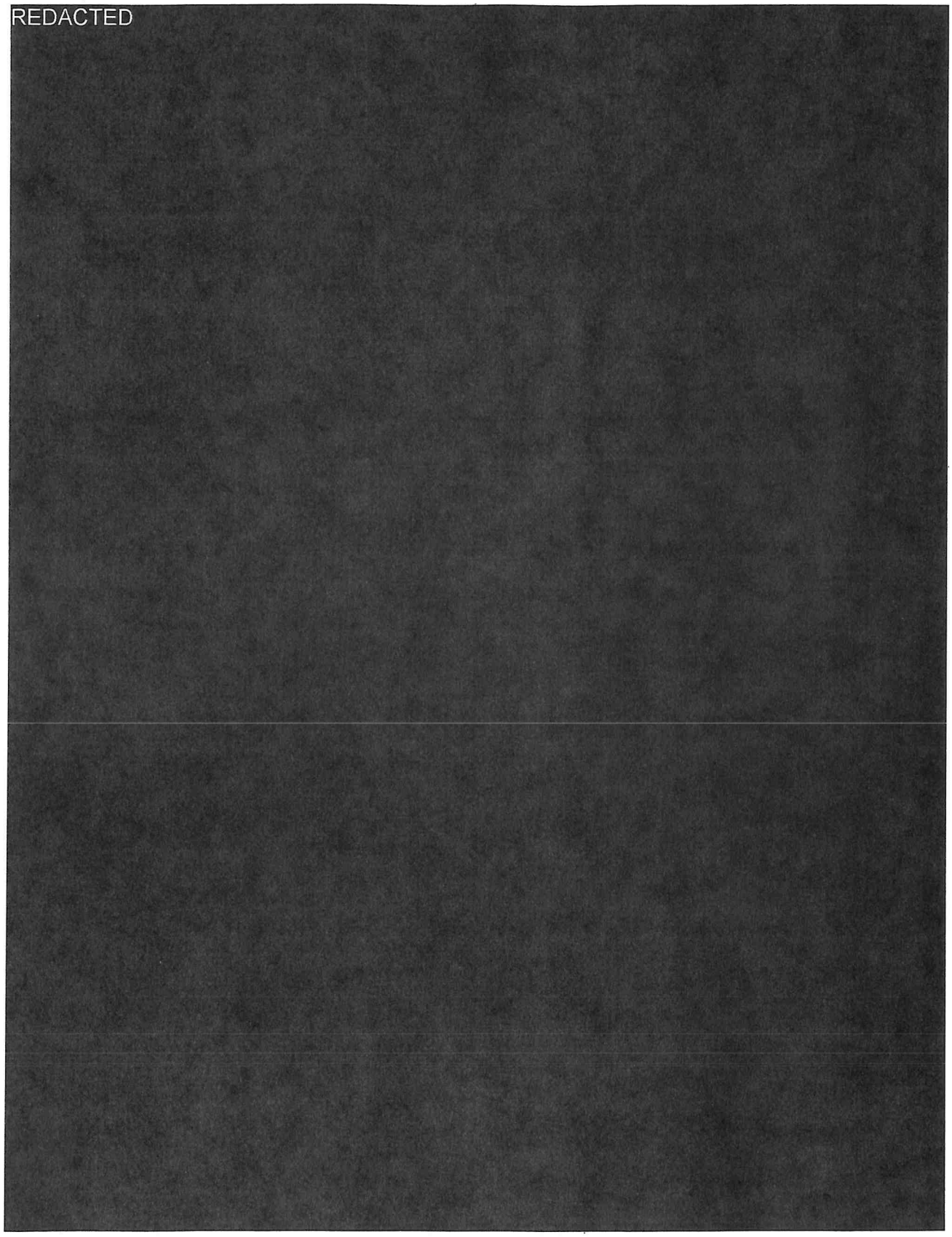

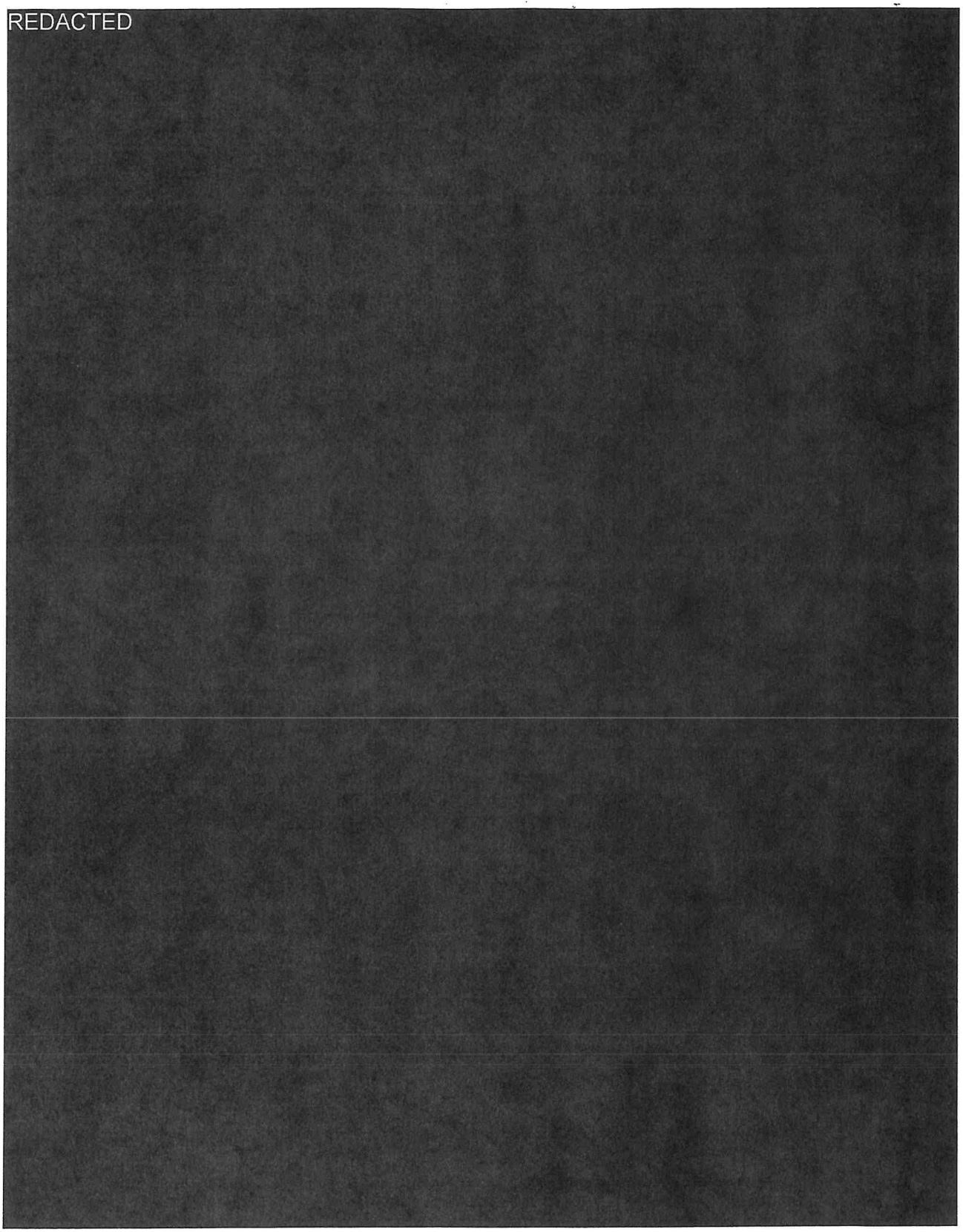
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RISPERDAL

Risperdal
& Comparative PIs

Clinical Reprints
Med Services

Overview of Mental Illness

Overview of the Psychotic Disorders

Roy Steinhouse, M.D.
Professor of Psychiatry
Temple University School of Medicine

Observations of mental illness have been with us since man began drawing pictures and recording his history. Older theories of mental illness included

A. Demon Possession
B. Divine punishment
C. Faulty bodily humors
    1. blood
    2. black bile
    3. yellow bile
    4. phlegm
D. Abnormal brain anatomy and phrenology
E. Abnormal psychology

Newer Theories Include

A. Genetic-neurophysiological-neurotransmitters-anatomic abnormalities
B. Modern psychoanalytic-Ego Psychology, Object Relations Theory, self psychology
C. Cognitive-behavioral
D. Faulty "systems"

Mental illness is ubiquitous

A. 10-20% of women will have a major depression in their lives
B. 8-12% of men will have a major depression in their lives
C. 1% of the population is schizophrenic
D. 0.6% of the population is Bipolar (manic-depressive)
E. There are 8-16 million alcoholics in the U.S.
F. About 30,000 people commit suicide in the U.S. every year (8th leading cause of death)
G. Of the 10 leading causes of disability in the world, five are psychiatric conditions
    1. Alcohol use
    2. Obsessive-compulsive disorder
    3. Major depressive disorder
    4. Schizophrenia
    5. Bipolar affective disorder

The economic costs of mental illnesses in the U.S. are staggering

Mental illness, alcohol, substance abuse and dementia cost over $300 billion dollars for care, lost productivity, police and court costs annually

The Human costs include

- A. Suicide
- B. Crime
- C. Abuse
- D. Wasted lives
- E. Pain and suffering of families and significant others

Psychotic Disorders

- A. Schizophrenia
- B. Delusional Disorder
- C. Schizoaffective Disorder
- D. Schizophreniform Disorders
- E. Brief Psychotic Disorder
- F. Shared Psychotic Disorders (Folie a deux: Symbiotic Psychosis)
- G. Psychosis due to general medical conditions
- H. Delirium and Dementia
- I. Substance Induced Psychosis
- J. Psychotic Depression
- K. Borderline Personality Disorder
- L. Bipolar Disorder
- M. Rare Psychoses

Psychotic Disorders: Schizophrenia

I. History

- A. Emil Kraeplin (1896) – coined term "dementia praecox" to label the chronic deteriorating illness that is now called schizophrenia
- B. Eugene Bleuler (1911) – coined term "schizophrenia" and described the "4 A's" autism, ambivalence, associations (loose), and affect (blunted)
- C. Kurt Schneider (1930's) – described "first rank" symptoms of schizophrenia
  1. Thought broadcasting
  2. Thought insertions
  3. Thought withdrawal
  4. Auditory hallucinations
  5. Delusions
  6. Control of patient's behavior/impulses from an outside source

II. Signs and Symptoms

- A. Thought Disorder
  1. Disturbance of thought content
     - a. Delusions
       1. Persecutory (they're out to get me)
       2. Reference (they're talking about me)
       3. Religious
       4. Grandiose

5. Somatic

b. Hallucinations

1. Auditory: single or multiple voices, perceived as coming from outside the head; must be more than one or two words; auditory hallucinations are the most common
2. Other senses: tactile, visual, gustatory, and olfactory. (Visual gustatory, and olfactory hallucinations in the absence of auditory hallucinations suggest a medial problem.)

c. Poverty of thought

2. Disturbance of thought process

a. Loose associations (thoughts not connected), sometimes referred to as "derailment
b. Blocking (sudden disruption in train of thought)
c. Neologism (new word created by patient, often combining syllables of other words, for idiosyncratic reasons)
d. Clang association (association of words similar in sound but not in meaning)
e. Glossolalia (also known as "speaking in tongues")
f. Verbigeration (meaningless repetition of specific words or phrases)
g. Perseveration (persisting response to a prior stimulus after a new stimulus has been presented)
h. Echolalia (repeating of words/phrases of one person by another)

B. Other disturbances associated with Schizophrenia

1. Affect
   a. range
   b. appropriateness
   c. stability
2. Volition
   a. impairment in self-initiated, goal-directed behavior
   b. ambivalence
3. Interpersonal Functioning
   a. withdrawn, detached, impaired social functioning
   b. autism – retreat into an inner world
   c. loss of contact with reality
4. Sense of self
   a. Poor/blurred "boundaries" (Am I him, or is he me?)
   b. Depersonalization, derealization
5. Psychomotor behavior
   a. catatonia (mutism, rigidity, "waxy flexibility")
   b. excitement, increased spontaneous activity, agitation
   c. mannerisms

C. "Positive" Vs "Negative" symptoms

1. Positive (or productive): active psychotic symptoms such as delusions, hallucinations, loose associations

2. Negative (or deficit): flattening affect, alogia (poverty of speech or content of speech), avolition (lack of initiation of activity), apathy

III. DSM-IV Criteria
- A. Characteristic symptoms: 2 or more of the following, present/active for significant portion of a one month period
  1. Delusions
  2. Hallucinations
  3. Disorganized speech
  4. Grossly disorganized or catatonic behavior
  5. Negative symptoms
- B. Functioning in work, social relations or self-care impaired since onset or if gradual onset, patient fails to achieve expected levels of functioning
- C. Duration: continuous signs present for at least 6 months: includes 1 month of active symptoms (criterion A) and prodromal or residual symptoms (i.e.: negative symptoms or attenuated forms of positive symptoms – odd beliefs, unusual perceptual disturbances)
- D. Not schizoaffective disorder or psychotic affective disorder
- E. Not due to a substance or medical condition

IV. Classification of Types
- A. Paranoid
  1. Preoccupations with 1 or more delusions; content usually organized around a theme
  2. No disorganized speech; no disorganized or catatonic behavior; no flat or inappropriate affect
- B. Disorganized
  1. All of the following are present: disorganized speech, disorganized behavior, flatter/inappropriate affect
  2. Not catatonic; delusions or hallucinations may be present but are not systematized
  3. More extreme impairment of functioning; insidious onset; chronic course
- C. Catatonic
  1. Symptoms include 2 of the following
     a. Motor immobility evidenced by catalepsy or stupor
     b. Excessive purposeless motor activity
     c. Extreme negativism or mutism
     d. Peculiarities of voluntary movement evidenced by posturing, stereotyped movements, prominent mannerisms or grimacing
     e. Echolalia or echopraxia
- D. Undifferentiated – prominent psychotic symptoms that cannot be better classified as paranoid, disorganized or catatonic type
- E. Residual
  1. Absence of prominent psychotic symptoms
  2. Continuing evidence of negative symptoms (flat affect, alogia, avolition) or positive symptoms in attenuated form

F. Obsessive-Compulsive Type

V. Differential Diagnosis
- A. Other affective and psychotic disorders
- B. Substance-induced psychotic states (medications, drugs of abuse, alcohol)
- C. Medical conditions
  1. Delirium
  2. Dementia
  3. Deficiency states: B12, folate, thiamin niacin
  4. Neurologic: Parkinson's, Huntington's chorea, epilepsy, strokes, tumors
  5. Endocrinopathies
  6. Metabolic: hepatic, uremic, hypercalcemic, hypoglycemic, hyponatremic

VI. Epidemiology
- A. Lifetime prevalence is 1 to 1.5%
- B. Sex: males≥females
- C. Socioeconomic factors: higher prevalence in lower classes, but similar incidence across all classes indicates "downward drift" as a result of impaired functioning
- D. Region: urban>rural: prevalence increases with population density. 1/3 to 2/3 if homeless thought to be schizophrenic
- E. Suicide: 50% attempt, 10% are successful

VII. Course and Prognosis
- A. Onset: peak onset in males: 15-25 years, females 25-35 years: rare before age 10 or after 50
- B. Prodrome: acute psychosis may be preceded by prodromal symptoms which can be present for years; however, not all patients with schizophrenia hve an insidious onset
- C. Prognosis
  1. Good prognosis vs. poor prognosis:

	Good Prognosis	Poor Prognosis
Onset	Acute, late	Insidious
Precipitants	Clear	None
Premorbid work & social history	Good	Poor
Symptoms	Affective, positive, catatonic	Withdrawn, autistic, Negative
Marital	Married	Never married
Family history	Affective disorder	Schizophrenia
Social supports	Good	Poor
Other		Neurologic sx Abnormal CT, EEG, Etc:h/o Perinatal trauma:h/o assaultiveness

VIII. Etiology

A. Biological theories

1. Dopamine hypothesis - current leading hypothesis for the etiology of schizophrenia postulates that hyperactivity of the dopamine system in the mesolimbic and mesocortical areas is linked to psychosis
   a. Supported by these observations:
      1. Antipsychotic drugs block the dopamine receptor
      2. Antipsychotic potency correlates with D2 receptor affinity
      3. Dopamine agonists can cause psychosis (e.g, amphetamines, L-dopa)
      4. Plasma HVA (homovanillic acid), a dopamine metabolite, correlates with severity of psychotic symptoms
   b. Problems with the dopamine hypothesis
      1. Antipsychotics treat psychotic symptoms in other conditions, not just schizophrenia
      2. Antipsychotics are less effective for negative symptoms
      3. D2 receptor gene is not linked to schizophrenia
      4. "Atypical" antipsychotics have decreased D2 receptor affinity
   c. Current theories now include D1 receptor antagonism and/or 5HT2 antagonism: LSD is a 5HT2 agonist
   d. What is the role of glutamate?

2. Neuroanatomic structural correlates
   a. CT scan: lateral and 3rd ventricle enlargement in 10 to 50% with schizophrenia: 10 to 35%show cortical atrophy. This is independent of treatment, irreversible, and non progressive
   b. MRI studies suggest changes in the temporal lobe; these structural changes are associated with negative symptoms, neuropsychiatric impairment, more neurologic signs, and poorer premorbid function
   c. Regional blood flow and PET scan findings show decreased blood flow/glucose utilization in the frontal lobes
   d. 3 primary regions involved in schizophrenia, neuroanatomically, are the frontal lobes, limbic system, and basal ganglia
3. EEG abnormalities: increased spike activity with activation; nonspecific abnormalities. Suggests increased sensitivity to sensory input
   Infectious hypothesis: infection causing congenital anomalies complications at birth followed later by psychosis
4. Genetic: family and twin studies support this but concordance is not 100%

B. Psychosocial theories

1. Disturbed relationship with family (mother) and peers
2. Social class: Drift vs. Breeder hypothesis (do central urban areas attract schizophrenics or tend to produce them?)

IX. Treatment

A. Neuroleptic (antipsychotic) medications

1. Typical antipsychotics (Mellaril, Haldol, Thorazine) treat signs and symptoms of schizophrenia, are more effective for positive symptoms
2. Atypical antipsychotics (Clozaril, Resperdal, Zyprexa) may be more effective for negative symptoms
3. Typicals are useful in other psychotic disorders
4. Know a few of these medications well: dosages, side effects, etc.

B. Hospitalization
1. frequently required in schizophrenia
   a. a safe, protected environment
   b. reduction in stress (e.g., from chaotic home environment)
   c. a structured setting
   d. more intensive nursing care, monitoring/observation

C. Psychosocial
1. Supportive therapy: help manage demands of daily life; to improve medication compliance
2. Family involvement
   a. education about the illness
   b. intervene in high "EE" (expressive emotion) families that are hostile, critical, overintrusive, overinvolved, chaotic
   c. presumption that families cause schizophrenia is untrue

D. Behavioral interventions
1. Used to encourage appropriate social behavior
2. Vocational training/promotion of skills

PSYCHOTIC DISORDERS

Delusional Disorder
1. DSM-IV Criteria
   a. Presence of non-bizarre delusion for at least 1 month
   b. Criterion A for schizophrenia has not been met
   c. Functioning is not markedly impaired and behavior is not bizarre
   d. If mood episodes are present, they have been brief relative to delusions
   e. Not due to a substance or medical condition
2. Types
   a. Erotomanic - that another person often famous, loves the patient
   b. Grandiose-delusion of inflated self-importance
   c. Jealous - that the sexual partner is unfaithful
   d. Persecutory - that the patient (or associate) is being intentionally mistreated or harmed
   e. Somatic - that the patient has some physical defect or disease
   f. Mixed
   g. Unspecificied
3. Epidemiology
   a. Prevalence is about 0.03%
   b. Sex ratio: slightly more common in women than men
4. Course

a. Onset: average onset between 40-55, but can occur between 20 and 90
b. 50% recover, 20% improve, 30% chronic (the persecutory type tends to be chronic)
c. Follow-up suggests that the disorder does not change to schizophrenia or mood disorder

5. Etiology
   a. Risk factors: immigration, emigration, deafness, blindness, isolation, low socioeconomic status
   b. Psychological history may include physical abuse, emotional abuse, cruel or erratic parenting
   c. No regular biologic defect in this disorder
6. Treatment
   a. Hospitalization for suicidal/homicidal ideation
   b. Antipsychotics (syndrome may be med. resistant)
   c. Psychotherapy (syndrome may be therapy resistant)

II. Schizoaffective Disorder
1. DSM-IV Criteria
   a. An uninterrupted period of illness during which there is either a major depressive episode, a manic episode or a mixed episode present with psychotic symptoms meeting criteria A for schizophrenia
   b. During the same period of illness, there have been delusions or hallucinations present for at least 2 weeks in the absence of prominent mood symptoms
   c. Symptoms that met criteria for a mood episode are present for a substantial portion of the total duration of the active and residual phase of the illness
   d. Not due to a substance or medical condition
2. Course
   a. outcome for schizoaffective-bipolar type may be better than for depressed type
   b. predictors of course and prognosis in schizoaffective-depressed type are similar to those for schizophrenia
3. Etiology
   a. none established remains a controversial disorder
   b. family studies find an increased frequency of schizophrenia and bipolar disorder in relatives of probands with schizoaffective-bipolar type
4. Treatment
   a. Hospitalization and supportive interventions as for other psychotic disorders
   b. Pharmacologic treatment:
      1. Bipolar type: combinations of mood stablizers and antipsychotics
      2. Depressed type: similar to treatment of psychotic depression (antidepressants and antipsychotics)

Schizophreniform Disorder

1. DSM-IV Criteria
   a. Psychotic symptoms (criterion A) as in schizophrenia
   b. The episode (including prodrome, active, and residual phases) lasts longer than 1 month but less than 6 months
   c. Does not meet criteria for affective disorder and not due to a medical condition
   d. If the patient meets criteria for both schizophreniform disorder and brief reactive psychosis, the diagnosis of brief reactive psychosis preempts and is diagnosed
   e. Schizophreniform disorder can be subtyped as "without good prognosis" or "with good prognosis" if 2 of the following are present:
      1. Psychotic symptoms began within 4 weeks of the first symptoms
      2. Confusion or perplexity at height of the episode
      3. Good premorbid functioning
      4. Absence of blunted or flat affect
2. Epidemiology
   a. Lifetime prevalence is 0.2%
   b. Sex ratio not established
3. Treatment
   a. Hospitalization, supportive treatment
   b. Antipsychotics are primarily drugs used
   c. After a first episode has cleared, a trial off antipsychotic is warranted

III. Brief Psychotic Disorder

1. DSM-IV Criteria
   a. Presence of 1 or more of the following:
      1. Delusions
      2. Hallucinations
      3. Disorganized speech
      4. Grossly disorganized or catatonic behavior
   b. Duration of the episode is at least 1 day but less than 1 month with full return to premorbid level of functioning
   c. Not better accounted for by mood disorder with psychotic features, schizophrenia, or schizoaffective disorder
   d. Not due to a substance or general medical condition
   e. Specify with 1 of the following if applicable:
      1. with marked stressor
      2. without marked stressdor
      3. with postpartum onset
2. Course
   a. Onset usually in young adulthood
   c. By definition the symptoms resolve quickly but may be followed by psychological sequelae, i.e., loss of self-confidence
3. Treatment
   a. Hospitalization may be required

b. Antipsychotics may be used sedatives/antianxiety meds are also useful and may be sufficient
c. Psychotherapy

IV. Shared Psychotic Disorder

1. DSM-IV Criteria
   a. A delusion that develops in the patient in the content of a close relationship with another person who already has an established delusion
   b. Delusion similar in content to the delusion of the primary case
   c. Not better accounted for by other psychotic disorder, mood disorder, substance, or medical condition
   d. Usually within families

2. Epidemiology
   a. Prevalence: very rare
   b. More common in women than men

3. Course: usually chronic

4. Etiology
   a. Biological vs psychological basis is unclear/unknown
   b. Involves a dyad of dominant and submissive person
   c. Because it occurs in families, there might be a genetic factor

5. Treatment
   a. First separate the dyad
   b. The delusions of the submissive partner may resolve with separation; if not, antipsychotics may be used; supportive treatment will be required after separation from the dominant partner on whom s/he depends
   c. Treatment of the dominant partner is difficult

<u>Psychosis Due to General Medical Condition</u>

The patient is ill primarily with a medical problem. As part of that syndrome - for example a hyperthyroid patient who is hallucinating - they have become psychotic

Central nervous system abnormalities can occur with multiple medical conditions- endocrine problems, autoimmune phenomena and central nervous system pathology being a few.

Treatment

1. correct the underlying medical abnormality
2. use of neuroleptic and other drugs to treat the psychosis or for behavioral control

Delirium and Dementia

Very common problems in a general hospital setting

Delirium	Dementia
Acute	Chronic
Cell alteration	Cell death
Reversible	Often irreversible

Both show problems with memory and cognition

Delirium - altered sleep wake cycle
Fluctuating consciousness
Labile affect
Quicker onset

23-33% of delirious patients are dead within 3 months - up to 50% are dead in one year

Treatment - proper timely diagnosis. Treat underlying cause. Use of neuroleptics for behavioral control and to treat psychosis if present.

Substance Induced Psychosis

Psychotic symptoms that appear in an individual secondary to substance intoxication - some offenders are alcohol (especially in withdrawal - D'T's (Delirium Tremens), Amphetamines, Cocaine, Hallucinogens, Phencyclidine.

One would expect that when the substance is fully metabolized, psychotic symptoms will clear. Treatment usually supportive - hydration, nutrition, reassurance. Medications as indicated and needed.

Depression with Psychotic Features

In a proportion of patients who develop the more severe depressions - Major Depressive Episode and Melancholia - psychotic symptoms may appear.

Can consist of various delusions with feelings of worthlessness, a sense that one is rotting away, etc.

Or can have hallucinations - usually auditory and of a self-deprecatory nature

The primary treatment is for the depression and would consist of antidepressants and/or electroconvulsive therapy (ECT). Neuroleptics can and are often used in the early stages of treatment to suppress the psychosis. Hopefully, neuroleptics can be withdrawn as the depression clears.

Borderline Personality Disorder

Old nomenclature - Pseudoneurotic Schizophrenia - An Axis 2 diagnosis - Character/Personality Disorder

a. Small percentage may have transient psychotic or psychotic-like symptoms.
May be a role for brief neuroleptic treatment.

Bipolar Disorder (Manic-Depressive)

An **Affective not a Thought** Disorder. Some patients with full blown mania or severe depression may have psychotic symptoms.

Bipolar I Disorder - the severe form usually requiring hospitalization.

Bipolar II Disorder - less severe, Hypomanic rather than manic. Usually managed as outpatient if patient is compliant.

Main treatment is with mood stabilizers - Lithium, Tegretol, Depakote.
Role for neuroleptics as adjunctive treatment and for management of psychotic symptoms.

Other Psychotic Syndromes - named for the person describing the syndrome, characterized by a certain type of delusion or other bizarre behavior, these syndromes have since been supplanted by other DSM-IV diagnoses

1. Capgra's syndrome: family members are imposters
2. Clerambault's syndrome: patient is loved by a famous person
3. Cotard's syndrome: belief that one has lost everything, that one has no internal organs, that one is dead
4. Autoscopy: hallucinations of seeing one's own body
5. Heutoscopy: delusion that one has a double (this double is also a Doppleganger)
6. Lycanthropy: delusion of being a werewolf
7. Fregoli's phenomenon: that persecutors or familiar persons can change into strangers

Reprint Workshop

REPRINT WORKSHOP

REPRINT WORKSHOP

Objectives

- What are FDAMA guidelines and how do they impact Janssen CNS Reps
- Review and understand Janssen's promotional/reprint guidelines
- Understand the 6 KEY areas of a clinical reprint
- The Janssen 3 - EFFICACY, SAFETY, DOSING

REPRINT WORKSHOP

- Title/Author/Sponsorship
- Abstract
- Introduction
- Methods
- Results
- Discussion/Conclusion

REPRINT WORKSHOP

Title/Author

- The basic thrust or purpose of the study
- Author names usually appear in the byline, usually just below the title
- Typically there is a maximum of six authors listed
- Most articles have contact information for one or more authors for additional requests/information

REPRINT WORKSHOP

Abstract

- Should answer the question "should I read the full article?" "Is it worth my while?"
- Best used as a roadmap for reading the article
- Often visually set off from the rest of the text by the use of boldface and/or a different type face.
- Summarizes the key content of the paper and is intended to provide a synopsis of the study and the author's conclusions

REPRINT WORKSHOP

Introduction

- States the purpose of the study, for example the hypothesis being tested.
- Establishes a context for understanding the results
- What is the key question being asked in the study?
- What other research led to the study e.g., Tran leading to Ho, Miller, Andreasen
- Why did the investigators think the study was important and worthwhile to perform

REPRINT WORKSHOP
Methods

Describes:

- How study was performed
- Who was studied
- What parameters were measured
- How the data were analyzed, including endpoints and statistical analysis

Is the endpoint relevant to the doctor's practice?

REPRINT WORKSHOP
Methods

What to ask yourself and what a doctor might ask you:

- What was the sample size
- What type of patients were admitted
- Was the study well-controlled
- What treatments did patients receive

REPRINT WORKSHOP
Results

- Typically states just the facts without commentary or interpretation
- Usually contains the statistical significance of the findings. P value at or below 0.05 denotes statistical significance

Ask yourself...

- How do these findings translate into features/benefits
- How will these findings impact my customers' prescribing behaviors
- Are there any findings that reflect negatively on my product
- Is there anything unexpected or ambiguous about the results that need to be examined

REPRINT WORKSHOP
Discussion/Conclusion

- The information contained in the discussion/conclusion is purely discretionary.
  - The authors are free to focus on what they feel are the important findings of the study.

Ask yourself..

- What conclusions did the author draw?
- What advantages/disadvantages did they note for your product and the competition?
- Are the results supported by other studies?

Be careful about making direct comparisons unless the data is head-to-head!

What is FDAMA?

(Food & Drug Administration Modernization Act)

Allows field dissemination* of select reprints if:

- Well-controlled study
- Published in a peer-reviewed journal
- Company has a planned sNDA for the studied use
- Approved via FDA-DDMAC

*See FDAMA Dissemination Procedures

Dissemination Procedures

NOTE:

The following information is for your information only. Details of this study regarding design, findings, and conclusions are not to be discussed with your customers.

Communication points regarding this study must be limited to:

- Name of the article
- What journal in which the article appeared
- Author of the article
- Medical use of the drug described in the article - If medical use of the drug is described in the article is mentioned, representatives MUST indicate that the medical use is not within product labeling

FDAMA Dissemination Procedures

- Reprint carrier will include the following:
  - Article
  - Bibliography
  - Package Insert
- DO NOT ADD/REMOVE any piece of information to/from the carrier.
- Requests for additional reprints must be ordered through Marketing Communications

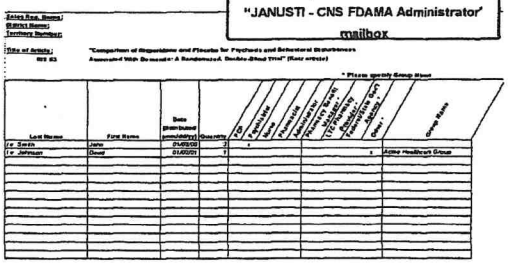
FDAMA Reprint Tracking Report

Must be e-mailed every 6 months to:

April and November

"JANUSTI - CNS FDAMA Administrator"

mailbox



Key Risperdal® Reprints

""The Effects of Risperidone on the Five Dimensions of Schizophrenia" - Marder, Davis

- Facts/Method
  - _____
  - _____
  - _____
- Efficacy
  - _____
  - _____
- Safety/Tolerability
  - _____
  - _____
- Dosing
  - _____
  - _____

"Risperidone Versus Olanzapine in Patients with Schizophrenia and Schizoaffective Disorder" – Conley, et al

- Facts/Method
  - _____
  - _____
  - _____
- Efficacy
  - _____
  - _____
- Safety/Tolerability
  - _____
  - _____
- Dosing
  - _____
  - _____

"Risperidone Versus Olanzapine for the Treatment of Mood Symptoms in Patients With Schizophrenia or Schizoaffective Disorder" – Myers, et al

- Facts/Method
  - _____
  - _____
  - _____
- Efficacy
  - _____
  - _____
- Safety/Tolerability
  - _____
  - _____
- Dosing
  - _____
  - _____

"Optimal Dosing With Risperidone: Updated Recommendations"- Williams

- Facts/Method
  - _____
  - _____
  - _____
- Efficacy
  - _____
  - _____
- Safety/Tolerability
  - _____
  - _____
- Dosing
  - _____
  - _____

"Differential Effects of Risperidone, Olanzapine, Clozapine, and Conventional Antipsychotics on Type 2 Diabetes: Finding from a Large Health Plan Database" – Gianfranceso, et al

- Facts/Method
  - _____
  - _____
  - _____
- Efficacy
  - _____
  - _____
- Safety/Tolerability
  - _____
  - _____
- Dosing
  - _____
  - _____

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  - _____
  - _____
- Safety/Tolerability
  - _____
  - _____
- Dosing
  - _____
  - _____

"Combination of a Mood Stabilizer With Risperidone or Haloperidol for Treatment of Acute Mania: A Double-Blind, Placebo-Controlled Comparison of Efficacy and Safety" – Sachs, et al

- Facts/Method
  - _____
  - _____
  - _____
- Efficacy
  - _____
  - _____
- Safety/Tolerability
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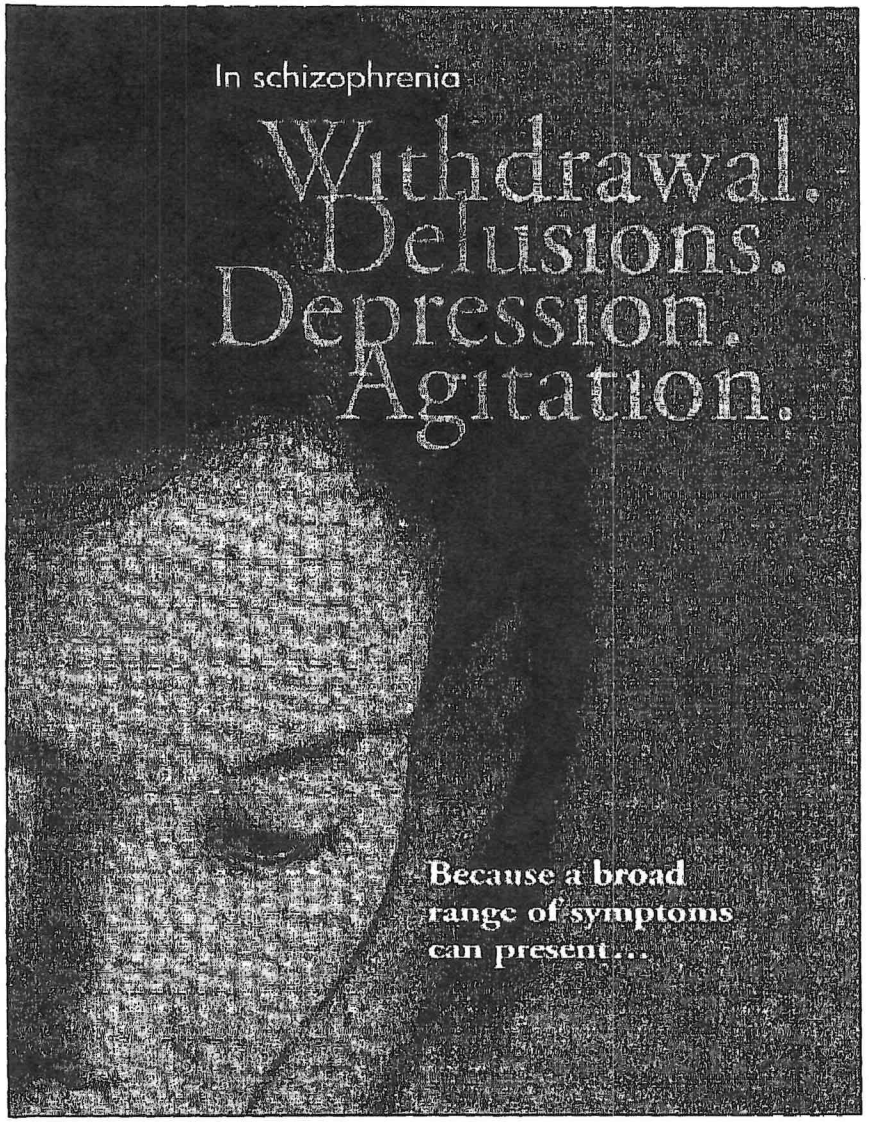
  - _____
- Dosing
  - _____
  - _____

Risperdal Sales Aid
Primer



RISPERDAL® (risperidone)

CNS Sales Aid Primer

Background information to help you maximize use of your new Sales Aid

Throughout this primer you will encounter background information, key messages, and sample sales calls that discuss the use of RISPERDAL for patients suffering from schizophrenia. It is important to understand that RISPERDAL is not approved for treatment outside of schizophrenia.

The information in this annotated guide is intended only for educational sales training purposes regarding RISPERDAL in general and is not intended to be used in a selling situation for RISPERDAL.

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RISPERDAL® (risperidone)

CNS Sales Aid Primer

Introduction

The purpose of this document is to help you maximize the use of your new RISPERDAL Sales Aid and ensure your success in delivering RISPERDAL core messages on every sales call. The RISPERDAL Cycle II sales materials introduce a brand-new image for RISPERDAL. Physicians associate the new RISPERDAL identity with higher-functioning patients and the mood and anxiety symptoms of schizophrenia. In addition, new and exciting clinical data are introduced to support the sales approach.

Note that "The #1 prescribed in its class" has been removed from every page of the Sales Aid and now appears on the back cover. In its place appears the new tagline, "Helping Turn Lives Around." This theme is now the focus of the new RISPERDAL campaign.

Core Selling Messages

- RISPERDAL has a unique receptor-binding profile (including effects on D_2, α_2, and 5-HT_{2A}) that makes it a well-suited atypical to treat mood and anxiety symptoms in patients with schizophrenia
- RISPERDAL significantly outperformed olanzapine on mood and anxiety symptoms in patients with schizophrenia at Week 8
- Low-dose RISPERDAL maintains efficacy while minimizing dose-dependent adverse events (ie, movement disorders)
- Differentiate RISPERDAL from the competition
  - —Low risk of diabetes
  - —Low incidence of daytime sedation
  - —9 years of trusted efficacy and no exacerbation of symptoms

Primary Objective: Broaden Potential Patient Population

In 2003, we must expand our market leadership. The new RISPERDAL campaign will support this objective by broadening our potential patient population and expanding into the higher-functioning schizophrenic patient.

Speak differently to physicians about the benefits of RISPERDAL, by focusing on its outstanding efficacy versus olanzapine in treating anxiety and depression symptoms in patients with schizophrenia without compromising tolerability. This will make physicians **think differently** about the brand, and ultimately, **behave differently** by prescribing RISPERDAL to the higher-functioning schizophrenic patient.

Good luck and good selling!

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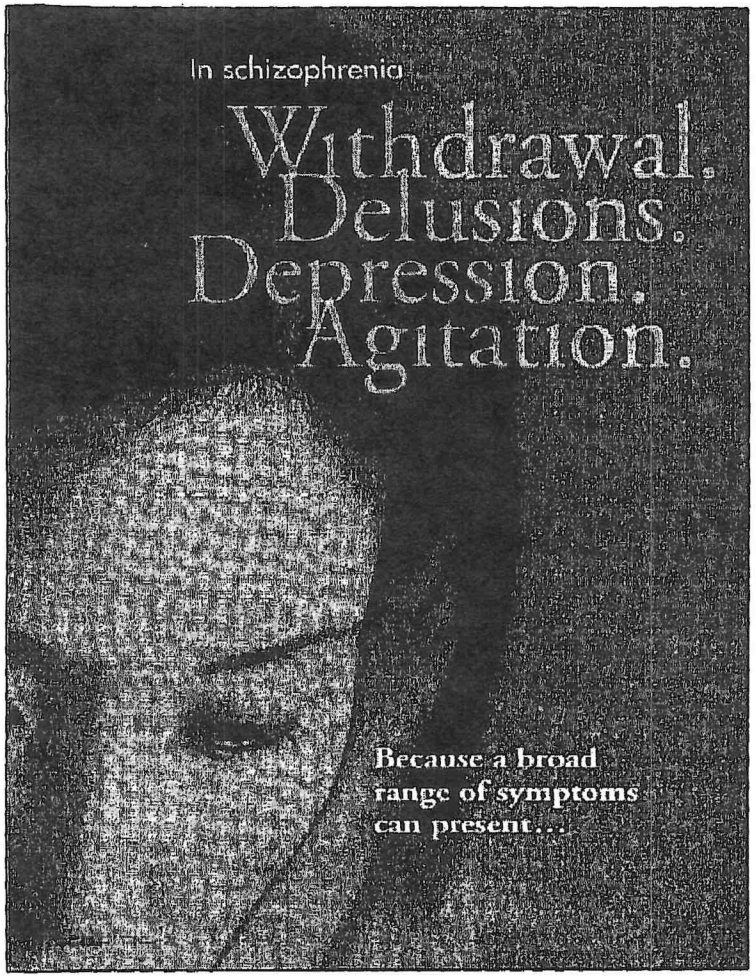

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RISPERDAL® (risperidone)

CNS Sales Aid Primer

Front Cover

Why This Information Is Important

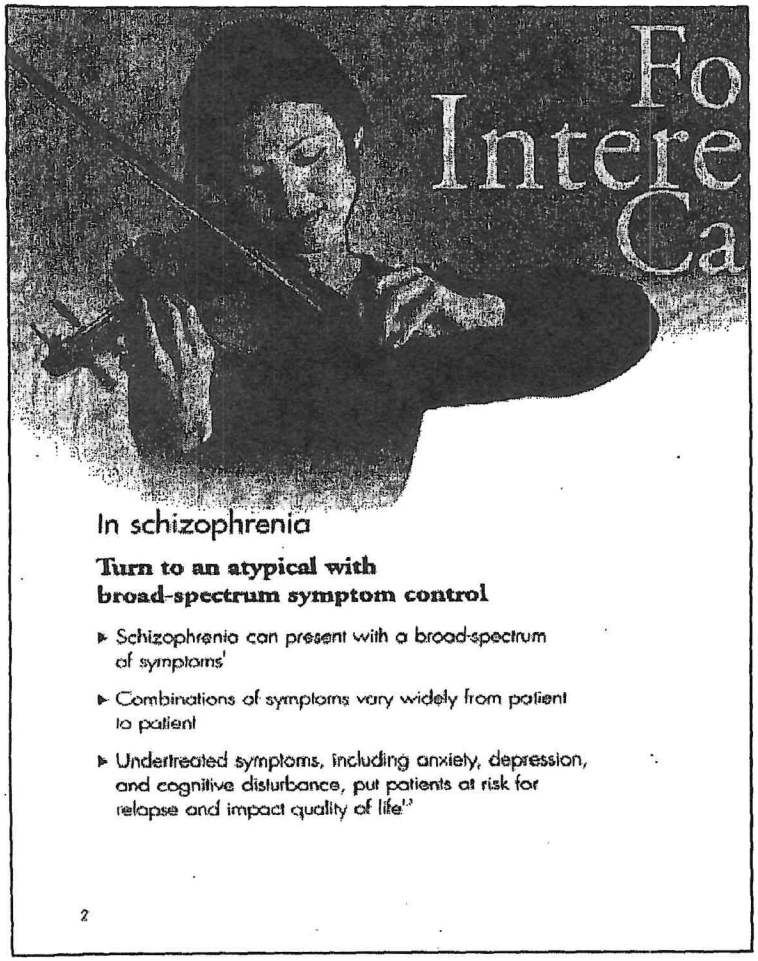
- Opens the discussion with a focus on the broad range of symptoms in schizophrenia that may present, especially depressive and anxious symptoms
  - —Many physicians tend to slot RISPERDAL as a treatment only for the positive and negative symptoms of schizophrenia
  - —Expands the physician's view of RISPERDAL to include the higher-functioning schizophrenic patient
  - —Begins to help physicians think of RISPERDAL differently
- Reflects our exciting new campaign graphics
  - —New brand personality
  - —Patient focus
- Evokes a variety of symptoms that may present in schizophrenia
  - —Withdrawal, delusions, depression, and agitation
  - —Represents 4 out of the 5 PANSS symptom clusters

Key Message

- Patients suffering from schizophrenia—whether they present with psychotic symptoms, such as delusions, or more mood-related symptoms, such as depression—may be appropriate candidates for low-dose RISPERDAL

Key Customer Action

- Visualize a specific patient suffering from anxious or depressive symptoms associated with schizophrenia for whom RISPERDAL is appropriate



RISPERDAL® (risperidone)

CNS Sales Aid Primer

Why This Information Is Important

- Plays off the front cover by highlighting the symptom reversal to positive characteristics—focused, interested, calm, and motivation
  - —Focuses on patient's abilities rather than his/her disabilities
  - —Graphically sets up the new campaign tagline, "Helping Turn Lives Around"
- Builds the case for the appropriateness of using an atypical with broad-spectrum symptom control in the treatment of schizophrenia
  - —Stresses uniqueness of each presenting patient and how unresolved symptoms of schizophrenia—even ones such as depression and anxiety—negatively impact patients' lives

Key Message

- Within schizophrenia, physicians can turn to an atypical with broad-spectrum symptom control to improve patients' lives—whether they present with psychotic symptoms, such as delusions, or primarily mood-related symptoms, such as depression

Key Customer Action

- Accept the appropriateness of utilizing an atypical, RISPERDAL, for a broad range of symptoms associated with schizophrenia

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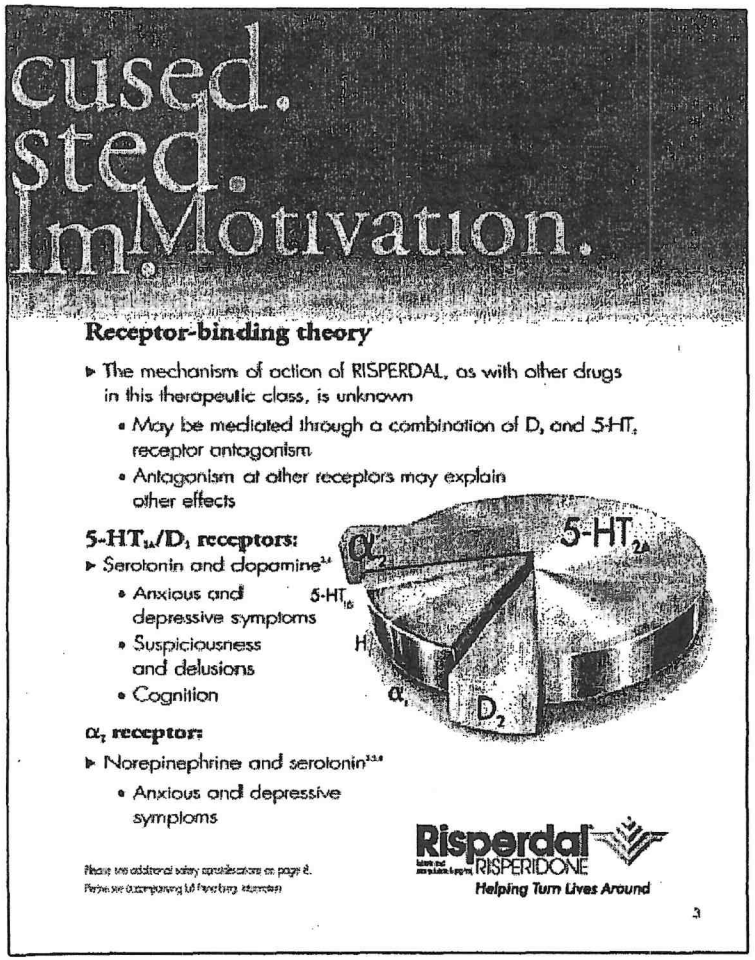

RISPERDAL® (risperidone)

CNS Sales Aid Primer

Why This Information Is Important

- Physicians must understand that the receptor-binding story provides a compelling theoretical and scientific basis to support the use of RISPERDAL in the treatment of anxious and depressive symptoms in patients with schizophrenia
  - —Confers credibility upon RISPERDAL as the brand moves further into a new market segment
- In market research, psychiatrists noted that the potency of RISPERDAL at the α_2-receptor site was highly relevant to the treatment of anxious and depressive symptoms of schizophrenia
  - —Antagonism at this site increases levels of serotonin and norepinephrine, a target of antidepressants and anxiolytics they are currently using
- Note: The Kapur chart will appear in a separate sales piece in which special emphasis will be placed on the benefits of low-dose RISPERDAL

Key Message

- The unique receptor-binding profile of RISPERDAL at low doses, including the α_2 receptor, makes it an ideal agent to treat anxious and depressive symptoms in patients with schizophrenia

Key Customer Action

- See RISPERDAL from a new perspective
  - —RISPERDAL has a relevant and solid pharmacological foundation through which it can be used to treat anxious and depressive symptoms in patients with schizophrenia

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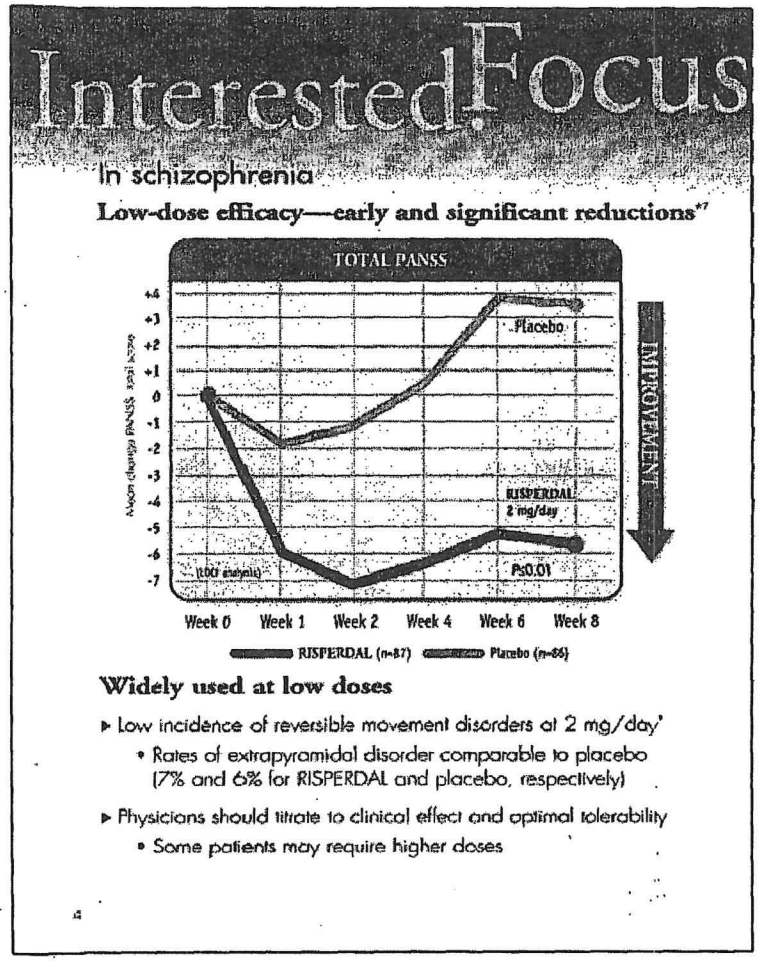

RISPERDAL® (risperidone)

CNS Sales Aid Primer

Why This Information Is Important

- Low-dose RISPERDAL provides early and significant reduction of symptoms associated with schizophrenia, without compromising tolerability
- Physicians were impressed that low doses of RISPERDAL demonstrated significant efficacy while keeping reversible movement disorders (EPS) at a rate comparable to placebo

Key Message

- Low-dose RISPERDAL effectively controls a range of symptoms associated with schizophrenia, with a rate of reversible movement disorders (EPS) comparable to placebo

Key Customer Action

- Gain an understanding that lower doses of RISPERDAL can provide the efficacy needed to control symptoms while minimizing concerns about reversible movement disorders (EPS) observed at higher doses

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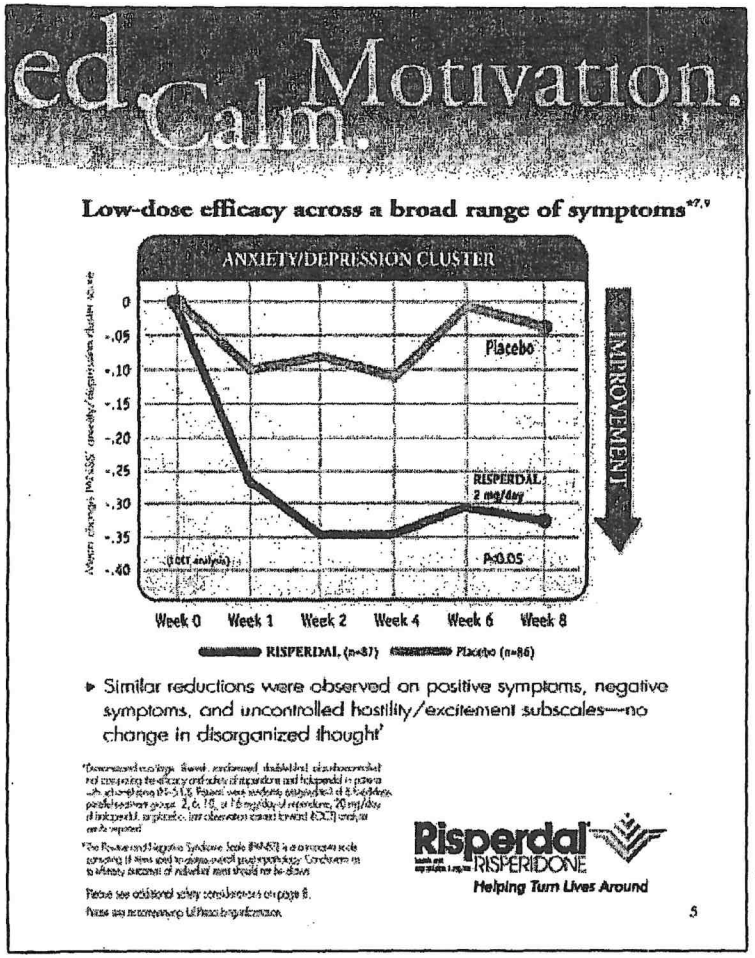

RISPERDAL® (risperidone)

CNS Sales Aid Primer

Why This Information Is Important

- Ensures that physicians understand the significance of these data and how they could impact their prescribing habits, especially at low doses
- The promotion of low-dose RISPERDAL is essential to the expansion of our leadership position
  - —Conveys to physicians that they can have improved tolerability without sacrificing efficacy
- Combat quetiapine by demonstrating the low-dose efficacy of RISPERDAL with a low incidence of daytime sedation

Key Message

- Low-dose RISPERDAL is a significantly effective agent in the treatment of anxious and depressive symptoms in patients with schizophrenia
- For the higher-functioning schizophrenic patient, RISPERDAL has minimal daytime sedation

Key Customer Action

- Full appreciation of all of the benefits associated with low doses of RISPERDAL in schizophrenia
  - —Effective control of anxious and depressive symptoms in patients with schizophrenia while minimizing reversible movement disorders (EPS)

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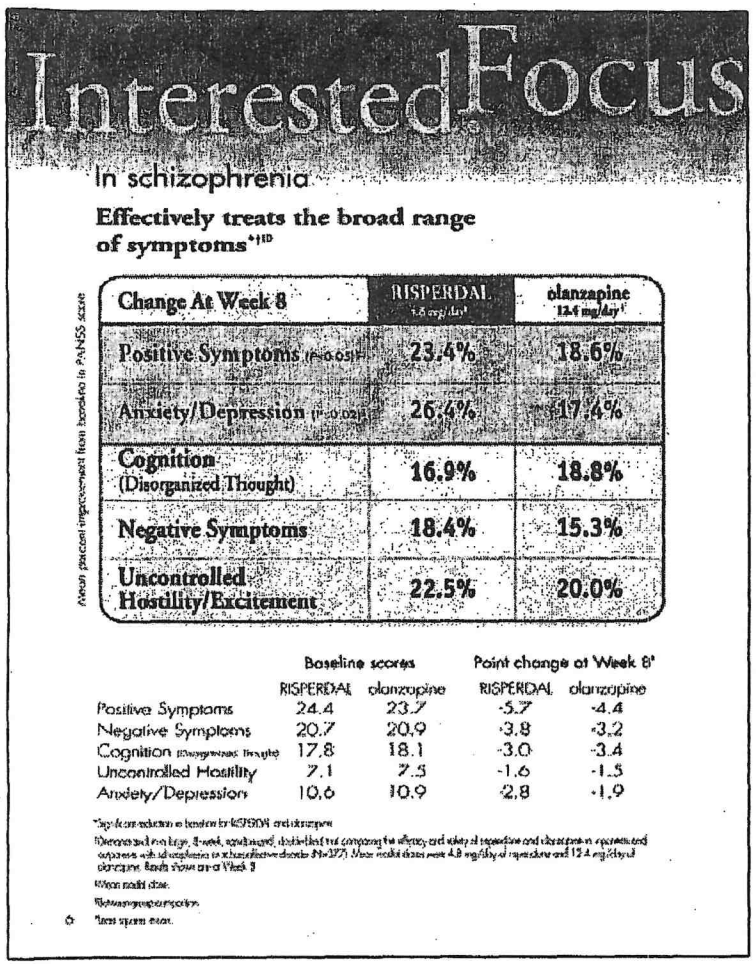

RISPERDAL® (risperidone)

CNS Sales Aid Primer

Why This Information Is Important

- RISPERDAL demonstrated significantly greater improvements in anxious, depressive, and positive symptoms in patients with schizophrenia versus olanzapine at Week 8
- Have physicians take this proven efficacy advantage into account when they weigh the risk/benefit ratios of RISPERDAL and other atypicals

—See page 9 of the Sales Aid for additional discussion on Safety & Tolerability

Key Message

- In a head-to-head, double-blind trial, RISPERDAL significantly outperformed olanzapine at Week 8 across a range of symptoms in patients with schizophrenia, specifically anxious, depressive, and positive symptoms

Key Customer Action

- Intention to prescribe RISPERDAL instead of olanzapine for the next appropriate patient in this population for whom they would consider prescribing an atypical

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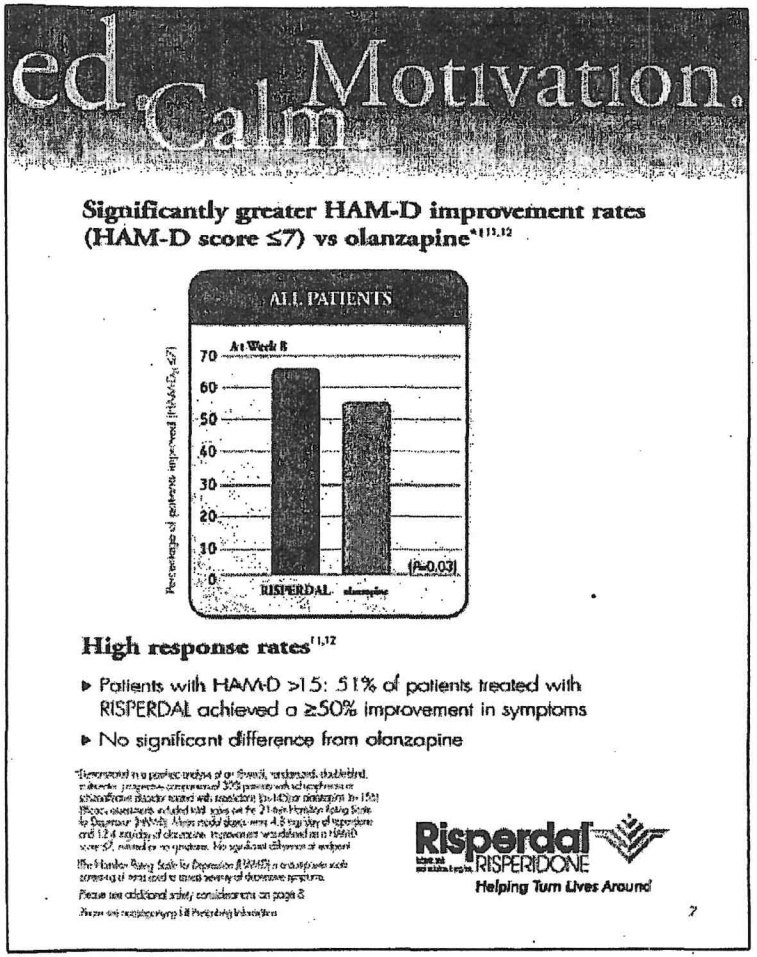

RISPERDAL® (risperidone)

CNS Sales Aid Primer

Why This Information Is Important

- RISPERDAL helped significantly more patients improve (HAM-D ≤7) than olanzapine in depressive symptoms associated with schizophrenia
  - —HAM-D ≤7 is the criterion commonly used to define remission in depression trials
  - —Provides a compelling reason to prescribe RISPERDAL over olanzapine
- For patients experiencing severe depressive symptoms associated with schizophrenia, RISPERDAL demonstrated significant efficacy in patients with higher levels of symptomatology
  - —More than 50% of patients with a HAM-D >15 showed a response to therapy (a ≥50% improvement in symptoms)
  - —Tells physicians RISPERDAL is efficacious for many schizophrenic patient types who present across a range of severity

Key Message

- RISPERDAL outperformed olanzapine in helping significantly more schizophrenic patients improve (HAM-D ≤7) their depressive symptoms at Week 8

Key Customer Action

- New appreciation of the benefits RISPERDAL offers versus olanzapine in this patient population when an atypical is deemed appropriate

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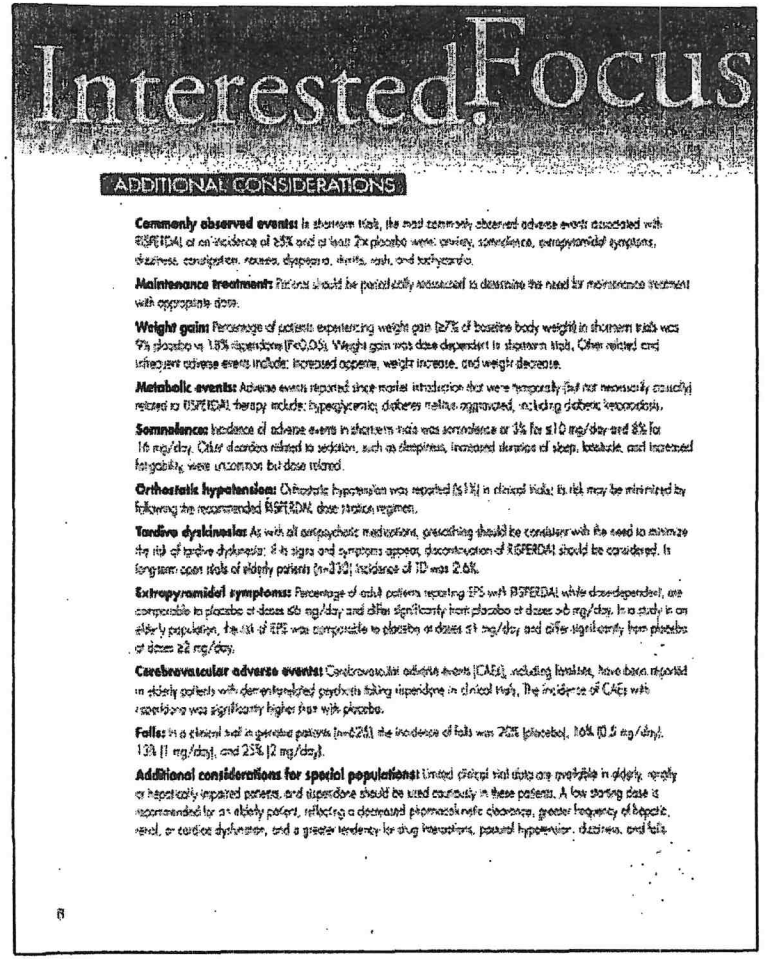

Interested Focus

ADDITIONAL CONSIDERATIONS

Commonly observed events: In short-term trials, the most commonly observed adverse events associated with RISPERDAL at an incidence of ≥5% and at least 2x placebo were: anxiety, somnolence, extrapyramidal symptoms, dizziness, constipation, nausea, dyspepsia, rhinitis, rash, and tachycardia.

Maintenance treatment: Patients should be periodically reassessed to determine the need for maintenance treatment with appropriate dose.

Weight gain: Percentage of patients experiencing weight gain (≥7% of baseline body weight) in short-term trials was 9% placebo vs. 18% risperidone (FeO,0.5). Weight gain was dose dependent in short-term trials. Other related and infrequent adverse events include: increased appetite, weight increase, and weight decrease.

Metabolic events: Adverse events reported since market introduction that were temporally (but not necessarily causally) related to RISPERDAL therapy include: hyperglycemic; diabetes mellitus aggravated, including diabetic ketoacidosis.

Somnolence: Incidence of adverse events in short-term trials was somnolence at 3% for ≤10 mg/day and 8% for 16 mg/day. Other disorders related to sedation, such as sleepiness, increased duration of sleep, lethargy, and increased fatigability, were uncommon but dose related.

Orthostatic hypotension: Orthostatic hypotension was reported (5.1%) in clinical trials; its risk may be minimized by following the recommended RISPERDAL dose titration regimen.

Tardive dyskinesias: As with all antipsychotic medications, prescribing should be consistent with the need to minimize the risk of tardive dyskinesia; if its signs and symptoms appear, discontinuation of RISPERDAL should be considered. In long-term open trials of elderly patients (n=332), incidence of TD was 2.6%.

Extrapyramidal symptoms: Percentage of adult patients reporting EPS with RISPERDAL while dose-dependent, are comparable to placebo at doses ≤8 mg/day and differ significantly from placebo at doses >8 mg/day. In a study in an elderly population, the risk of EPS was comparable to placebo at doses ≤1 mg/day and differ significantly from placebo at doses ≥2 mg/day.

Cerebrovascular adverse events: Cerebrovascular adverse events (CAEs), including fatalities, have been reported in elderly patients with dementia-related psychosis taking risperidone in clinical trials. The incidence of CAEs with risperidone was significantly higher than with placebo.

Falls: In a clinical trial in geriatric patients (n=225) the incidence of falls was 20% (placebo), 16% (0.5 mg/day), 13% (1 mg/day), and 25% (2 mg/day).

Additional considerations for special populations: Limited clinical trial data are available in elderly, renally or hepatically impaired patients, and risperidone should be used cautiously in these patients. A low starting dose is recommended for an elderly patient, reflecting a decreased pharmacokinetic clearance, greater frequency of hepatic, renal, or cardiac dysfunction, and a greater tendency for drug interactions, postural hypotension, dizziness, and falls.

8

RISPERDAL® (risperidone)

CNS Sales Aid Primer

Page 8

Why This Information Is Important

- Fair balance appears on a single page to organize your delivery; to allow you to focus on safety considerations; and to give you an opportunity to provide updated PIs
- Makes it easier for you to focus on the core messages for RISPERDAL and to utilize this piece as a single core-message detailer
- If this is the first call since label change (CAEs), please update physician on specifics of this new warning

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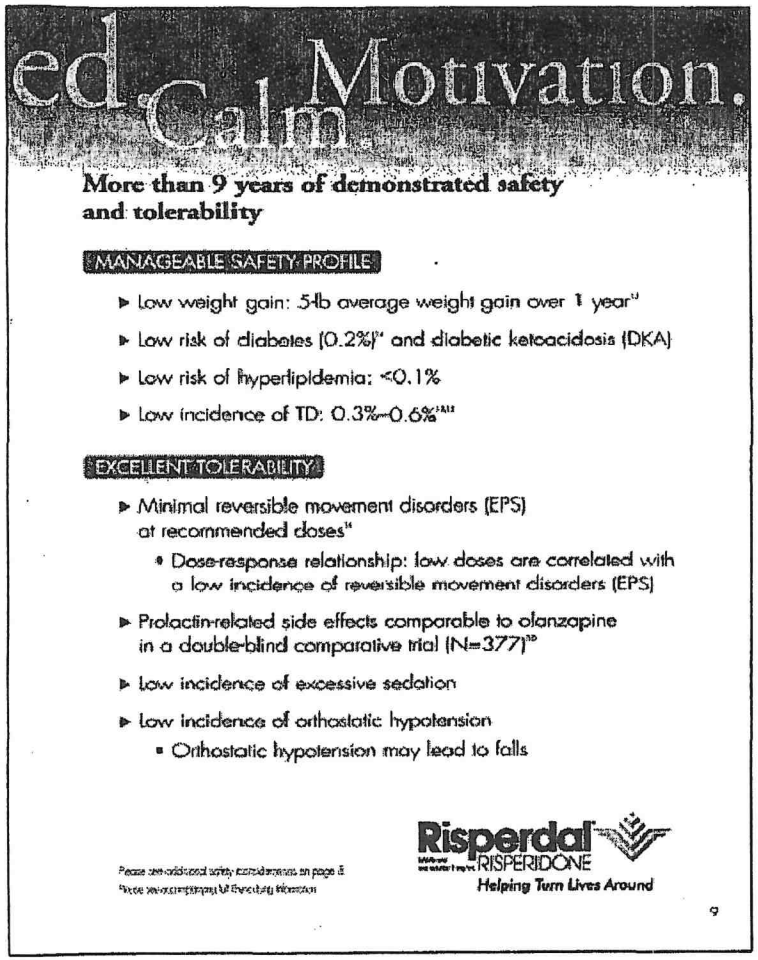

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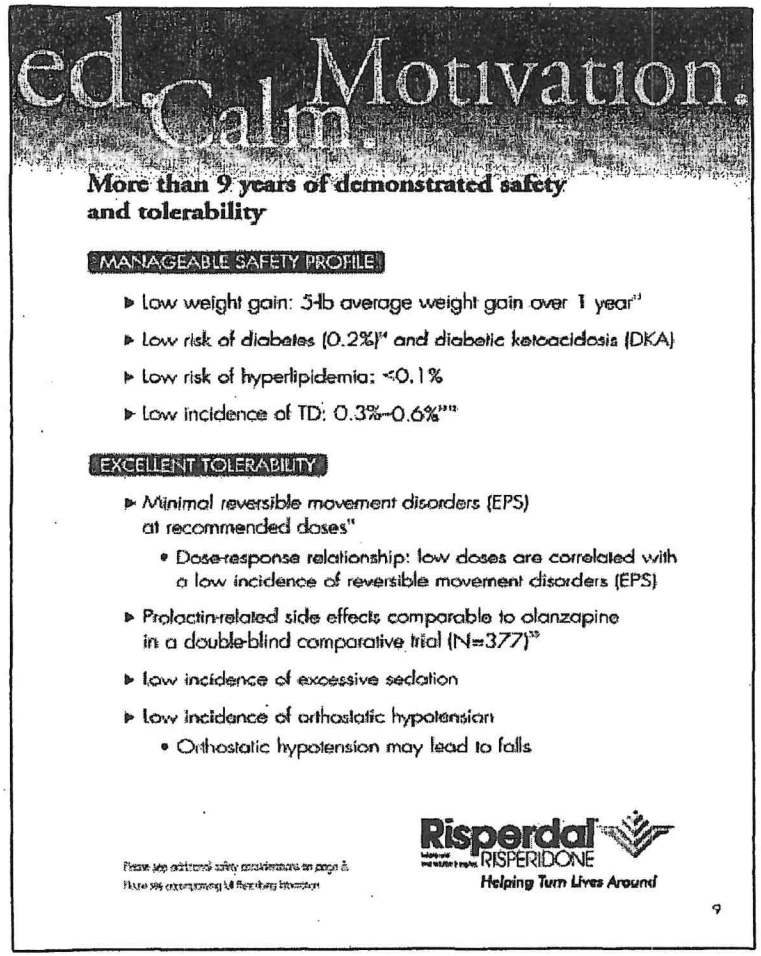
Why This Information Is Important

- Sets up the idea of putting these issues into perspective with regard to the risk/benefit ratio of RISPERDAL versus other atypicals
- A variety of safety and tolerability side effects associated with atypicals are of particular concern in this patient population
  - —Weight gain is still an issue in the atypical class, most notably with olanzapine
    - The low weight gain exhibited by RISPERDAL is in contrast to the increased weight gain observed in clinical trials with olanzapine
  - —Diabetes is another serious concern with atypicals that has been well documented in a number of case studies
    - Olanzapine is associated with a significant risk of diabetes and has also been linked to conditions such as diabetic ketoacidosis (DKA) and diabetic coma, irrespective of weight gain
    - Diabetes and other metabolic complications are not readily apparent, require testing, and may be difficult to manage
- RISPERDAL has been associated with a low risk of diabetes and DKA
  - —Olanzapine has also been linked to other metabolic disorders that require monitoring, such as hyperlipidemia, which increases the risk of cardiovascular disease
    - RISPERDAL is associated with a low incidence of hyperlipidemia



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RISPERDAL® (risperidone)

CNS Sales Aid Primer

Page 9 cont.

—Use the term *reversible movement disorders (RMD)* instead of EPS to convey that this may be a reversible tolerability concern and to distinguish it from the more devastating persistent movement disorders, such as tardive dyskinesia (TD)

- TD is usually a persistent movement disorder and one that RISPERDAL rarely causes

—At lower doses, RISPERDAL exhibits low incidences of RMD

- Physicians who see RMDs with RISPERDAL may have started the patient on too high a dose or titrated up too quickly
- Flexible dosing options with RISPERDAL allow physicians to achieve efficacy while minimizing RMDs

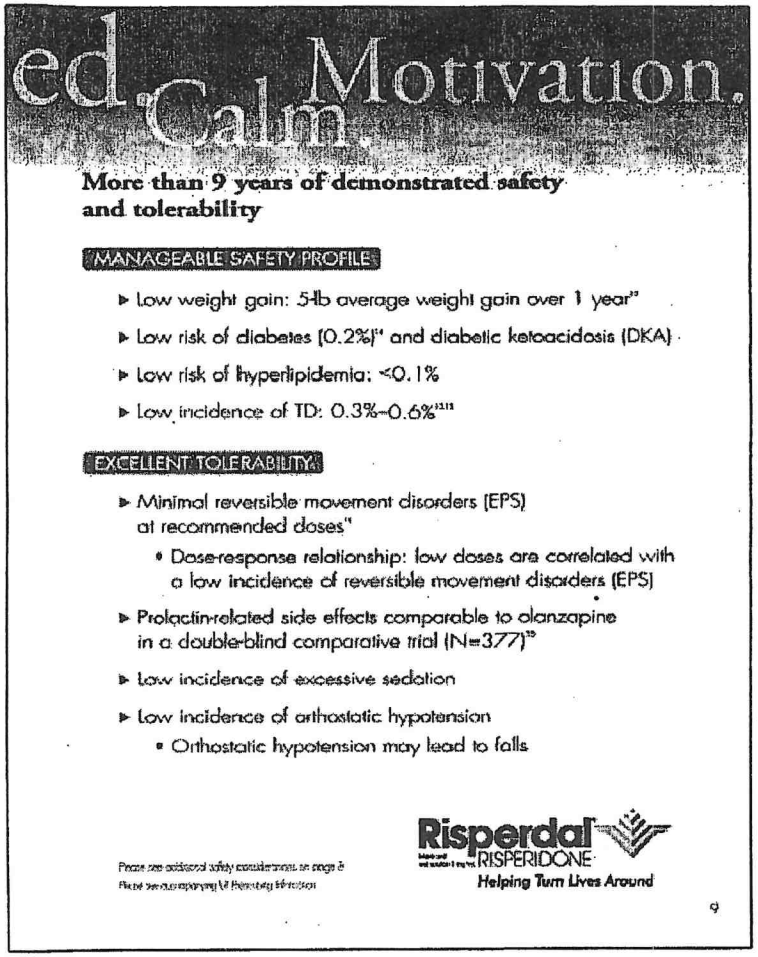
—Unlike many safety concerns and tolerability issues, physicians are alerted quickly to RMDs and can react appropriately to best manage patient outcomes

—Although RISPERDAL had a significant increase in prolactin levels in a double-blind, comparative trial versus olanzapine, RISPERDAL showed similar rates of prolactin-related side effects

- Supports the fact that increased prolactin levels may not be associated with prolactin-related side effects

—Encourages physicians to prescribe RISPERDAL over olanzapine due to:

- Comparability on this side-effect issue and superiority across a range of other side effects
- Superior efficacy demonstrated in the treatment of anxious and depressive symptoms associated with schizophrenia in a head-to-head trial at Week 8



—Daytime sedation is a side effect often associated with most atypicals; however, RISPERDAL shows a low incidence of this adverse event

- Daytime sedation should be avoided, especially with higher-functioning schizophrenic patients, particularly since it is a major reason for discontinuation
- Daytime sedative effects of atypicals, such as quetiapine or olanzapine, are often mistaken for efficacy because a sedated patient usually appears to be calmer
- Daytime sedation of a patient is counterproductive because it can limit daytime functioning, and long-term sedation can impair cognition

—RISPERDAL has a favorable risk/benefit ratio that makes it an outstanding option in the atypical class

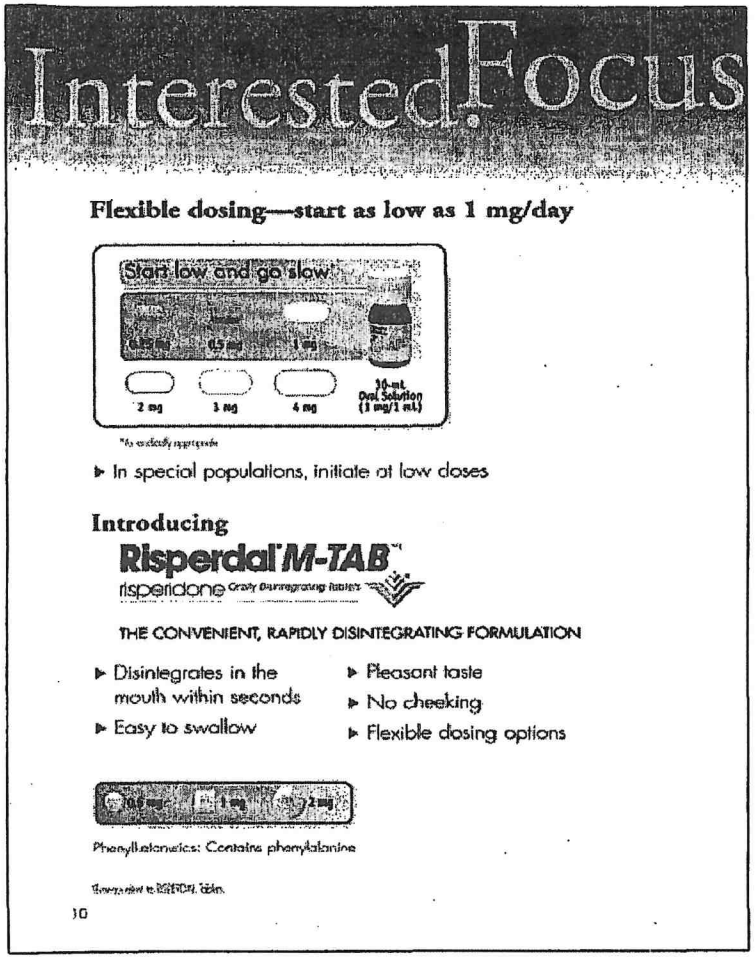
Key Message

- RISPERDAL delivers efficacy with a manageable safety profile and excellent tolerability

—When physicians evaluate the risk/benefit ratio of safety, tolerability, and efficacy among the atypicals, RISPERDAL is an outstanding choice

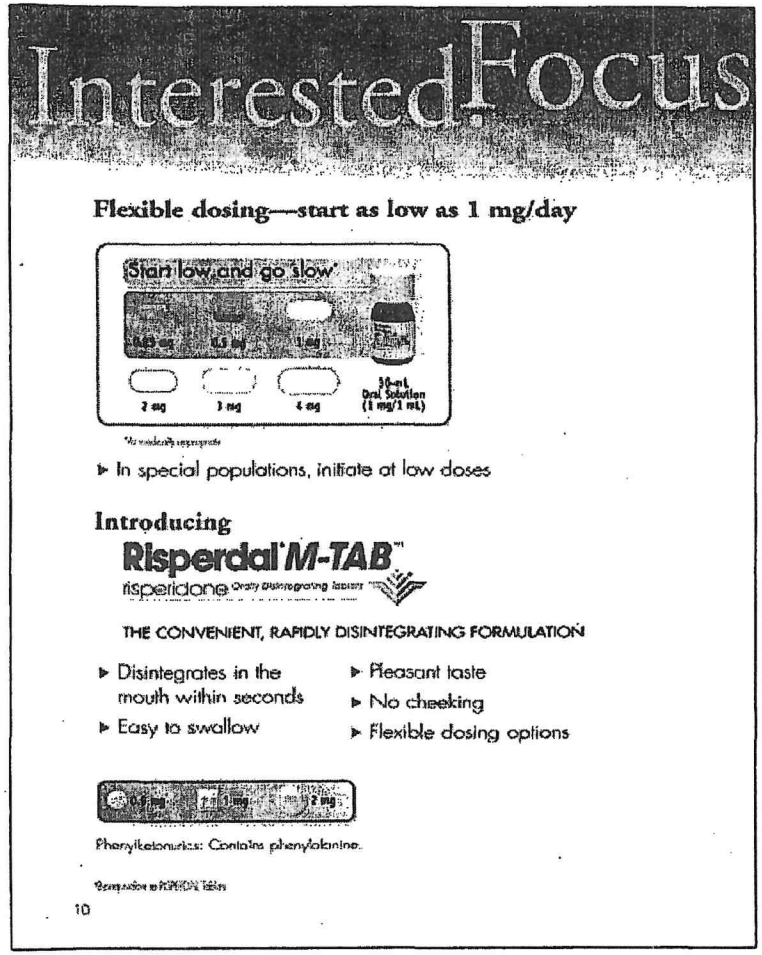
Key Customer Action

- Evaluate the risk/benefit ratio among the various atypicals and feel confident that RISPERDAL has an excellent safety and tolerability profile for the higher-functioning patient who suffers from anxious and depressive symptoms associated with schizophrenia



Why This Information Is Important

- RISPERDAL is the only atypical antipsychotic offering a full range of oral dosing options, allowing physicians to titrate to clinical effect and optimal tolerability.
- Many of our competitors (specifically quetiapine) do not provide the range of dosing options to help make low dosing easy and precise
  - —Flexible dosing makes it easy to prescribe the appropriate dose for a range of patient types (adults, special populations, etc) in any setting (acute care, office, hospital, etc)
- RISPERDAL now comes in an orally disintegrating tablet called Risperdal® M-TAB™
  - —Risperdal M-TAB provides the efficacy, safety, and tolerability of traditional RISPERDAL Tablets with the additional benefits of greater convenience and ease of use for physicians, staff, caregivers, and patients. RISPERDAL may be most appropriate for patients who can't or won't swallow pills, including:
    - Patients with difficulty swallowing (eg, elderly patients, neurological disorder patients)
    - Patients presenting in a crisis setting (eg, emergency room)
    - Patients who "cheek" their medication



CNS Sales Aid Primer

Page 10 cont.

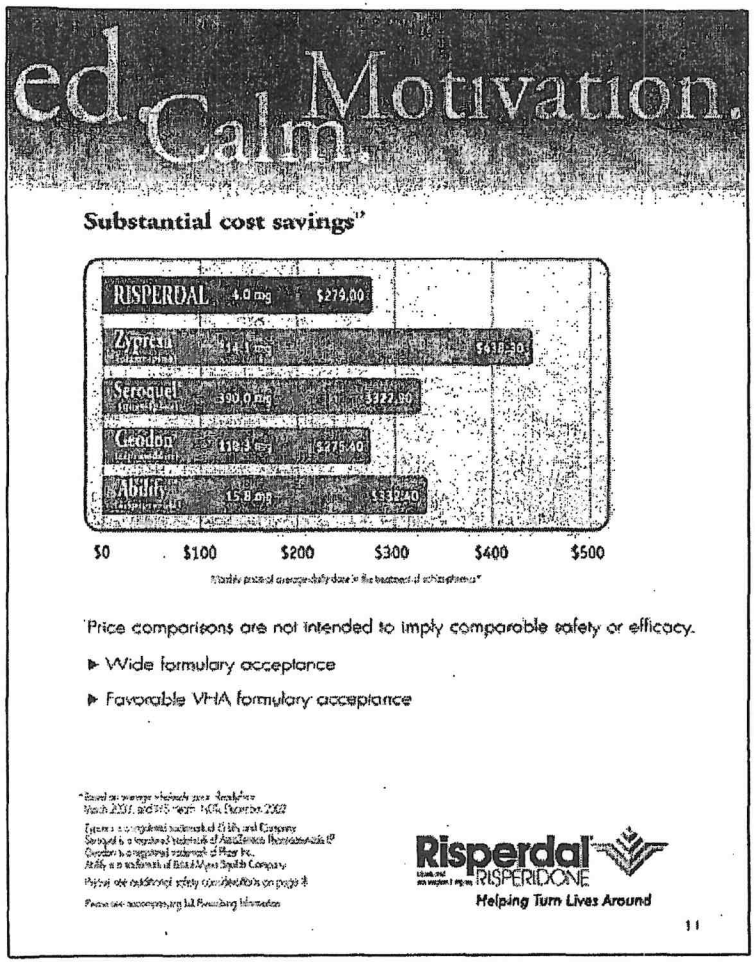
- Certain locations may be particularly appropriate for widespread use of Risperdal M-TAB, such as:
  - —Long-term care facilities
  - —Hospitals
  - —Office-based facilities—especially those with elderly or other patient populations that may experience difficulty swallowing

Key Message

- RISPERDAL is the only atypical antipsychotic offering a full range of oral dosing options, including new Risperdal M-TAB, which allows physicians to prescribe and easily titrate RISPERDAL for a variety of patient types

Key Customer Action

- Prescribe RISPERDAL because the wide range of dosing options offers easy and precise treatment for patients who suffer from anxious and depressive symptoms associated with schizophrenia



RISPERDAL® (risperidone)

CNS Sales Aid Primer

Page 11

Why This Information Is Important

- For an average daily dose, RISPERDAL is among the least expensive of all atypicals when used on a monthly basis
  - —An ideal choice for special-population patients, many of whom may lack pharmacy benefits or must comply with stringent formulary guidelines
- RISPERDAL has a wide formulary acceptance
  - —Easy for physicians to prescribe it for more of their patients

Key Message

- The monthly cost of RISPERDAL is less than the majority of its competitors; for example, the monthly cost of Zyprexa (olanzapine) is 57% more than RISPERDAL for a patient with schizophrenia
- RISPERDAL is accepted on a wide range of formulary plans

Key Customer Action

- RISPERDAL is an economical option for patients, both those with and without prescription benefits

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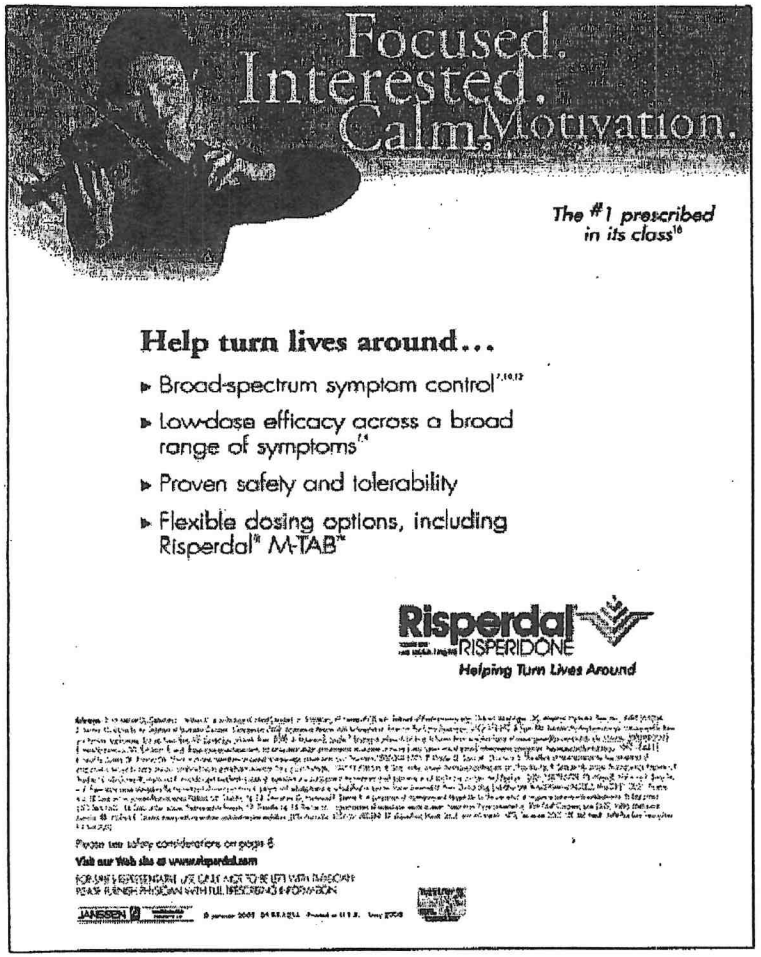

RISPERDAL® (risperidone)

CNS Sales Aid Primer

Back Cover

Why This Information Is Important

- Concludes every detail with a compelling close
  - —You will have established why RISPERDAL should be selected when a wide range of symptoms present in a broad variety of patients with schizophrenia
  - —Summarizes the key messages of your presentation and calls physicians to action with its "Help Turn Lives Around" headline
- Remember to review each section of the Sales Aid on every call to effectively communicate the core message points
  - —The broad-spectrum receptor activity of RISPERDAL is well suited to treat a wide range of symptoms present in schizophrenia, including anxiety and depression, because it is a potent atypical at the α_2-receptor site (Hertel, 1997) (Nasif, 2000) and the D_2- and 5-HT_{2A} -receptor sites (Richelson, 2000) (Stahl, 2000)
  - —Low-dose RISPERDAL demonstrated early and significant efficacy across symptoms in patients with schizophrenia, including anxiety and depression in schizophrenia
    - Rates of reversible movement disorders (EPS) were comparable to placebo at low doses
  - —RISPERDAL outperformed olanzapine in a head-to-head comparison by helping significantly more patients with schizophrenia improve (HAM-D ≤7) their depressive symptoms at Week 8

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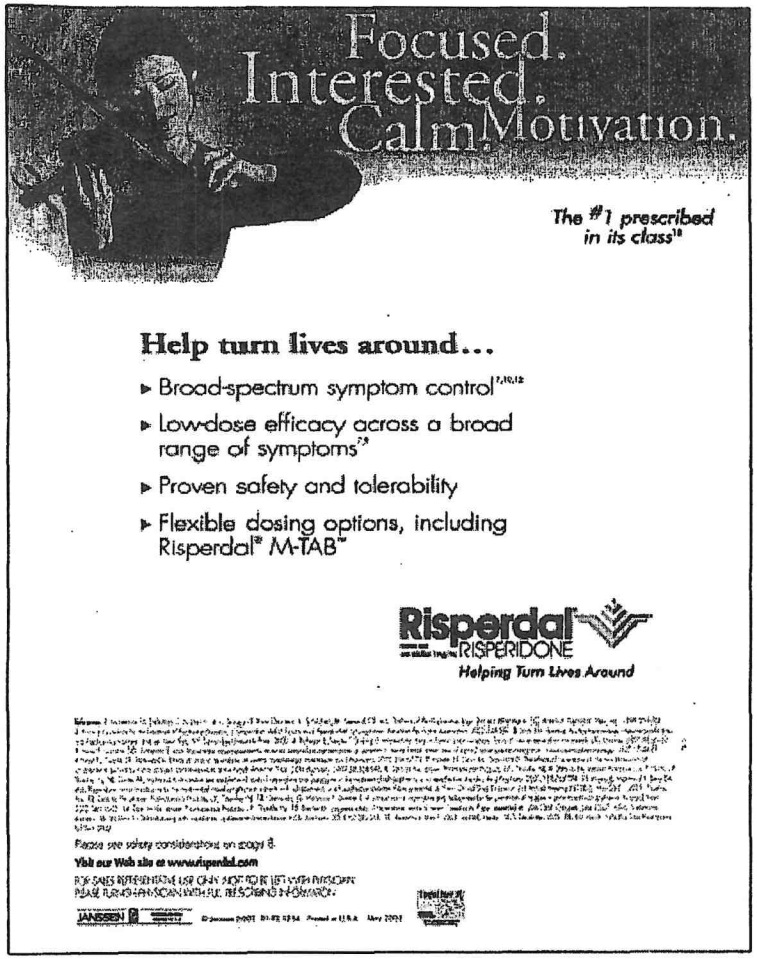

RISPERDAL® (risperidone)

CNS Sales Aid Primer Back Cover cont.

—RISPERDAL offers a wide range of flexible dosing options—unlike some of our competitors—including the introduction of new Risperdal M-TAB for additional convenience

- Remember to provide your physicians with an updated PI
- Differentiate from the competition:
  - —Low risk of diabetes
  - —Low incidence of daytime sedation
  - —9 years of trusted efficacy and no exacerbation of symptoms

Key Message

- RISPERDAL at low doses provides significant, effective, and safe treatment of anxious and depressive symptoms in patients with schizophrenia

Key Customer Action

- Full appreciation of the outstanding efficacy of RISPERDAL in treating a full range of symptoms of schizophrenia versus olanzapine
- Recognition of the excellent safety and tolerability profiles for RISPERDAL in the treatment of schizophrenia
- Agree to prescribe RISPERDAL as the best-choice atypical with a unique receptor-binding profile that includes α_2 receptors. This allows for optimal treatment of a broad range of symptoms in patients with schizophrenia, including anxious and depressive symptoms, even at low doses

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RISPERDAL® (risperidone)

CNS Sales Aid Primer

Brand Perspective

To achieve our strategic goal of gaining new ground in the anxious and depressive symptoms of schizophrenia segment in Cycle II of 2003, use the 3-way winning combination when detailing physicians:

1. Aggressively sell the benefits of low-dose RISPERDAL with a unique receptor-binding profile and compelling efficacy messages versus the competition.
2. Transition from the term EPS to *reversible movement disorders (RMD)* and minimize this tolerability concern by putting it into proper context.
3. Differentiate the risk/benefit ratio of RISPERDAL from atypical competitors in terms of broad-spectrum efficacy, excellent safety (low incidence of diabetes/DKA and weight gain), and tolerability (minimal reversible movement disorders and less daytime sedation) profiles to promote overall improvement.

By speaking to physicians differently, you will make them see RISPERDAL differently and expand their concept of appropriate patients for RISPERDAL. This shift of focus to the anxious and depressive symptoms in patients with schizophrenia continues in your latest Sales Aid. By utilizing this Sales Aid to its fullest potential, you can change physicians' perceptions and broaden their RISPERDAL prescribing patterns. Your hard work in the field will continue to ensure that RISPERDAL remains the #1 prescribed psychotropic in its class!

Sales Aid Tour

Welcome to Risperdal Training!!!

CNS IPT 2003

Risperdal RISPERIDONE
Helping Turn Lives Around

Receptor Binding... The Reason to Believe

Risperdal RISPERIDONE
Helping Turn Lives Around

Receptor Binding Profile of Antipsychotics:

DRUGS	+ D_2	+ 5-HT_{2A}	+ α_1	− Histamine H_1	− Muscarinic M_1	− α_1
Haloperidol	++++	+				++
Clozapine	++	+++	+++	++++	+++++	+++
Risperidone	++++	+++++	+++	++		+++
Olanzapine	+++	++++		++++	+++++	+++
Quetiapine	++	+	+	++++	+++	++++
Ziprasidone	++++	++++		+		++
Theoretical Effect of Blockade (antagonist)	Positive Sx decrease EPS Endocrine effects	Negative Sx decrease Mitigate EPS Improve Depressive Sx	Improve Depressive Sx	Sedation Weight gain	Memory dysfunction Anticholinergic effects Mitigate EPS	Orthostatic Hypotension Dizziness Reflex tachycardia

Adapted from : Richelson E. *J Clin Psychiatry* 1996;57(suppl 11):4-11.
Pickar D. *Lancet* 1995;345:557-562.

Risperdal RISPERIDONE
Helping Turn Lives Around

The Three Dimensions of Risperdal – Efficacy Theory

- D2 antagonist
  - Controls positive symptoms
  - Associated with movement disorders
- 5HT2a antagonist
  - Increases serotonin
  - Mitigates movement disorders
  - Treats depressive and anxiety symptoms
  - Improves cognition
- Alpha-2 antagonist
  - Risperdal is the most potent currently available atypical at the alpha-2 site
  - Increases norepinephrine
  - Increases serotonin (indirectly)
  - Treats depressive symptoms

Risperdal RISPERIDONE
Helping Turn Lives Around

The Three Dimensions of Risperdal – Safety Theory

Risperdal...

- Low affinity for H1
  - Low incidence of excessive sedation
  - Low weight gain
- No affinity for M1
  - Low incidence of anticholinergic side effects (dry mouth, blurred vision, urinary retention, etc)
  - Minimal cognitive impairment
- Low to moderate affinity for alpha-1
  - Low incidence of orthostatic hypotension
  - Orthostatic hypotension can lead to falls and fractures

Risperdal RISPERIDONE
Helping Turn Lives Around

Sales Aid

Risperdal RISPERIDONE
Helping Turn Lives Around

Trivia...

(1) Telling, when used alone, results in what percentage recall three hours later? ***70%***

How about three days later? ***10%***

(2) Showing, when used alone, results in what percentage recall three hours later? ***72%***

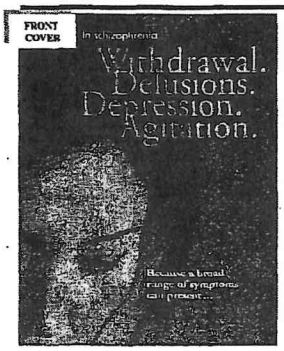
How about three days later? ***20%***

(3) Blend of telling and showing results in what percentage recall three hours later? ***85%***

How about three days later? ***65%***

Risperdal RISPERIDONE
Helping Turn Lives Around

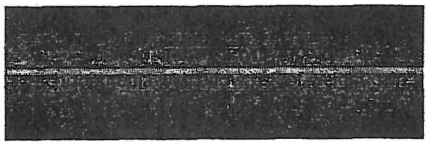
Risperdal Sales Aid Tour



- **Highlights?**
  - Receptor binding
  - Campaign graphics focusing on patient functioning and symptoms
  - Tagline of *"Helping Turn Lives Around"*

Risperdal RISPERIDONE
Helping Turn Lives Around

RISPERDAL Core Positioning Statement



Risperdal RISPERIDONE
Helping Turn Lives Around

Interested Focused Calm Motivation

PAGE 2

In schizophrenia

Turn to an atypical with broad-spectrum symptom control

- Schizophrenia can present with a broad spectrum of symptoms[1]
- Combinations of symptoms vary widely from patient to patient
- Undertreated symptoms, including anxiety, depression, and cognitive disturbance, put patients at risk for relapse and impact quality of life[2]

- **Why this is important**
  - Highlights symptom reversal
  - Highlights how unresolved symptoms negatively impact patients' lives
  - Gain agreement from physician about the need to treat the broad range of symptoms in schizophrenia.

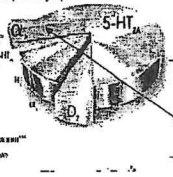
Risperdal RISPERIDONE
Helping Turn Lives Around

Interested Focused Calm Motivation

PAGE 3

Receptor-binding theory

- The mechanism of action of RISPERDAL, as with other drugs in this therapeutic class, is unknown
  - May be mediated through a combination of D_2 and 5-HT_2 receptor antagonism
  - Antagonism at other receptors may explain other effects
- 5-HT_2/D_2 receptors:
- Serotonin and dopamine[3]
  - Anxious and depressive symptoms
  - Suspiciousness and delusions
  - Cognition
- α_1 receptor:
- Hypotension and syncope[4]
  - Anxious and depressive symptoms



Why this is important...
Receptor-binding provides a potential rationale for the efficacy of Risperdal in the treatment of anxious and depressive symptoms in patients with schizophrenia giving physicians a "Reason to Believe"

Dr. what makes Risperdal different? Antagonism of the alpha-2 receptor site is theorized to be highly relevant in the treatment of the anxious and depressive symptoms of schizophrenia

Risperdal RISPERIDONE
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Interested Focused Calm Motivation

PAGE 3

Receptor-binding theory

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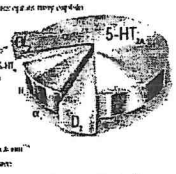


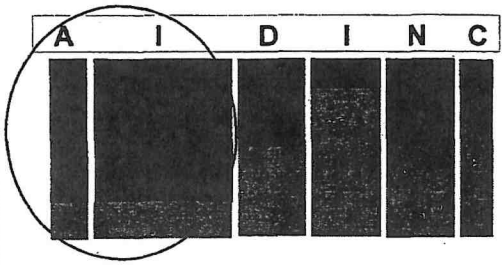
Key Feature:
The *unique* binding is theorized to make Risperdal an ideal agent to treat the mood, anxiety, and other symptoms associated with schizophrenia

What would be the benefit of this selling feature?

Risperdal RISPERIDONE
Helping Turn Lives Around

Practice

A I D I N C



Work as a team to create examples of Interviewing questions utilizing the front cover and pages 2-3

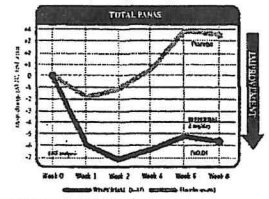
Risperdal RISPERIDONE
Helping Turn Lives Around

Interested Focused Calm Motivation

PAGE 4

hrenia

Low-dose efficacy—early and significant reductions[1]



Widely used at low doses

- Low incidence of movement disorders at 2 mg/day[1]
  - Rates of extrapyramidal disorder comparable to placebo (5% and 4% for RISPERDAL and placebo, respectively)
- Physicians should titrate to clinical effect and optimal tolerability
  - Some patients may require higher doses

Key point

This demonstrates the effectiveness of 2mg Risperdal in total PANSS and the mood and anxiety symptoms of schizophrenia with a low incidence of movement disorders

Suggested probe...

Doctor, can you share with me how this information compares with your experience with other atypicals?

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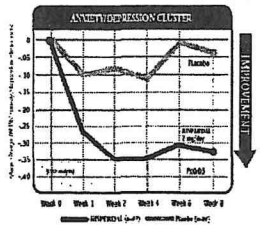
Interested Focused Calm Motivation

PAGE 5

Low-dose efficacy across a broad range of symptoms[1]



- Similar reductions were observed on positive symptoms, negative symptoms, and uncontrolled hostility/excitement subscales—no change in disorganized thought[1]

Key Feature:

Risperdal at low doses demonstrated a reduction in anxiety and depressive symptoms associated with schizophrenia

Suggested dialogue:

How would you utilize this information to differentiate Risperdal vs. Seroquel?

Risperdal RISPERIDONE
Helping Turn Lives Around

Interested Focused Calm Motivation

Page 6

izophrenia

Effectively treats the broad range of symptoms[1,2]

Change At Week 8	RISPERDAL	olanzapine
Positive Symptoms	23.4%	18.6%
Anxiety/Depression	26.4%	17.4%
Cognition (Disorganized Thought)	16.0%	18.0%
Negative Symptoms	18.4%	15.3%
Uncontrolled Hostility/Excitement	22.5%	20.0%

	Baseline scores		Mean change at Week 8	
	RISPERDAL	olanzapine	RISPERDAL	olanzapine
Positive Symptoms	24.4	22.7	-5.7	-4.2
Negative Symptoms	20.7	20.8	-3.8	-3.2
Disorganized Thought	17.8	16.1	-2.8	-2.9
Uncontrolled Hostility	7.1	7.5	-1.6	-1.5
Anxiety/Depression	16.6	15.9	-4.4	-3.0

Key Feature:

In a head-to-head trial, Risperdal demonstrated statistically significant improvement in the positive and anxiety/depression symptoms associated with schizophrenia

What is the benefit to the patient?

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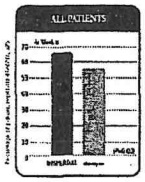
Page 7

Significantly greater HAM-D improvement rate (HAM-D score ≤7) vs olanzapine[1,2]



High response rates[1,2]

- Patients with HAM-D ≥15; 51% of patients treated with RISPERDAL achieved a ≥50% improvement in symptoms
- No significant difference from olanzapine

Key Feature:

A high percentage of patients taking Risperdal achieved a HAM-D score ≤7 – a common criteria used to define remission in depression trials

Doctor, how does Risperdal compare to other atypicals in the treatment of depressive symptoms associated with schizophrenia?

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Page 6 and 7 Messages

- In a head to head trial Risperdal significantly outperformed olanzapine across a range of symptoms in patients with schizophrenia, specifically anxious, depressive and positive symptoms.
- Risperdal helped significantly more patients improve as measured by HAM-D ≤7 (a common criteria used to define remission in depression trials)
- Demonstrates Risperdal's efficacy in reduction of depressive symptoms in schizophrenia measured by the HAM-D scale which is familiar to psychiatrists

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Interested Focused Calm Motivation

Page 8 RELEVANT CONSIDERATIONS

Check in with your customers to proactively discuss Risperdal's safety profile

Doctor, do you have any questions or concerns about ... (CAE, EPS, TD)

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Interested Focused Calm Motivation

Page 9 ...an 9 years of demonstrated safety ...and tolerability

MANAGEABLE SAFETY PROFILE

- Low weight gain: 5lb average weight gain over 1 year*
- Low risk of diabetes (0.2%)** and diabetic ketoacidosis (DKA)
- Low risk of hypolipidemia: <0.1%
- Low incidence of ID: 0.3%–0.6%**

EXCELLENT TOLERABILITY

- Minimal treatable movement disorders (EPS) at recommended doses*
  - Dose-response relationship: low doses are correlated with a low incidence of treatable movement disorders (EPS)
- Prolactin-related side effects comparable to olanzapine in a double-blind comparative trial (N=377)*
- Low incidence of excessive sedation
- Low incidence of orthostatic hypotension
  - Orthostatic hypotension may lead to falls

"Risperdal offers you and your patients an excellent safety profile with less weight gain vs. Zyprexa and minimal sedation"

What is the benefit of this selling feature?

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Interested Focused Calm Motivation

Page 10

...ivailable dosing—start as low as 1 mg/day

- In special populations, initiate at Low dose

Introducing Risperdal M-TAB Risperidone

THE CONVENIENT, RAPIDLY DISINTEGRATING FORMULATION

- Disintegrates in the mouth within seconds
- Easy to swallow
- Pleasant taste
- No chewing
- Flexible dosing options

Doctor, Risperdal offers your patients control over a broad range of symptoms of schizophrenia. Risperdal is also available in the largest number of delivery systems providing many options for your patients

Remember M-Tab in the acute setting!

Close for business:
Doctor, now that we've discussed the advantages of Risperdal, what I'm telling you do is prescribe Risperdal for patients that present with symptoms such as... associated with schizophrenia instead of (Zyprexa, Seroquel, Abilify, etc...)

Risperdal RISPERIDONE
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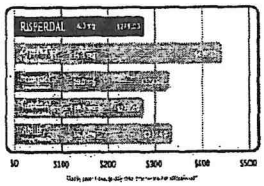
Interested Focused Calm Motivation

Page 11

Substantial cost savings*



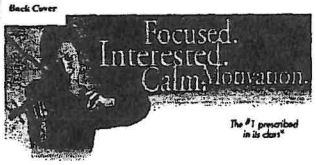
Price comparisons are not intended to imply comparable safety or efficacy.

- Wide formulary acceptance
- Favorable VHA formulary acceptance

Risperdal RISPERIDONE
Helping Turn Lives Around

Interested Focused Calm Motivation

Back Cover



Key Feature:
Risperdal provides *significantly more effective therapy with important safety and tolerability advantages for treating the mood and anxiety symptoms associated with schizophrenia*

Help turn lives around...

- Broad spectrum symptom control**
- Provides efficacy across a broad range of symptoms*
- Proven safety and tolerability
- Flexible dosing options including Risperdal® M-TAB®

Risperdal RISPERIDONE
Helping Turn Lives Around

Sales Aid Exercise

- Break into 6 groups
- Each group takes one spread
  - Opening and Closing
  - Receptor Binding Spread
  - Low dose Spread
  - Conley Spread
  - Safety Spread
  - Dosing and Cost Spread
- Identify key messages and role play spread

Risperdal RISPERIDONE
Helping Turn Lives Around

Key Supporting Messages

- Risperdal has a unique receptor binding profile (D2, 5HT2A and alpha-2)
- For higher functioning patients, Risperdal delivers early and significant relief across the full range of symptoms associated with schizophrenia at low doses – while minimizing the perceived liabilities of the higher doses
- More Risperdal patients achieve complete resolution of depressive symptoms of schizophrenia compared to Zyprexa
- Risperdal has a favorable risk / benefit ratio

Risperdal RISPERIDONE
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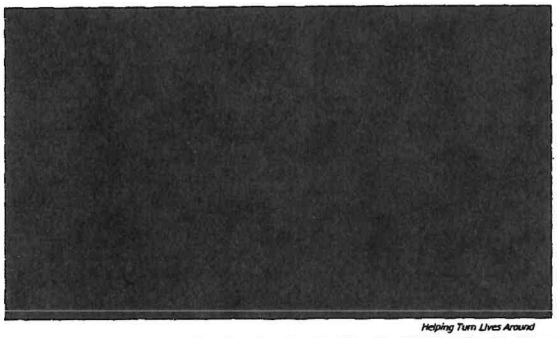
Role Play

Risperdal RISPERIDONE
Helping Turn Lives Around

Sales Training Detail



Helping Turn Lives Around

Role Play Scenario One

Dr. Green -Psychiatrist
Location: CMHC

APS- 90

Risperdal	25%
Zyprexa	18%
Seroquel	42%
Geodon	13%
Abilify	2%

Reserves Risperdal for tough to treat patients. Been using more Seroquel.

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Role Play Scenario Two

Dr. White- Psychiatrist
Location: Psychiatric Institution and Private Practice

APS- 50

Risperdal	24%
Zyprexa	50%
Seroquel	20%
Geodon	4%
Abilify	2%

Doctor has been using more Zyprexa for patients because he is concerned with EPS.

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Role Play Scenario Three

Dr. Yellow- Psychiatrist
Location: Private Office

APS- 90

Risperdal	25%
Zyprexa	25%
Seroquel	23%
Geodon	17%
Abilify	10%

Lately Dr has begun to use all of the atypical options. Does not believe there is a difference in efficacy.

Risperdal RISPERIDONE
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Seroquel Workshop

CNS IPT Seroquel Workshop

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Seroquel Current Perceptions

2003
APS Annual Tracking Study

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Study Overview & Methodology

- Primary objective: Understand current antipsychotic prescribing practices
  - Where products are being used
  - Attribute ratings of products
- Baseline research conducted in 2001, Wave 2 in 2002 and Wave 3 in spring 2003.
- In-office interviews were conducted with 108 primary care physicians and 251 psychiatrists
- All physicians were recruited from Janssen target lists

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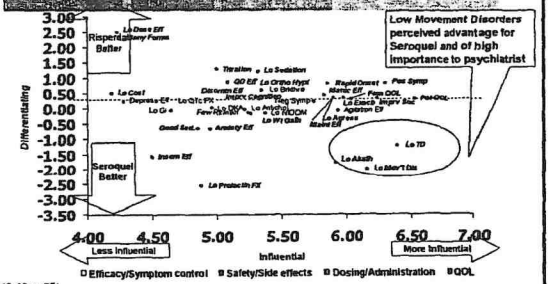
RISPERDAL vs. SEROQUEL – 2003
- Psychiatrists -



Q12, 13; n=251
* Attribute is bolded and italicized if significant difference between drugs
Base: Psychiatrists

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Seroquels two highest areas of use are in Mood and Anxiety.

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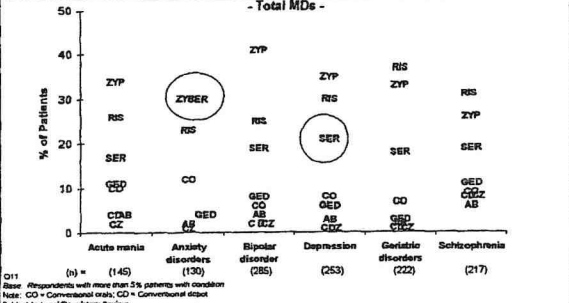
DISTRIBUTION OF PATIENTS ON ANTIPSYCHOTICS BY PRODUCT* AND DIAGNOSIS - 2003
- Total MDs -



Q11
Base: Respondents with more than 5% patients with condition
Note: CO = Conventional oral; CO = Conventional depot

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Perceived Advantages and Disadvantages of Seroquel

PSYCHs

Key Advantages
- Improves sleep
- Lower/lack of EPS
- Effective for agitation
- Effective for mood/anxiety symptoms

Key Disadvantages
- Sedation
- Difficult/slow titration
- Poor efficacy

Q19,20; only options selected by 10% or more are shown

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Undesirable sedation is perceived to be the most frequent antipsychotic side effect; leads to regimen changes in half of cases

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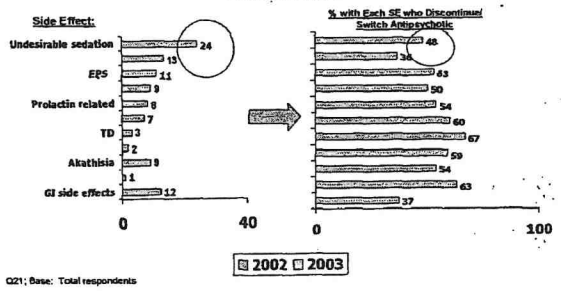
RATE AND IMPACT OF ATYPICAL ANTIPSYCHOTIC SIDE EFFECTS

- Percent of Patients -



Q21; Base: Total respondents

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Annual Tracking Study Recap

- PCP perceive minimal differences between Risperdal and Seroquel.
- Psychiatrist perceive Seroquel to be safer then Risperdal.
- Seroquel used most frequently for Mood and Anxiety symptoms of schizophrenia.
- **Top perceived advantages of Seroquel for PCP and Psych**
  - **Mood and Anxiety symptoms of schizophrenia, low movement disorders, sleep and effective for agitation (sedates and calms)**
- **Undesirable sedation perceived as the most frequent APS side effect with 50% discontinuation rate.**

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Previous Seroquel Work Shops

- **Data Highlights**
  - **Receptor binding data**
  - **Movement disorder comparisons**
  - **Sleep data**

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Receptor Binding Profiles

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	D_2	5-HT_{2A}	α_2
RISPERDAL	++++	+++++	+++
Seroquel	++	+	+
Zyprexa	+++	++++	—
Geodon	++++	++++	—

Adapted from : Pickar D. *Lancet* 1995;345:557-562.

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Receptor Binding Profiles

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	α_1	H_1	M_1
RISPERDAL	+++	++	—
Seroquel	++++	++++	+++
Zyprexa	+++	++++	+++++
Geodon	++	+	—

Adapted from : Pickar D. *Lancet* 1995;345:557-562.

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Atypical Antipsychotics Adverse Effects: Reversible Movement Disorders (EPS)

	Drug		Placebo
	Dose (mg/day)	Percent EPS	Percent EPS
Risperdal	2	13%	13%
	6	16%	
Seroquel	150	6%	16%
	300	4%	
	600	8%	

Comparisons based upon package inserts are not based on head-to-head trials and, therefore, direct comparisons can not be made.

*Dose ranged from 10 to 200 mg/day during short-term, placebo-controlled trials

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Similar Rates of TD, a Persistent Movement Disorder

Medication	Adult Schizophrenia	Elderly Patients
Risperidone	0.3%-0.6%[1,4]	2.6%[5]
Quetiapine	No data available	2.7%[6]

Comparisons are not based on head-to-head trials and, therefore, direct comparisons can not be made.

[1]Conventional antipsychotics (mainly haloperidol and thioridazine).
[1]Csernansky JG et al. *N Engl J Med.* 2002;346:16-22.
[4]Brecher M. Poster presented at: CINP Congress; June 23-27, 1996; Melbourne, Australia.
[5]Jeste DV et al. *Am J Psychiatry.* 2000;157:1150-1155.
[6]Jeste D et al. Poster presented at: Annual Meeting of AAGP; 2000; Miami, Florida.

These materials are for educational purposes only not to be utilized in a selling situation

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Importance of Serotonin in Sleep

- Serotonin, 5HT, is theorized to be an important neurotransmitter in initiating and maintaining sleep

Dophaide JA. Sleep disorders. In: Koda-Kimble MA, Young LY, eds. Applied Therapeutics: The Clinical Use of Drugs. 7th ed. Baltimore, MD: Lippincott Williams & Wilkins. 2001: 75:1-22.
Dursun SM, et al. *J Psychiatry & Neuroscience* 1999;24(4):333-337. Yamashita H, et al. *Psychiatry Research* 2002;109:137-142.

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Risperdal Effects on Sleep

- Study
  - Dursun (1999)
- Control groups
  - RIS – 8 pts
  - CONV – 8 pts
  - Control – 8 pts
- Evaluations
  - VAS (VAS = Visual Analog Scale), sleep quality, AM sleepiness, Actigraphy
- Results
  - RIS improved sleep quality, AM sleepiness and reduced movements vs. conventionals

Dursun SM, et al. *J Psychiatry & Neuroscience* 1999;24(4):333-337

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Risperdal Sales Aid vs. Seroquel

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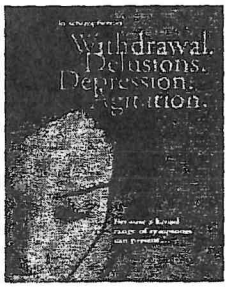
Front Cover and Inside Spread



- **Seroquel Objections** - Efficacy for Mood and Anxiety symptoms and Calming of Agitated patients with schizophrenia
- Utilize front spread to Approach and Interview the physician to uncover and target symptoms they are treating with Seroquel.
- Inside spread can be a vehicle to begin Demonstrating Risperdal's excellent efficacy.

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Receptor Binding Spread

- Demonstrate Risperdal's unique receptor binding profile (A2 and 5HT2a) affinity.
- Demonstrate Risperdal's robust D2 activity.

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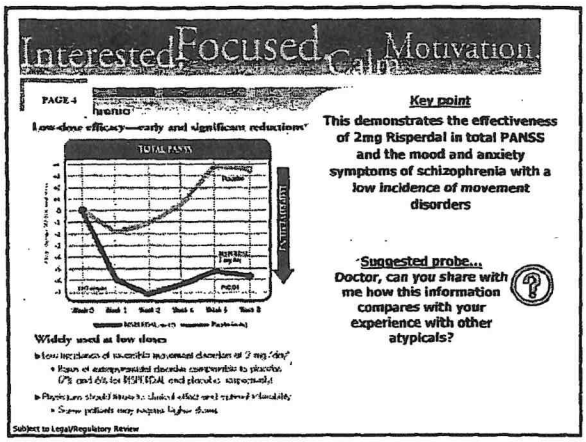
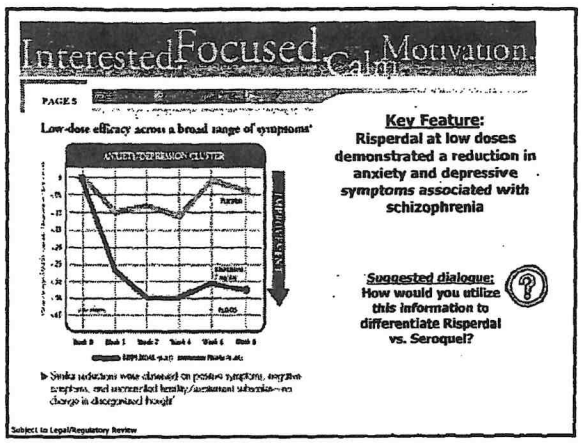
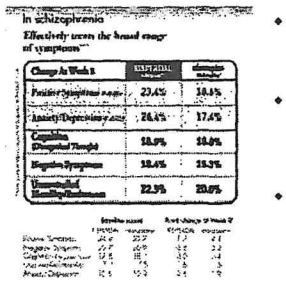


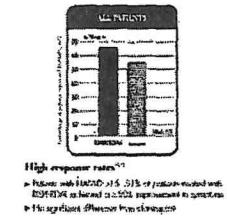


Conley Data (PANSS)



- **Seroquel Objections** – Efficacy in Mood and Anxiety symptoms and calming of agitated patients with schizophrenia.
- Demonstrate efficacy vs. another atypical as seen in (PANSS) anxiety/depressive and positive symptom results in schizophrenia at week 8.
- Not a direct comparison to Seroquel but demonstrates efficacy vs. an atypical comparator in the target symptoms.

Conley Data HAM-D



- **Seroquel Objection** – Efficacy in Mood and Anxiety symptoms of schizophrenia.
- Risperdal helped significantly more patients improve as measured by HAM-D ≤7 (a common criteria used to define remission in depression trials)
- Demonstrates Risperdal's efficacy in reduction of depressive symptoms in schizophrenia measured by the HAM-D scale which is familiar to psychiatrists

Movement Disorders Data

More than 9 years of demonstrated safety and tolerability

MANAGEABLE SAFETY PROFILE

EXCELLENT TOLERABILITY

- **Seroquel Objection** – Movement disorders especially concerns with eventual TD.
- Use when Demonstrating or Negotiating Risperdals low rates of movement disorders.
- Make specific reference to low incidence of TD rates when Negotiating or Demonstrating.
- Point out overall risk benefit profile low incidence of diabetes and low weight gain.

Additional Considerations

More than 9 years of demonstrated safety and tolerability

MANAGEABLE SAFETY PROFILE

EXCELLENT TOLERABILITY

- **Seroquel Objections** – Sedation good for calming or helps to improve sleep.
- Highlight Risperdal's efficacy and improved sleep quality while minimizing undesirable sedation.
- Highlight Risperdals low Fall rates in geriatric studies.

Risperdal M-TAB and Dosing Spread

- Make comparison to Risperdals easy dosing and titration vs. Seroquels variable dosing and titration.
- Risperdal has flexible dosing formulations including the new convenient Risperdal M-TAB.
- Point out what these dosing benefits can mean acutely agitated patients, cheekers, or those who have trouble swallowing.

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Back Cover

- Utilize back cover to confirm agreed upon benefits.
- Close for the specific patient type you were focusing on.

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Sales Aid Key Points vs. Seroquel

- Efficacy
  - Utilize front cover and page 2 to position Risperdal for the M&A symptoms of schizophrenia where Seroquel gets significant utilization.
  - Utilize page 3 to highlight Risperdal's unique receptor binding profile.
- Safety/Tolerability
  - Low risk of TD, Diabetes/DKA, weight gain
  - Paint the picture of how excessive sedation can impact QOL.
  - Low movement disorders at low doses.
- Dosing
  - Highlight RISPERDAL's flexible dosing options & emphasize 1mg start.
- Close
  - Recap key agreed upon benefits (Efficacy / Safety / dosing) and ask for a trial on the symptoms physicians reserve for Seroquel.

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Handling Seroquel Objections

Interviewing and Negotiating

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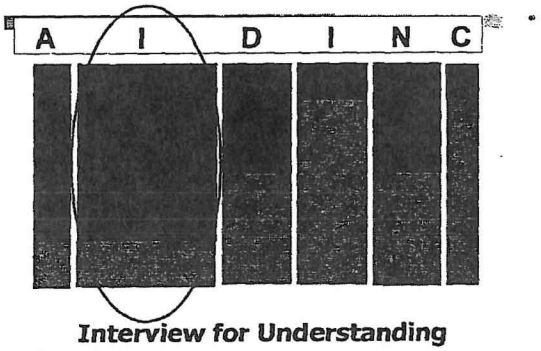
Handling Seroquel Objections



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Example: Interviewing To Uncover Symptoms vs. The Sleep Objection

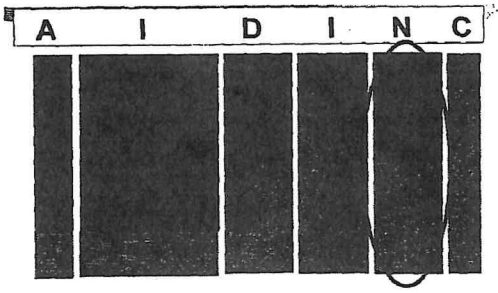
If a doctor says sleep → it is likely a smokescreen or they are treating sleep secondary to other psychotic symptoms because 90+% of Seroquel business is for treating symptoms other than sleep.

Interview - to uncover the symptoms they are treating with Seroquel

Are you using Seroquel just for sleep or are you using it to treat other symptoms as well?

- **Remember, sleep only represents 4% of the business, so we to need to probe deep to uncover the additional symptoms physicians are treating**
- **Once we uncover the symptoms, we own the call**
- **Call should now shift into Negotiation phase (see next two slides)**

Handling Seroquel Objections



Negotiating - Restate, Empathize & **Respond**

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Example: Negotiate with available resources vs. the Sleep Objection

Doctor initially said sleep → Through probing you have determined *sleep is a smoke screen or secondary goal and the primary goal is* mood and anxiety symptom management

Restate and Empathize- shows your alignment with the customers goal

Respond and Validate– Utilize sales aid, key reprints and workshop data

Restate and Empathize - DR efficacy and improved sleep are desirable goals and I can *appreciate what they must mean to your patients overall functioning.*

Respond – DR can we discuss a different way to accomplish this goal for your patients that you may prefer. Risperdal provides efficacy and can improve sleep quality while *minimizing undesirable sedation.*

Validate - Hit key points from the sales aid and by referencing peer reviewed data.

If the DR agrees with the data or if it even sounds reasonable to them - CLOSE !!!

Table Activity

Pre-call Planning and Role Play for Success

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Table Activity Instructions

- Break Into into 3 groups Ex. 10 reps (2 groups of 3) & (1 group of 4)
- Assign each group one of the other remaining Seroquel objections.
  - 1) Movement disorders 2) Mood & Anxiety symptoms of schizophrenia 3) Sedation to control Agitation in schizophrenia.
    - We already walked through the sleep objection.
- Assumption - The objection was discovered on a previous call so the reps will focus the next call on overcoming the objection.
- Each group will complete the following:
  - Pre-call plan an interview question to ensure complete understanding of the objection. (Flip chart)
  - Pre-call plan their negotiating strategy including specific resources (Flip chart)
  - Report out to the team their pre-call plans, including an example role play of the overall call applying the interview and negotiation plans. 20 min

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Background Information Grid

Comparisons are my based on head-to-head trials and limitations about comparisons are not to be made educational purposes only not to be utilized in a selling situation.

M&A Symptoms of Schizophrenia	Sedation For Agitation	Movement Disorders
Sales Aid: • Unique Receptor Binding -(alpha 2) as well as Sif2a • Efficacy of Risperdal at 2mg/day – Marder/Davis spread • Efficacy superior to Zyprexa in M&A sxs of schizophrenia, positive sxs. • Undesirable Sedation – Negative impact on patient outcomes / falls	**Sales Aid:** • Receptor Binding *Superior D2 Activity symptom control at low doses and M-Tab* • *Undesirable Sedation* – Negative impact on patient outcomes/Falls	**Sales Aid:** • Efficacy of Risperdal at low doses. • *Low dose means low rates of reversible movement disorders.* • *Optimal Risk / BenefR Ratio (low incidence of Diabetes, weight gain, reversible movement disorders)* • Promotes better outcomes
Key Reprints: Conley – Risperdal superior to Zyprexa for treating M&A symptoms associated with Schizophrenia – PANSS and HAM-D Note: Not a direct comparison to Seroquel but it proves high efficacy with target symptoms.	**Key Reprints:** Williams - Receptor binding affinity (Kapur) Carrier – 2 mg Risperdal oral solution + 2 mg oral lorazepam showed comparable efficacy and time to sleep to 5mg IM Haloperidol and 2mg IM lorazepam.	**Key Reprints:** Conley- Comparable rates of reversible movement disorders with Zyprexa, another atypical perceived to have low rates of reversible movement disorders.
Previous Workshop Data: N/A	**Previous workshop Data:** - Receptor binding data negative effects H1 sedation.	**Previous Workshop Data:** Movement disorder comparisons Elderly TD Risp 2.6 vs. Ser 2.7

Abilify Workshop

RISPERDAL
"Acting Like the Market Leader"

Aripiprazole Workshop

IPT 2003

Risperdal RISPERIDONE
Helping Turn Lives Around

The information in this presentation is intended for educational sales training purposes only and is not intended to be used in a selling situation for Risperdal.

Risperdal RISPERIDONE
Helping Turn Lives Around

Aripiprazole Workshop Objectives

- Familiarize ourselves with key Abilify product information
- Understand Abilify selling strategy
- Understand how to sell against Abilify
- **Grow Risperdal Share!**

Risperdal RISPERIDONE
Helping Turn Lives Around

Aripiprazole Background

- Dosing: QD 15 –30 mg/day
- **MOA (unknown)**
- "Dopamine-system stabilizer"
  - **may** act as a ***partial agonist*** at D2 and 5HT1a receptors
- 5HT2a Antagonism:
  - May help mitigate reversible movement disorders (EPS)
  - May improve negative symptoms
- Unpredictable dose-response relationship to efficacy and safety

Risperdal RISPERIDONE
Helping Turn Lives Around

BMS Selling Strategy

- Emphasize "partial agonist" activity
  - balances dopamine and seretonin with minimal adverse events
- Marketing focused on New Beginnings
- Efficacy:
  - Focus on improving basic, everyday life activities
  - Efficacy vs. placebo and active competitors in both short- and long-term studies
  - Will sell efficacy in L-T maintenance vs. placebo (FDA approval)
- Differentiate on safety
  - Minimal movement disorders (EPS)
  - Favorable weight gain profile
  - Not associated with hyperprolactinemia

Risperdal RISPERIDONE
Helping Turn Lives Around

Background: Key Findings

- **Unpredictable dose-related Efficacy**
  - Aripiprazole has **not** consistently shown superiority over haloperidol in studies
  - insufficient response at a starting dose of 15mg, increasing the dose may not improve efficacy (Carson et al)
  - Aripiprazole did not distinguish from placebo in all of its pivotal trials (Kane, JCP).
- **Unpredictable dose-related Side Effects**
  - Side-effect cannot be predicted along a dose curve (ie: adjusting dose may not decrease side effects/EPS).
  - In a study comparing Aripiprazole and RISPERDAL to placebo, Aripiprazole had higher levels of akathesia and tremor vs. placebo than were seen with Risperdal vs. placebo. Neither drug produced significant reversible movement disorders (EPS) (Potkin, et al 2003).

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Aripiprazole Communication Points

- A lack of predictable dose-related efficacy and safety in high and low doses.
- In 1 of four pivotal trials aripiprazole did not demonstrate consistent *superiority vs placebo.*
- Aripiprozole 30 mg/day was not consistently superior to placebo in PANSS negative Subscale Scores (Kane, JCP).
- Unpredictable dose-effect on EPS at 10mg, 15mg, 20mg & 30Mg.
- Dose adjustments not recommended before 2 weeks due to long half life.
- Unclear starting dose

Risperdal RISPERIDONE
Helping Turn Lives Around

Strategies

- ***Sell the Efficacy and Safety of Risperdal FIRST on every Call!***
- Probe for reasons why doctor is trying Abilify
  - Patient has been tried on Risperdal before, did not respond
    - *Define unresponsive: not effective, experience side effects?*
    - What dose started at? How quickly titrated? Ending dose?
    - Retry Risperdal at 1mg/day, go slow, use .25 and .5 to titrate to effect
  - Possible safety advantage
    - Probe to uncover concerns about Risperdal safety and tolerability
    - Question dose, number of patients, titration
    - Sell safety benefits and excellent tolerability of Risperdal w/sales aid

Risperdal RISPERIDONE
Helping Turn Lives Around

Strategy/Key Messages

USE RISPERDAL CORE SALES AID

- **Predictability**
  - RISPERDAL has proven dose-related efficacy and safety.
- **Efficacy**
  - Significantly greater HAM-D improvement rates (HAM-D≤7) vs Olanzapine in pos sxs, mBa sxs of schizophrenia demonstrated in d-b, placebo controlled trial (Sales Aid – Conley page)
  - RISPERDAL has proven superior efficacy to placebo (See Marder/Davis spread for efficacy of 2mg dose in 8-week study)
  - Excellent efficacy for over 9 years & over 50 million prescriptions.
- **Safety**
  - Incidence of reversible movement disorders comparable to placebo at 2mg (and at ≤6mg) in adults. No statistical difference in reversible movement disorders in head to head trial with olanzapine (Conley study – reprint carrier).
  - Prolactin-related side effects comparable to Olanzapine in d-b trial (Conley, safety page)
  - Low weight gain: average 5lbs
  - Low incidence TD, risk of diabetes/DKA, hypertipidemia

Risperdal RISPERIDONE
Helping Turn Lives Around

Strategy/Key Messages

- Dosing
  - Start as low as 1mg, titrate to effect
  - Can adjust dose to increase efficacy, tolerability
- **Close for more Risperdal patients!!!**

Risperdal RISPERIDONE
Helping Turn Lives Around

Settings Workshop

OVERVIEW OF SETTINGS

RISPERDAL

OVERVIEW OF SETTINGS
OBJECTIVES

- Define the different customer settings that representatives may encounter
  - CMHC
  - State Hospitals
  - ER/Acute Care
  - Private Practice
  - Child & Adolescents
  - Geriatrics
- Discuss the importance of the setting as well as the Key Players, Key Issues, and Strategies to use in each setting

RISPERDAL

COMMUNITY MENTAL HEALTH CENTERS

RISPERDAL

Community Mental Health Centers

- Found in the majority of M-Rep territories
- Provide services to patients with chronic mental disorders in an outpatient setting
- Emphasis on outpatient care and prevention of hospitalization
- Generally funded by State and Federal Funding - Medicaid is Primary Payer
- Large indigent patient population
- Represents bulk of growth potential for Risperdal

RISPERDAL

CMHC: Key Players

Patient Management Team often Consists of:

- PSYCHIATRISTS
- NURSE/NURSE PRACTITIONERS
- PSYCHOLOGISTS
- CASE MANAGERS/SOCIAL WORKERS

RISPERDAL

CMHC: Key Areas

- Medication Clinic
- Day Treatment/Partial Hospitalization
- Psychosocial Rehabilitation
- Vocational Services - supported employment
- Injection Clinic - Haldol/Prolixin
- Crisis Stabilization Unit/Intake

RISPERDAL

CMHC: Key Issues

- Breaking "Habits" - leaving patient on what docs at Hospital Rx
- Redefining "OK", stable
- Switching Patients from Neuroleptics to Risperdal
- Realistic Trial of Risperdal
- Heavy use of Decanoates - Compliance issues
- Access - Doctors are extremely busy and often rotate through other settings

RISPERDAL

CMHC: Strategies

- Identify the key CMHCs within territory
- Identify key players
- Find out from which hospitals patients are being referred - community/state/academic med ctrs
- Partner for high call frequency
- Maximize on Group Selling situations
  - Inservices: Risperdal Consta administration
  - Teletopics
  - DLNs
- Refer to Constant Access for billing/distribution issues

RISPERDAL

CMHC: Strategies

- POSITION RISPERDAL AS FIRST LINE
- GAIN SWITCHES FROM COMPETITION
- BE A RESOURCE TO THE CMHC
  - Patient Assistance Program/Constant Access
  - Coupons
  - Samples

RISPERDAL

STATE HOSPITALS

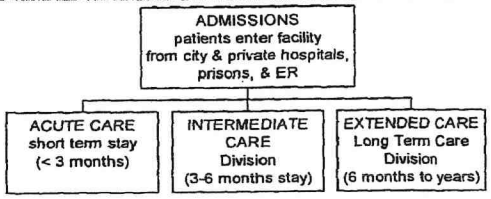
RISPERDAL

STATE HOSPITALS

- Covered by I, M, L Reps
- Provide settings of care for patients with varying diagnoses
  - Adult (Acute/Chronic)
  - Forensic
  - Child/Adolescent
- Length of stay varies based on patient
- Funded by state

RISPERDAL

State Hospitals: Clinical Treatment Pathways



- Discharge planning can involve Psychiatrist, Social Worker, Nurses, Therapist
- Try to establish stability in outpatient setting so patient is not "lost in the system"

RISPERDAL

State Hospitals: Key Players

- Director of Psychiatric Services
- Chief of Psychiatry
- Affiliated Psychiatrists
  - Admitting Physicians
- Pharmacists
- Nursing Staff
- Social Workers/Case Managers
- P&T Committee Members
- CME Coordinator

RISPERDAL

State Hospitals: Key Areas

- Adult Unit
  - Chronically Mentally Ill patients
  - Refractory Patients
- Forensic Unit
  - Patients transferred from Prison system
  - Often display hostile/aggressive behavior
- Child/Adolescent Unit
  - Patients with ADHD, PDD, CD, ODD
- MR/DD
  - Patients often display aggression and self-injurious behavior

RISPERDAL

State Hospitals: Key Issues

- Pharmacy Budget is a *BIG* issue
- State formularies drive physicians medication preferences
- Large Conventional use - cost and habit
- Heavy decanoate use - compliance issues
- Sedation is sometimes a "good" side effect

RISPERDAL

State Hospitals: Strategies

- Determine who are the decision makers
  - Director of Psych Services?
  - Pharmacists?
  - State P&T Members?
- Provide Pharmacoeconomic data
- Maximize on Group Selling situations
  - Grand Rounds
  - Teletopics
  - Satellite Programs: DLN, Psych Link

RISPERDAL

State Hospitals: Strategies

- POSITION RISPERDAL AS FIRST LINE
- GAIN SWITCHES FROM THE COMPETITION
  * Conventionals
- BE A RESOURCE TO THE STATE HOSPITAL
  - Speakers for Grand Rounds
  - Patient Assistance Program

RISPERDAL

EMERGENCY ROOM

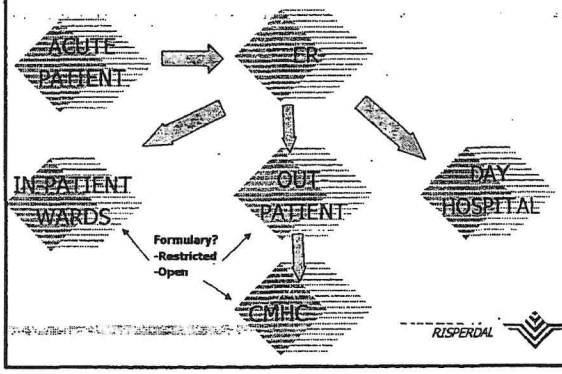
RISPERDAL

EMERGENCY ROOM

- Covered by both M, L- and I-Reps
- Not necessarily psychiatrists
  - Internal Medicine
  - Emergency Physician
  - Psych Liaison
- Treat patients who are acutely psychotic (or "appear psychotic"), agitated, or aggressive
  - Drug/Alcohol Abuse
  - Diabetic Shock
- Time and cost sensitive

RISPERDAL

Patient Flow Chart



RISPERDAL

EMERGENCY ROOM: Key Players

- Psychiatrist/Resident
  - Attending
  - Consultant
- ER Physicians
- Nurses
- Social Worker
- Pharmacist
- P&T Members

RISPERDAL

EMERGENCY ROOM

- Key Areas
  - Triage
  - 23 Hour Beds
- Key Issues
  - ER physicians are habitual writers of the Haldol/Ativan cocktail
  - Using PO medication is not protocol in many ER
  - Fear that Risperdal PO will not work as fast as IM
  - Formulary status of Risperdal M-TABs
  - Difficult to get time with entire treatment team

RISPERDAL

ER: Key Strategies

- Check formulary status of Risperdal M-TABs & OS
- Uncover established protocol
- Sell entire ER staff with Currier study
- Discuss benefits of oral therapy over IM
- Provide samples (if possible) and plan an in-service
- Utilize attending psychiatrist's experience with Risperdal to sell advantages of M-TABs, or OS.
- Patients started on Risperdal in the ER *today* will be Risperdal outpatients *tomorrow*!

RISPERDAL

ER: Currier Reprint

Efficacy

- Agitation based on PANSS scores declined significantly at 30 and 60 minutes in both treatment groups
- No significant difference in 5 agitation subscales of the PANSS or CGI scores between the haloperidol IM and RISPERDAL liquid groups
- Time to sleep...no difference between groups

Safety

- No cases of dystonia in the RISPERDAL group, 1 case of dystonia in the haloperidol group

Dosing

- RISPERDAL = 2 mg RISPERDAL oral solution + 2 mg p.o. lorazepam
- Haloperidol =5 mg IM haloperidol + 2 mg of IM lorazepam

RISPERDAL

ER: Key Strategies

- POSITION RISPERDAL AS FIRST LINE
- GAIN SWITCHES FROM COMPETITION
- BE A RESOURCE TO THE ER
  - Currier Study
  - M-TAB Placebo cards
  - Oral Solution Samples
  - Inservices (Dosing)

RISPERDAL

PRIVATE PRACTICE

RISPERDAL

PRIVATE PRACTICE

- Covered by M & L-Reps
- Provide care to patients who are generally higher functioning
- Less of a "Team Approach" - more individualized care
- Payment comes through private insurance or fee-for-service
- Treat across diagnoses - more mood disorders and depression

RISPERDAL

PRIVATE PRACTICE

- Key Players
  - Psychiatrist
  - Psychologist
  - Nurse, NP, PA
  - Receptionist
- Key Issues
  - Patients less tolerant of side effects
  - Not treating schizophrenia as much
  - Patient self-image is a stronger focus
  - Cost of medication can be a concern

RISPERDAL

PRIVATE PRACTICE - Strategies

- Sell on efficacy for *symptoms* not diagnosis
- Safety/tolerability: Weight gain, excessive daytime sedation
- Show cost comparisons among atypicals
- Maximize selling time by appointments and lunches
- Coupons and samples are always helpful

RISPERDAL

PRIVATE PRACTICE - Strategies

- POSITION RISPERDAL AS FIRST LINE
- GAIN SWITCHES FROM COMPETITION
- BE A RESOURCE TO THE PRIVATE PRACTICE
  - Approved Reprints/Medical Services
  - Coupons/Samples

RISPERDAL

CHILD & ADOLESCENT PHYSICIANS

RISPERDAL

Child & Adolescents

- Can be covered by all CNS reps
- Provide treatment to patients who are under the age of 18
- Most are diagnosed with a "Behavioral Disorder" or a "Mood Disorder"
- Can see initial stages of psychosis
- Provide therapy for children and families
- Generally paid through private insurance

RISPERDAL

Child & Adolescents

- Key Players
  - Psychiatrist
  - Social Worker
  - Psychologist
  - Family Therapist
- Key Areas
  - Teaching Hospitals, State Hospitals, and Private Psychiatric Hospitals may have specific units
  - Outpatient (CMHC, Private Practice)
  - Private Residential Homes

RISPERDAL

Child & Adolescents

- Key Issues
  - NO INDICATION
  - Fear of using "antipsychotics"
  - Difficult to treat - diagnosis often unclear
- Key Strategies
  - Sell on *symptoms* not diagnosis
  - Utilize Medical Services for studies
  - Develop relationships now - key for future

RISPERDAL

Child & Adolescents

- POSITION RISPERDAL AS FIRST LINE
- GAIN SWITCHES FROM COMPETITION
- BE A RESOURCE TO THE C&A PSYCHIATRISTS
  - Medical Services requests
  - Samples/Coupons
  - CME Programs - Teletopics/DLN

RISPERDAL

GERIATRIC PSYCHIATRISTS

RISPERDAL

GERIATRIC PSYCHIATRISTS

- Covered by ElderCare
  - Partner with both M- and I-Reps
- Rotate through various settings - Key Areas
  - Nursing Homes
  - Teaching/Community Hospitals
  - State Hospitals
  - Private Practice
- Provide services to elderly patients who suffer with varying diagnoses
  - Alzheimer's - Dementia
  - Psychosis - Depression

RISPERDAL

GERIATRIC PSYCHIATRISTS

- Key Issues
  - Not specifically indicated for dementia
  - Geriatric patients can be medically compromised
  - May still be unsure of dosing schedule
- Key Strategies
  - Dosing is key - less is better
  - Sell on *symptoms* not on diagnosis
  - No anticholinergic or QT prolongation
  - Partner with ElderCare reps on high prescribers

RISPERDAL

GERIATRIC PSYCHIATRISTS

- POSITION RISPERDAL AS FIRST LINE
- GAIN SWITCHES FROM COMPETITION
- BE A RESOURCE TO THE GERIATRIC PSYCHIATRIST
  - FDAMA Approved Reprints
  - Medical Services
  - Inservices

RISPERDAL

Summary

- Always deliver the core message - no matter what setting
- Focus on specific symptoms
- Utilize *all* resources that are available
  - Sales Aid - Patient Assistance Program
  - FDAMA Reprints - Inservice Opportunities
  - Medical Services - Speaker Programs
- Determine need at each setting and tailor your calls to their needs

RISPERDAL

Negotiation Workshop

Negotiation Workshop

Risperdal Objection Handling

ON YOUR MARK...
GET READY...
GET SET...

RISPERDAL OBJECTION HANDLING

GO!
DEVOUR THE COMPETITION

RISPERDAL OBJECTION HANDLING

KEY STEPS:

#1 Restate

#2 Empathize

#3 Respond

Probe – Clarifying Question
Tell what other Physicians have found
Share specific data (TOOLS?)
Answer the objection

Confidential: Sales training only, not to be used in a selling situation

Key Objections

1. All Atypicals are the same
2. Reversible Movement Disorders (EPS) may lead to Persistent Movement Disorder (TD)
3. All Atypicals cause Diabetes
4. Risperdal® causes prolactin increases
5. Risperdal® is not sedating enough

"All Atypicals Are the Same"

Probes

- What do you mean by "they are all the same?"
- How do you define efficacy?
- If they are all equal, how do you decide which atypical to Rx?
- What symptoms are you trying to treat with Drug X?
- When you prescribe Drug X, what benefits do you get from that drug that you don't get from RISPERDAL?

Tools to Use

Support Versus Atypicals

- Sales Aid
  - Conley
- Koro Reprint
- Gianfrancesco Reprint

All 3 studies can be distributed to customers

"Reversible Movement Disorders (EPS) Leading to Persistent Movement Disorder (TD)"

Probes

- What is your strategy in handling Reversible Movement Disorders (EPS)?
- What is EPS? Get into a discussion about reversible vs. persistent movement disorders.
- How often do you see these side effects?
- What is the patient's symptoms?
- How long has the patient been on THAT dose?
- Tell me how they were titrated?

Tools to Use

- Sales Aid
  - Conley
  - RISPERDAL has minimal reversible movement disorders at recommended doses
  - Refer to Proper Dosing - titrating with .25mg or .5mg
  - 9 Years of RISPERDAL Use in 51 Million Prescriptions
    - Persistent Movement Disorder (TD) for RISPERDAL is 0.3%
    - All Atypicals have similarly low rates of TD
- Williams Reprint

"All Atypicals Cause Diabetes"

Probes

- Do you screen for hyperglycemia/diabetes?
- Have any of your patients developed diabetes or any lipid abnormalities on any of the atypicals?
- What precautions do you take if you have a patient who has a higher risk of developing diabetes? (family history, etc.)

Tools to Use

- Sales Aid
  - 0.2% in double-blind + open-label trials (n=2607)
  - Minimal Case Reports (3 reported cases to date)
- Koro Reprint
- Gianfrancesco Reprint
- Teletopics on metabolic abnormalities

"RISPERDAL Causes Prolactin Increases"

Probes

- Approximately how many patients have you treated with RISPERDAL?
  - How often have you seen prolactin-related side effects with your patients?
- Are you seeing actual prolactin-related side effects?
- Is the side effect you are seeing actually related to prolactin increases, or specifically to RISPERDAL?
- What do you do if you see prolactin-related side effects?
- What is your concern for the long term?

Tools to Use

- Sales Aid
  - Conley
  - 9 Years of Experience in over 51 million prescriptions worldwide
- Medical Services

"RISPERDAL Is Not Sedating Enough"

Probes

- What symptoms are you trying to treat?
- How often do your Risperdal patients complain that they are not getting a good night's sleep?
- What leads you to believe that your patients on Risperdal will not get a good night's sleep?
- What is your ultimate goal – to sedate your patients or best treat the symptoms that prevent them from sleeping well?
- Somnolence rates for Risperdal are low, and these are measured during the day. So if Risperdal patients are not sleepy during the day, aren't they getting a good night's sleep?

Tools to Use

- Risperdal Core Sales Aid
- Yamashita & Durson, et al sleep studies (For information only. Not to be used in a selling situation).

More on... Sedation

Sedation and APS efficacy are two separate issues. It's important to have control over sedation to ensure patients can be active participants in the assessment process to determine the underlying problem, the cause of their psychotic behavior.

Sedation has been linked to a higher risk of falls and fractures in the elderly.

Sedation is a short term goal. APS efficacy should be the long term goal. Risperdal has the fastest onset of action amongst the atypical antipsychotics.

Final Realistic Objection

"That's not my clinical experience."

- Validate physician's experience
- Not every patient has the same experience on each drug
- In fact, clinical studies have shown...
- Reemphasize that RISPERDAL has 9 years of experience in 51 million prescriptions worldwide
- Probe to find out why the physician had that experience - dosing, titration
- Utilize tools to overcome physician's perception of RISPERDAL

Key Take Aways

- Improve probing and listening skills & Sell with Integrity
  - Asking the right questions
  - Asking the right number of questions
  - Restate, Empathize, Respond
- Close for agreement and expanded use of RISPERDAL

Administration

Adverse Event Training

Drug Safety and Surveillance

Adverse Drug Experience
Training
by Medical Services

Overview

- ✓ Safety and Surveillance - Historical Perspective
- ✓ J&J Drug Safety and Surveillance
- ✓ FDA Regulations - Adverse Events
- ✓ Reporting Adverse Drug Experiences to Janssen Medical Services
- ✓ Janssen Adverse Event Reporting Obligations
- ✓ J&J Adverse Event Records Retention
- ✓ Case Studies
- ✓ Q&A

Learning Objective

To assure that Janssen Pharmaceutica is in compliance with the FDA reporting regulations and that adverse drug experience reports (ADEs) are complete, accurate and timely.

Safety Surveillance Historical (Reactive) Perspective

- ✓ Voluntary Reporting to FDA
- ✓ Thalidomide
- ✓ Diethylstilbestrol (DES)
- ✓ Baycol – drug removal
- ✓ 1992 Introduction of MEDWATCH Program (FDA Medical Products Reporting Program)

Purpose of NDA Adverse Drug Experience Regulations and Reporting

- ✓ To obtain additional information on adverse events that may not have been detected prior to marketing.
- ✓ To modify the labeling of drug products.
- ✓ To communicate safety information.
- ✓ To avoid under-reporting to FDA

FDA Definitions Adverse Drug Experience

- ✓ Any adverse event associated with the use of a drug in humans, whether or not considered drug related, including the following:
- ✓ An adverse event occurring in the course of the use of a drug product in professional practice

Adverse Drug Experience (continued)

- An adverse event occurring from drug overdose whether accidental or intentional
  - ◆Example - A patient put on another Duragesic patch without removing the old one and experienced nausea and vomiting.

Adverse Drug Experience (continued)

- An adverse event occurring from drug withdrawal
  - ◆Example: A patient is titrated off Duragesic 25 mcg/hr patches and the clinician reports that three days later the patient experiences symptoms of withdrawal including insomnia, nausea, abdominal pain, cramps and vomiting.

Adverse Drug Experience (continued)

- Any failure of expected pharmacological action
  - ◆Example: A patient was started on Duragesic 25mcg/hr on 1/1/01 and called to report no pain relief on 1/8/01.

Adverse Drug Experience (continued)

- Pregnancy exposure
- Captured as ADEs and followed up to determine the outcome of the pregnancy
- Any abnormal outcomes are reportable ADEs
  - ◆Example: A patient calls to ask a question and mentions she is expecting a baby.

Serious Outcomes

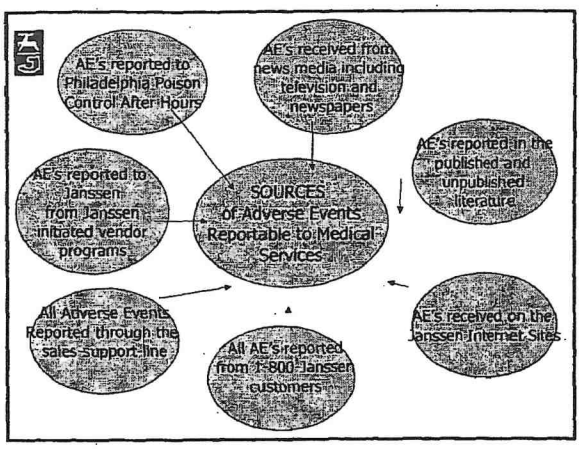
- ✓Death
- ✓Life-threatening
- ✓Inpatient hospitalization
- ✓Prolongation of existing hospitalization
- ✓Persistent or significant disability/incapacity
- ✓Congenital anomaly/birth defect
- ✓Important medical events/other

The Elements for ADE Reporting

- ✓An identifiable patient
- ✓An identifiable reporter
- ✓A J&J suspect drug
- ✓An adverse event or fatal outcome

FDA Postmarketing 15-Day Alert Reports

✓The clock starts <u>when the first J&J company representative learns of the report!</u>



ADE Reporting Process for all Employees

- 1-800-SSL-5514
- Written correspondence can be faxed to 609-730-3138 (retain fax confirmations)
- Information required for a report:
  - HCP's name, specialty, address and phone #
  - Adverse Event
  - Patient Demographics (gender, age)
  - Janssen drug
  - Transmissions no later than 1 business day

Product Quality Complaint

Terry Meisner
Process Manager
Medical Services

What is a PRODUCT QUALITY COMPLAINT?

✓A complaint is any discrete concern that questions the identity, quality, reliability, safety, efficacy or performance of a product

✓A complaint may allege an AE, injury or malfunction associated with the use of the product

✓It may also involve the design, packaging, advertising or promotion of the product

What is reportable?

✓**PACKAGING** - the primary or secondary packaging is reported to have a missing or defective component

✓**PHYSICAL** - the actual product is reported to be defective

✓**SUSPECTED FOREIGN MATERIAL** - a foreign object is found within the product or packaging of a product

Reporting an Product Quality Complaint

- ✓Report all Product Quality Complaint to Medical Services
- ✓Sales Support Line: 1-800-SSL-5514, Press 3, then 3

Adverse Event Reporting

- The Sales Representative is speaking with physician who mentions he no longer prescribes Risperdal in his elderly patients since he had a woman last month experience orthostatic hypotension and fall and break her hip.

  The Physician states that he can not be sure the fall was caused by Risperdal, but he prefers to take a conservative approach on this one.
- **Representative Response:** "Doctor, orthostatic hypotension is certainly a concern when treating the elderly. Our package labeling includes this event and recommends a starting dose of 0.5 mg may minimize this risk of falls. I will, however, report this the our Safety department."
- ***** Regardless of whether the physician feels the fall was related to the use of Risperdal, the representative has the minimum reporting information (a patient, a drug, an event and a reporter). Call this adverse event into Medical Services at 1-800-SSL-5514 prompt #3.***

Product Quality Reporting

- The Sales Representative is in a large chain pharmacy. The pharmacist mentions that his last shipment of Risperdal 1 mg. Tablets were yellow in color and usually white. He asked the representative if Janssen had changed the color?
- **Representative response:** "Thank you for sharing this information with me. Janssen has not communicated any changes in the tablet appearance for Risperdal. This is potentially a serious packaging complaint and needs to be reported to our Quality Assurance Department. Please hold on to the product, you will be notified by QA to retrieve the product for investigation. They will arrange a credit for you through your wholesaler. Do you have the lot number?"
- ***** The Sales Representatives report all product quality complaints to Medical Services by calling 1-800-SSL-5514, prompt # 3. Providing a lot number allows QA to track and trend that complaint.***

Medical Information Request

- The Sales Representative is asked by a physician about the efficacy of Risperdal use to treat Bi-Polar Disorder.
- **Representative Response:** "I appreciate your inquiry doctor. As you know, Risperdal is not indicated for the treatment of Bi-Polar Disorder. Our Medical Services Department would be happy to research this information for you. Please complete this information request form and sign at the bottom. A summary of the information will be mailed to you in 3-5 business days. If at that time you have additional questions, please call 1-800-JANSSEN and one of our professionals would be happy to assist you."
- ***** This information was spontaneously requested by the HCP. All unsolicited requests for information outside the package labeling will be managed by Medical Services and communicated directly to the physician. To ensure compliance, retain the signature on file.***

SAFETY TRAINING ASSESSMENT EXERCISE

Please respond to the following multi-choice questions. (Circle the most accurate response) Your completion of this exercise will assist Medical Services in measuring the training effectiveness of this program.

QUESTIONS

1. Which of the following is the purpose of FDA regulations for collecting and reporting adverse events.
   A. To obtain additional safety information on the use of a prescription drug.
   B. To modify drug label, if necessary.
   C. To recall a drug from the market.
   D. To inform physicians on new information.
   E. All of the above.

2. Does the definition of an Adverse Drug Experience include:
   A. Accidental or intentional drug overdose even without an ADE.
   B. Drug withdrawal.
   C. Lack of drug efficacy.
   D. Whether or not drug is related to ADE.
   E. All of the above.

3. Is a report of a patient's death, if being treated with a J&J drug, always reportable to Medical Services?
   A. Yes
   B. No
   C. Sometimes
   D. Only when considered related or associated to the adverse event.

4. When does the time clock start for reporting an adverse event?
   A. A patient notifies their physician.
   B. A consumer calls and leaves a voice mail on a weekend.
   C. The date the AE is reported in a medical journal.
   D. When the first J&J company representative learns of the report.
   E. All of the above.

5. What are the consequences to J&J if the company does not comply with the Federal Regulations on Adverse Event Reporting?
   A. Class action law suit
   B. Potential imprisonment of company officers or monetary fines
   C. Drug taken off the market
   D. FDA could put on "hold" any new company drug approvals
   E. All of the above

6. We require which of the following key pieces of information to classify the event reportable.
   A. A patient
   B. An event
   C. A product
   D. A reporter
   E. All the above

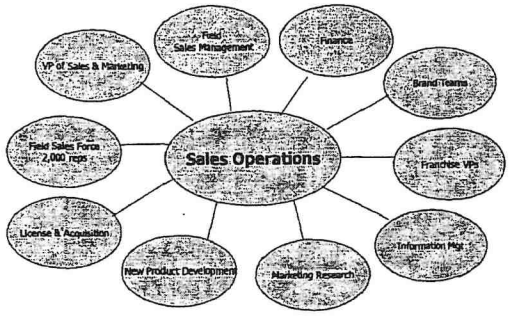
NAME: _____ _____ _____
Print Signature Territory

Business Analytics

CNS BUSINESS ANALYTICS

Understanding the business of your territory.

Sales Operations



Sales Operation's Responsibilities

- Sales Compensation
- Sales Territory Deployment
- Monthly Sales Reports
- Call Planning & Call Activity Tracking
- Market Share Forecasting/Analysis
- Promotional Response Models
- Rep/DM Business Analysis Training
- Sales Force Productivity & Capacity Models
- New Business Opportunity Analysis

Objectives

- Review and understand all data sources that are delivered to the field.
- Be able to turn this data into actionable information to enable you to leverage your business.
- Develop short & long term strategies that will help you impact physicians and your bonus payouts.

What are your objectives ?

AGENDA

- Tracking Prescriptions
- Sales Reports
- Case Study
- Q&A

TYPES OF DATA TRACKED

- Prescription Data
  - Retail (TRX or NRX) Xponent®
    - Physician > Prescription > Pharmacy
  - Mail Order
    - Physician > Prescription > Mail Order
  - DDD (Institutional Sales)
    - Hosp. Physician > Prescription > Hosp. Pharmacy

TRACKING PRESCRIPTIONS

IMS
(International Marketing Services)

- Located in Philadelphia
- IMS Contracts with 34,000 pharmacies each year
- Pharmacies report on a weekly/monthly basis
  - Computer systems linked to pharmacies
  - All major pharmaceutical companies use IMS
  - A minimum of 6 weeks is required to retrieve the prescription data and deliver to the companies.
  - Prescriptions are tracked to rep's territory/zip code

IMS SAMPLE AUDIT

- Approximately 50,000 stores in the retail universe
- IMS contracts with 34,000 retail and mail order pharmacies
- Geospatial statistical projection methodology is used to estimate the non-reporting pharmacies

Collecting Data

Elements Collected from Pharmacies

- Physician DEA
- Store ID
- Rx Fill Date
- New/Refill Indicator
- Product NDC Number
- Rx Size

Rx Matching

- Credit the right doctor with each prescription
- Credit the right Sales Rep with each Rx
  - DEA Number
  - ME Number
  - Name/Zip Code combination
  - Prescriber ZIP Code
  - Store ZIP Code
- Match Traveling Rxs back to the territory of origin

Multiple Office Prescribers

- DEA first match identifies location
- ME Number ties it back to the physician
- Physician can have multiple DEA numbers
  - Once tracked back to physician:
    - If physician is profiled, that territory will receive credit.
    - If multiple reps have physicians profiled, all will receive shared credit.
    - If the physician is not profiled by any representative, the territory that has the responsibility for that zip code will receive credit.

DDD

- Account level information for institutions
- Shows drug sales from the distributor to the individual account
- Reported in units (pill, ml, patch, etc)
- Over 30 years of use in the pharmaceutical industry

DOLLARIZATION

- Known as Janssen Dollars
- Based on daily consumption (DACON) and average cost per day
- The competition is converted to the cost of Risperdal
- Levels the playing field by removing the influence of price
- Dollarization is used during the Deciling process

Decile Methodology

- Physician's prescriptions are dollarized using the standard Janssen dollarization process.
- Physicians' dollar potential is summed for the last 12 months and sorted in descending order.
- All physician specialties are segmented into 10 buckets, each containing equal sales potential.
- Each segment is assigned a decile value between 00 and 90.
- The bottom decile is segmented again to enhance targeting capabilities (10,11,12,13,14).

Deciling

APS Market - All Specialties

Decile	Average $ Value	Total $ Value	# of Prescribers	Cumulative % of Business
90	$ 534,925	$ 263,718,025	493	10%
80	$ 309,784	$ 264,245,953	853	20%
70	$ 220,606	$ 263,624,020	1,195	30%
60	$ 163,491	$ 263,874,952	1,614	40%
50	$ 119,137	$ 264,007,507	2,216	50%
40	$ 84,210	$ 263,912,904	3,134	60%
30	$ 53,529	$ 264,539,441	4,942	70%
20	$ 27,276	$ 265,473,831	9,733	80%
10	$ 12,118	$ 263,245,904	21,724	90%
0	$1,346	$ 272,224,990	202,243	100%

•Janssen CNS currently targets all psychiatrists deciles 20-90. This is approximately 90% of the total psychiatry business.

Decile Comparison Across Janssen Products

	APS MARKET	PPI MARKET	ALZ MARKET	CP MARKET	AFO MARKET
Decile	Mean $	Mean $	Mean $	Mean $	Mean $
90	$ 534,925	$ 214,179	$ 39,279	$ 495,418	$ 41,568
80	$ 309,784	$ 119,001	$ 19,143	$ 206,714	$ 21,501
70	$ 220,606	$ 86,500	$ 12,760	$ 104,841	$ 14,709
60	$ 163,491	$ 67,844	$ 9,322	$ 58,272	$ 10,855
50	$ 119,137	$ 54,665	$ 7,086	$ 36,204	$ 8,232
40	$ 84,210	$ 43,892	$ 5,427	$ 23,728	$ 6,252
30	$ 53,529	$ 34,279	$ 4,077	$ 15,535	$ 4,663
20	$ 27,276	$ 24,995	$ 2,918	$ 9,642	$ 3,290
14	$ 16,433	$ 19,629	$ 2,308	$ 6,927	$ 2,578
13	$ 13,403	$ 17,661	$ 2,102	$ 6,059	$ 2,329
12	$ 10,897	$ 15,656	$ 1,897	$ 5,243	$ 2,084
11	$ 8,831	$ 13,645	$ 1,699	$ 4,466	$ 1,844
10	$ 7,079	$ 11,550	$ 1,507	$ 3,709	$ 1,602
0	$ 1,346	$ 1,884	$ 555	$ 671	$ 699

CONFIDENTIALITY

- Data is for your use only
- Must not be discussed with:
  - Pharmacy
  - Physician
  - Competitors

BRAIN TEASER

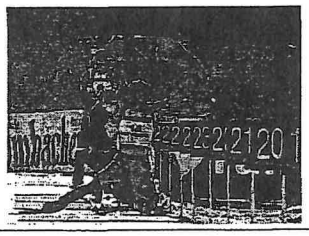
A boy and a girl born on the same calendar day of the same year with the same parents are not twins.

How is this possible?

AVAILABLE REPORTS

- NRx / TRx / DDD Volume Share
- Risperdal Outlet Report
- IMS Early View

Introducing Volume/Share Reports

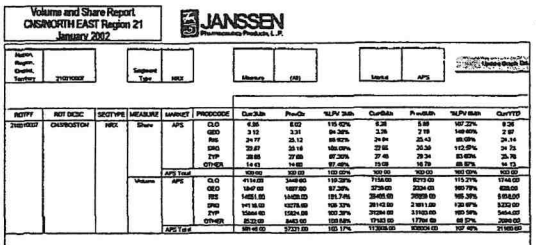


Keeping **YOU** focused and **"in Control"**

VOLUME SHARE REPORT

- Monitor TRx, NRx, & DDD share & volume for our products and competitive agents
- Total APS volume, rolling 3 months current vs. previous quarter & current 6 months vs previous 6 months
- Good overall trend and YTD, LYTD data
- Compare territory to district, region and nation

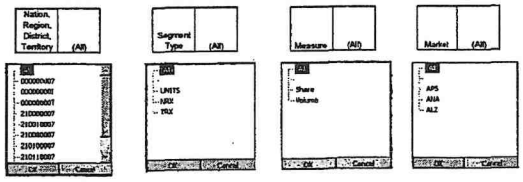
New Volume/Share Report



Includes:

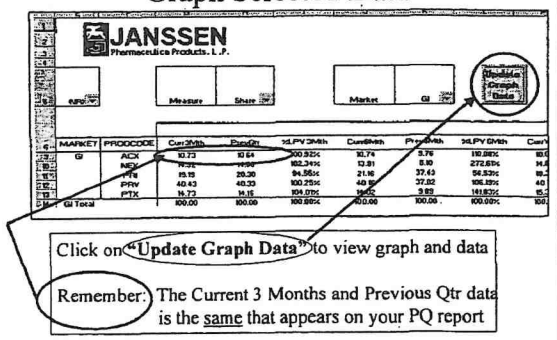
- Share Point Change
- Current 3 Months
- Previous Quarter
- % LPV and % LPS
- Current & Previous 6 Months
- Current & Previous YTD
- 12 Current Months of Data

Data Analysis Options

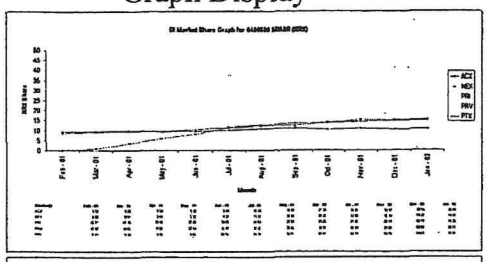


- Different combinations of data may be selected with the use of drop down boxes
- Select one or all of your markets from one report

Graph Selected Data

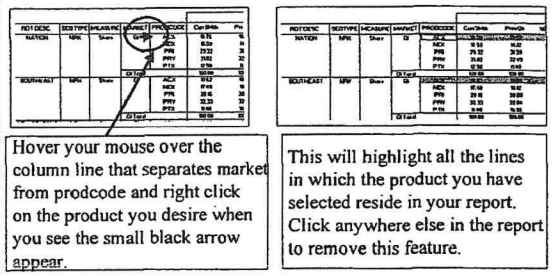


Graph Display



- Graphs 12 **individual months** of sales data
- Competitive products are included
- Prints graph and data to one page

New Terms and Features



Hover your mouse over the column line that separates market from prodcode and right click on the product you desire when you see the small black arrow appear.

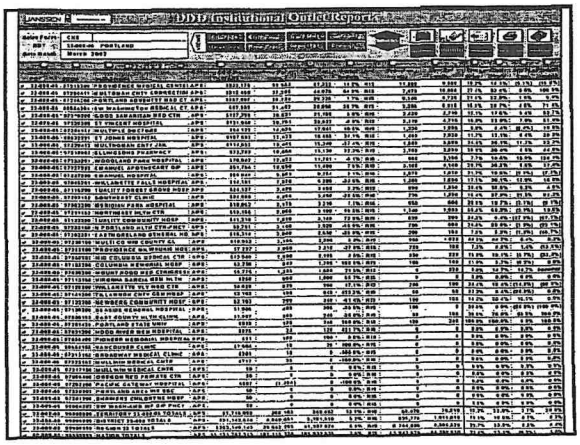
This will highlight all the lines in which the product you have selected reside in your report. Click anywhere else in the report to remove this feature.

WHY USE VOL SHARE REPORTS ?

- NRX report allows you to look at short term trends in your territory
- DDD report allows you to look at long term trends in your territory
- DDD/NRX/TRX reports tracks the competitors' activity in your territory
- These reports enable you to identify your APS market potential

RISPERDAL OUTLET REPORT

- Summary of institutional sales
- Total APS volume, rolling 6 months current vs. previous for individual accounts in territory
- Current Market & Product Units
- Current & Previous Share & Share Change
- Measures Risperdal and APS market; not individual competitors

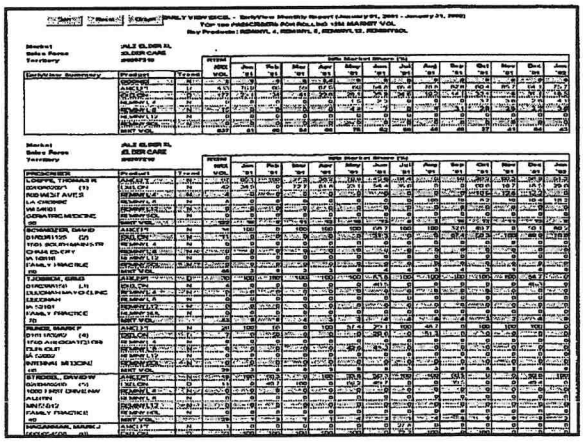


WHY USE OUTLET REPORT ?

- Identify the accounts being used to calculate your PQs
- Determine the accounts where you will be spending your time
- Identify current trends at each of your institutions
- Determine buying patterns based upon 24 months of history

IMS EARLY VIEW

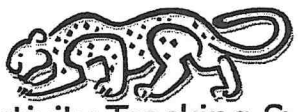
- Allow analysis of individual physician's prescribing trends for Risperdal and competition
- Identify high prescribing physicians in your territory
- Use to measure effectiveness of marketing plans and speaker programs



WHY USE EARLY VIEW ?

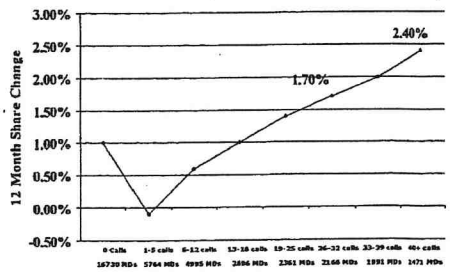
- Allows you to identify immediate impact of detailing and resource utilization at the physician level
- Gives you more recent prescribing patterns than the current decile information
- To be used as a trending report not a targeting tool

JANSSEN · Pharmaceutica Products, L.P. ·

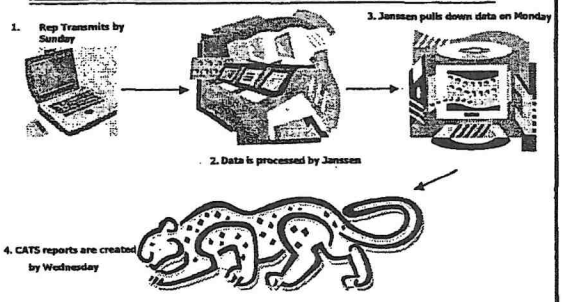


Call Activity Tracking System

NRX 12 Month Share Change vs Call Activity



CATS Generation Process



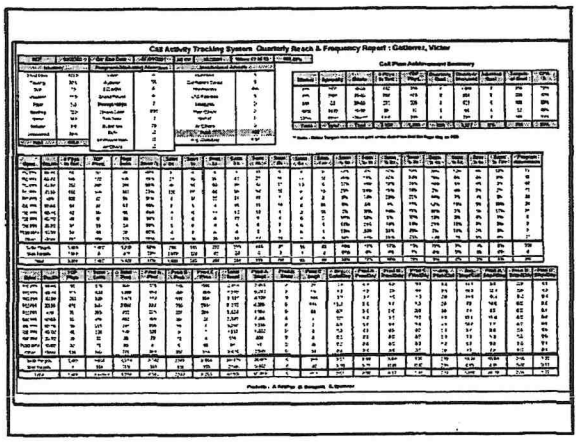
Call Plan Achievement

of doctors seen the right number of times

# of TOP Physicians (Rep Target "Yes")

CATS Basics

- Data is as good as its inputs
- Company Targets = guide for reps
- Rep Target "Yes" dictates CPA
- Workload should = 385 ± 10%
- Time Lag – CATS is one week behind



Itinerary

RDT	6160704	Qtr End Date	09/31/2002	AS OF	3/24/02	Week 12 of 13
Itinerary		Programs/Marketing Attendees		Institutional Activity		
Field Days	42.5	Video	0	Hospitals	0	
Training	2.0	Speaker	0	Out Patient Clinics	0	
Sick	0.0	CD ROM	0	Pharmacies	121	
Vacation	5.0	Grand Round	0	LTC Facilities	0	
Fleet	0.0	Preceptorships	0	Hospices	0	
Meeting	6.6	Dine-n-Dash	0	Pain Clinics	0	
Other	2.0	TeleTopic	0	CMHC	0	
Holiday	3.0	In-Service	0	All Others	0	
Unreported	0.0	DLN	0	Total	121	
Total	60.0	On-Patient Web	0	Avg. Calls/Day	2.85	
		All Others	0			

- Shows how are you spending your time and where
- # and types of Programs
- # of Pharmacy and Total Institution calls per day

CPA

Call Plan Achievement Summary

Market	Specialty	Decile	# Phys in Terr	TOP Phys	Quarterly Goal	Quarterly Workload	Adjusted Goal	Targets at Goal	CPA %
PPI	PCP	40-50	83	74	3	222	3	39	51%
PPI	PCP	20-30	51	29	2	58	2	24	83%
PPI	GE	20-30	12	10	3	30	3	4	40%
Other	Other	Other**	101	0	2	0	2	0	0%
Total	Total	Total	247	113	N/A	310	N/A	68	60%

** Note - Other Targets that are not part of the Call Plan that the Reps flag as YES

- Shows TOP physicians by grouped decile and Quarterly Goal
- Shows your Workload (TOP * Quarterly Goal) by grouped decile.
- Shows you the number of targets at Goal vs TOP Physicians
- Shows your achievement of the frequency goal (CPA = Targets @ Goal / TOP Physicians) by grouped decile

Physicians Seen

Specialty	Decile	# Phys in Terr	TOP Phys	Phys Seen	Seen %	Seen 0x	Seen 1x	Seen 2x	Seen 3x	Seen 4x	Seen 5x	Seen 6x+	Seen 7x+
PC PPI	80-90	9	9	9	100%	0	1	2	4	1	1	0	0
PC PPI	60-70	26	24	23	96%	1	0	8	8	5	0	2	0
PC PPI	40-50	48	41	40	98%	1	2	21	9	5	1	2	0
PC PPI	20-30	31	29	27	93%	2	3	7	14	2	1	0	0
PC PPI	<20	78	0	0	0%	0	0	0	0	0	0	0	0
GE PPI	80-90	3	3	3	100%	0	1	0	1	1	0	0	0
GE PPI	60-70	0	0	0	0%	0	0	0	0	0	0	0	0
GE PPI	40-50	5	4	4	100%	0	2	0	1	0	1	0	0
GE PPI	20-30	4	3	3	100%	0	2	1	0	0	0	0	0
GE PPI	<20	7	0	0	0%	0	0	0	0	0	0	0	0
Other	Other	21	0	0	0%	0	0	0	0	0	0	0	0
Total Targets		113	113	109	96%	4	11	39	37	14	4	4	0
Non-Targets		134	0	21	16%	113	10	3	5	3	0	0	0
Total		247	113	130	53%	117	21	42	42	17	4	4	0

- Provides Total and # of TOP Physicians and your Reach (seen)
- Shows Frequency by decile to track your CPA
- Shows where you are short or excessive in Frequency
- Shows Frequency for Target vs. Non-Target Activity

Total Calls

Specialty	Decile	TOP Phys	Total Calls	Total Pres	Prod A Pres	Prod B Pres	Prod C Pres	Total Smpl	Prod A Smpl	Prod B Smpl	Prod C Smpl	Avg Calls/Day
PC PPI	80-90	9	39	66	26	14	26	331	144	166	42	0.9
PC PPI	60-70	24	72	172	72	30	70	742	306	400	36	1.7
PC PPI	40-50	41	109	282	107	47	108	1,063	540	380	143	2.5
PC PPI	20-30	29	77	198	72	37	71	636	306	276	54	1.7
PC PPI	<20	0	0	0	0	0	0	0	0	0	0	0.0
GE PPI	80-90	3	8	10	8	1	1	72	72	0	0	0.2
GE PPI	60-70	0	0	0	0	0	0	0	0	0	0	0.0
GE PPI	40-50	4	10	15	10	2	3	18	18	0	0	0.2
GE PPI	20-30	3	4	4	4	0	0	72	72	0	0	0.1
GE PPI	<20	0	0	0	0	0	0	0	0	0	0	0.0
Other	Other	0	0	0	0	0	0	0	0	0	0	0.0
Total Targets		113	300	709	290	131	275	2,948	1,458	1,215	275	7.05
Non-Targets		0	45	99	43	18	41	397	189	145	54	1.01
Total		113	345	808	342	148	320	3,345	1,656	1,360	329	8.07

Products: A. Aciphex B. Risperdal C. Remicyl

- How many **Calls** were made and to whom
- How many **Presentations** were made and to whom
- How many **Samples** were left and with whom
- How many **Calls Per Day** were made
- **Targets vs. Non-Target Activity**

Total Calls (continued)

Prod A Pres/Day	Prod B Pres/Day	Prod C Pres/Day	Avg Pres/Call	Avg Smpl/Call	Prod A Smpl/Day	Prod B Smpl/Day	Prod C Smpl/Day
0.6	0.3	0.6	2.5	13.5	3.4	3.9	1.0
1.7	0.7	1.7	2.4	10.3	7.2	9.4	0.9
2.5	1.1	2.5	2.4	9.8	12.7	8.9	3.4
1.7	0.9	1.7	2.5	8.8	7.2	8.4	1.3
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.2	0.0	0.0	1.3	9.0	1.7	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.2	0.1	0.1	1.5	1.8	0.4	0.0	0.0
0.1	0.0	0.0	1.0	18.0	1.7	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7.04	3.08	6.68	2.36	9.83	34.51	28.69	6.47
1.01	0.35	0.85	2.30	9.23	4.68	3.41	1.27
8.05	3.44	7.53	2.36	9.75	38.95	32.00	7.74

Products: A. Aciphex B. Risperdal C. Remicyl

- How many **Product presentations** per day were made
- How many **Presentations Per Call** were made
- How many **Samples Per Product Per Day** were given
- Target vs. Non-Target Activity as well as Total Activity

DELIVERY SCHEDULE

Deliverables	Source	Approximate Delivery Date
Early View	Excel Document Attached to E-mail Directly From IMS	20th of each month
TRx, NRx, DDD & TCO Reports	Excel Document Attached to E-mail Sent from Home Office	25th of each month
PQ Report & President's Trophy Ranking	.PDF File Attached to E-mail	25th of each month
Bonus Payout	J&J Shared Services	2nd Thursday of June, Sept, Dec & March

Case Study

- Answer the following questions about your Territory.
- If you cannot complete the questions during this session, take the time after hours to prepare yourself to know your Territory.
- Once you complete this Territory analysis, send it to your DM and field trainer to assist you in creating your TOP.

Objectives

- Review and understand all data sources that are delivered to the field.
- Be able to turn this data into actionable information to enable you to leverage your business.
- Develop short & long term strategies that will help you impact physicians and your bonus payouts.

THANK YOU

On behalf of Sales Operations...

CNS Territory Analysis Workshop

1. In your territory, for the current 3 months, which product is leading the APS market in...

Unit Share _____	Share = _____
% of LPV for Uinit Shr_____	% LPV = _____
Unit Volume _____	Volume = _____
% LPV for Unit Vol _____	% LPV = _____
NRx Share _____	Share = _____
% LPV of NRx Shr _____	% LPV = _____
NRx Volume? _____	Volume = _____
% LPV for NRx Vol_____	% LPV = _____
TRx Share _____	Share = _____
% LPV for TRx Shr _____	% LPV =_____
TRx Volume _____	Volume = _____
% LPV for TRx _____	% LPV = _____

2. What is the NRx % growth of the APS Market in your Territory for the current 3 months?
   A) Which product is currently driving this market growth?
      Product _____ % Growth (%LPV) _____
   B) What is your RISPERDAL growth for the current 3 months?

   C) How does your RISPERDAL growth compare to your Market growth for the current 3 months?

3. Which product would you consider to be your main competition based on the current 3 month period and why?
   Offices - (NRx)

   Hospitals -(Units)

4. What is the NRx Share trend for your main competitor for the last 6 months?
   Risperdal?
5. What is the NRX Volume trend for your main competitor for the last 6 months?
   Risperdal?
6. What is the Units Share trend for your main competitor for the last 6 months?
   Risperdal?
7. What is the Unit Volume Trend for your main competitor for the last 6 months? Risperdal?

8. In your territory, for current 3 months, how many APS NRxs make 1 Market share point? (hint – take 1% of market total of NRx for 3 months)

9. What does the answer in #8 mean to you in your territory?

10. List the top 5 Hospitals in your territory according to APS WAC$.

A	WAC $=
B	WAC $=
C	WAC $=
D	WAC $=
E	WAC $=

11. List the following for each of the above accounts:

	Curr Mkt Units	Curr Prod Units	Curr RIS Share	Curr Shr Pt Change
A				
B				
C				
D				
E				

12. List the top 3 hospitals in Market growth. What is their Risperdal growth?

A	% =	RIS %=
B	% =	RIS %=
C	% =	RIS %=

What does this tell you about your Risperdal business?

13. List the top 3 hospitals in Risperdal growth. What is their market growth?

A	% =	Mkt %=
B	% =	Mkt %=
C	% =	Mkt %=

What does this tell you about your Risperdal business?

14. List the top 5 physicians who write for your main competitor in question 3.

A	# NRx=
B	# NRx=
C	# NRx=
D	# NRx=
E	# NRx=

Do they write more or less Risperdal NRxs than the competition?

15. List the top 5 Risperdal NRx writers in your territory & RIS Trends (U, D, N)

A	# NRx=	Trend=	Comp=
B	# NRx=	Trend=	Comp=
C	# NRx=	Trend=	Comp=
D	# NRx=	Trend=	Comp=
E	# NRx=	Trend=	Comp=

Which competitive product do they write the most?

CNS Territory Analysis Workshop

FDAMA

What is FDAMA?

(Food & Drug Administration Modernization Act)

Allows field dissemination* of select reprints if:

- Well-controlled study
- Published in a peer-reviewed journal
- Company has a planned sNDA for the studied use
- Approved via FDA-DDMAC

*See FDAMA Dissemination Procedures

Dissemination Procedures

NOTE:

The following information is for your information only. Details of this study regarding design, findings, and conclusions are not to be discussed with your customers.

Communication points regarding this study must be limited to:

- Name of the article
- What journal in which the article appeared
- Author of the article
- Medical use of the drug described in the article - If medical use of the drug is described in the article is mentioned, representatives MUST indicate that the medical use is not within product labeling

FDAMA Dissemination Procedures

- Reprint carrier will include the following:
  - Article
  - Bibliography
  - Package Insert
- DO NOT ADD/REMOVE any piece of information to/from the carrier.
- Requests for additional reprints must be ordered through Marketing Communications

FDAMA Reprint Tracking Report

Must be e-mailed every 6 months to:
April and November
"JANUSTI - CNS FDAMA Administrator" mailbox

Sales Rep. Name:
District Name:
Territory Number:

Title of Article: "Comparison of Risperidone and Placebo for Psychosis and Behavioral Disturbances Associated With Dementia: A Randomized, Double-Blind Trial" (Katz article)
RIS 63

* Please specify Group Name

Last Name	First Name	Date Distributed (mm/dd/yy)	Quantity	PCP	Psychiatrist	Nurse	Pharmacist	Administrator	Pharmacy Benefit Manager *	LTC Pharmacy Provider *	Federal/State Gov't Agency *	Other *	Group Name
i.e. Smith	John	01/02/00	3		x								
i.e. Johnson	David	01/02/01	1									x	Acme Healthcare Group

JJRIS 00431917
Confidential/Produced in Litigation Pursuant to Protective Order

Driving Dynamics
Advanced Driving School

This is Your Course Confirmation

There are three things you need to do to prepare your car for the course. They are extremely important, and *they must be* done in order for you to participate.

1. **Prior to arrival, increase your tire pressure to 40 pounds.**
2. **Remove all loose articles from vehicle interior. (Samples in your trunk are OK.)**
3. **Arrive with at least 1/2 tank of fuel.**

Car preparation is a safety issue and your responsibility before you arrive.

Please pay attention to your assigned class *(date, time, place and tire pressure).* If you need to change your time, please see your advisor to ensure the class size remains the same *(no more then 16-18 per class).* If your tire pressure is not at 40 psi, you will be instructed to drive to the nearest gas station, which will increase the class end time.

Please be on time for your designated start time. If you are late, it may not be possible to admit you to the class

With your cooperation the class will end before 5:00.

DRESS: Check the weather and dress accordingly. The class will run rain or shine, so we recommend sneakers, casual dress and rain gear if needed. You will be outside most of the day.

MEALS: Lunch will be deli sandwiches. If you have other dietary requirements, please bring your own lunch or beverages.

We regret that we cannot supply coffee in the morning, but sodas and water will be available throughout the day.

Cellular phone use is restricted to the lunch break only. We need your attention all day so that we can certify that you have successfully completed the course.

We look forward to having you in the class.

Directions to:
Johnson & Johnson

From the South:
From the Regency Hyatt or Marriott, go north on Route 1.
About 7.5 miles north of the Regency Hyatt, (5 miles north of the Marriott), you will see a large blue water tower on your right.
About three miles further, you will see a L'Oreal building on your right. (There is a white L'Oreal sign).
Just after the L'Oreal sign, turn right at the light onto Aaron Road. This leads you into the J & J facility. We will be in the parking lot in front of the building.
Park near the Driving Dynamics trailer.

For the trailer – go past Aaron Rd. to the next road – Commerce Drive.

From the North:
J&J is on Route 1 about 7 miles south of where it intersects with Route 18.
You will see a large white J&J sign on the left. Take the jughandle at Arron Rd., just past J&J and cross over to the building.

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You will see a large white J&J sign on the left. Take the jughandle at Arron Rd., just past J&J and cross over to the building.

Directions to
Sovereign Bank Arena
Trenton, NJ

- From the Regency Hyatt, go South on Rte. 1
- About 2 1/2 miles south of the Regency, the road divides. There are green signs over the road. Stay in one of the two left lanes. (But if you end up on the right, don't panic. Stay to the left, and the roads re-combine).
- About three miles further, the road divides again. Bear left on Rte. 1 South, Trenton.
- After another 3 1/2 miles, you will see signs for Downtown Trenton, and go under two overpasses.
- Shortly after the second overpass, turn right on Rte. 129. (There are two right turns next to each other. Rte. 129 is the second right).
- Stay on Rte. 129 only a short distance. Take the first right turn onto Hamilton Avenue. The Arena will now be on your left, and the parking lot on your right.
- Take the first right turn into the parking lot.
- You will see lots of orange cones and the Driving Dynamics trailer. Park near the trailer.