

# Using clinical research to inform regulatory decisions for OTC drugs: Understanding consumer behavior

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Disclosure: Speaker is a consultant to Sigma Tau Research, Merck Research Laboratories, McNeil Consumer and Specialty Pharmaceuticals, GSK Consumer Products, PEGUS Research, Consumer Health Products Association, Kowa Research, Calistoga Pharmaceutical, Indigo Pharmaceuticals

# Potential risks and benefits of OTC access

*Mis-diagnosis*  
*Delay in treatment*  
*Drug interactions*  
*Off label use*  
*Accidental poisonings*  
*Use during pregnancy*  
*Diversion from optimal care*



*Improved access to effective drugs*  
*Lower costs*  
*Increased efficiencies in healthcare system*  
*Greater consumer autonomy*  
*Improved consumer education*

Do the benefits of availability of the drug without involvement of a learned intermediary out weigh the risks?

# Guiding consumer self-management of therapy

- The OTC product label is the critical tool for informing consumers as to the proper use of an OTC drug
  - May be the sole source of information at time of purchase
  - Must guide all aspects of self-management of therapy, related to both indication and drug
- Thus, design and validation of the OTC label central to an OTC development program and regulatory decision making

# Key Data to Support OTC Switch: Demonstrating that the Label is Effective

Label Development: Identify the key messages that must be communicated to consumer to allow drug to be used properly

INDICATION: Why should the drug be used?  
Allow consumer self-diagnosis

WARNINGS When NOT to use due to individual consumers health status: Condition requires higher level care or use of drug not safe for individual

DIRECTIONS for use

WARNINGS When to discontinue use: Condition changes and now requires higher level of care or drug adverse event

***Selection  
Decision***

***Deselection  
Decision***

# Developing the OTC Label

- Develop wording for the key messages and organize into proposed label
- Can typical consumer understand the label?

Tool: Label Comprehension Study

# Label comprehension studies

- Study participants provided proposed label(s) and asked series of questions about the drug.
  - Participants answer based on their understanding of label
  - Multiple choice, open-ended and scenario based questions included
  - Each question designed to address one key message
  - Results tabulated to assess effectiveness of each communication objective (percent correct)
- Study recruitment designed to enroll population similar to consumers who would consider the product
  - Low literacy consumers included
  - Varied ethnicity/insurance status/socioeconomic status
  - Populations enriched for groups of special interest (e.g. those at risk)

## Label Comprehension Study: OTC Switch of Omeprazole for Heartburn (Gastric reflux)

Design: 504 participants – provided proposed label and asked pre-specified questions

Special cohorts of interest:

- Consumers with frequent heartburn (n = 197)

- Consumers who did not have frequent heartburn (n = 104)

- Low literacy consumers - 7<sup>th</sup>-8<sup>th</sup> grade reading level (n=154)

- Consumers with potential safety contraindications – interacting drugs, pregnant, breast feeding (n = 117)

# Label Comprehension Study: OTC Switch of Omeprazole for Heartburn

Q: You expect to have a very stressful day at work. You usually get heartburn on stressful days like this. You want to take Prilosec 1 to prevent your heartburn on this day. Thinking about this situation, when is the best time to take Prilosec 1?

Correct/Acceptable: 81% Incorrect: 19%

Objective: Drug does not work immediately – label must communicate this. Study result led to label refinement prior to further studies

# Label Comprehension Study: OTC Switch of Omeprazole for Heartburn

Q. You suffer from seizures and are taking a medicine called phenytoin to help control your seizures. You also routinely suffer from heartburn several times per week. You have just heard about this new product Prilosec 1 for the prevention and relief of heartburn. If you were the person described in this situation and you wanted to use Prilosec 1 to prevent or treat your heartburn, what would you do now?

90% correct or acceptable (would not use or would ask their doctor)

Objective: Need to avoid a potentially dangerous drug interaction.

# Label Comprehension Study: OTC Switch of Omeprazole for Heartburn

However, with a similar scenario with phenytoin replaced by Prozac which is NOT on the label >50% responded would not use of would ask their doctor

What are we measuring? Comprehension or universal tendency towards “safe” response in the testing scenario

# Does proposed label guide consumer behavior in the use of the OTC candidate?

**Self-selection and Actual Use Studies:** Clinical trials that determine how consumers would make decisions and use the drug in real-world OTC setting

Major endpoints are behaviors

- Will consumers appropriately self-select
- Will consumers self-manage the course of therapy

# Actual Use Studies: Design

- Core design elements:
  - Participants recruited through pseudo-marketing
  - Participants visit mock pharmacy to see product display, product packaging with proposed label
  - Consumer makes decision whether product appropriate for them and if they wish to purchase
  - Key demographic data collected after primary endpoint decision
  - Consumer may purchase product and use
  - May return to purchase additional product
  - Data collected on purchase, use and response to changes in condition during use
  - Minimize cuing or introduction of bias during data collection

# Orlistat for weight loss – key behaviors of interest

- Would orlistat be used with meals as required for efficacy?
- Would consumers exceed the maximal daily dose?
- Would consumers adhere to chronic therapy?
- Would consumers use a multi-vitamin as directed?
- Would drug interactions be avoided?
- Would non-overweight or young consumers abuse the weight loss product?

## ***Flow of research subjects in orlistat OTC actual use study***

**703 Subjects screened at sites**

*Eligibility assessed*

**681 Eligible subjects**

*Asked "...medicine is appropriate for you to use?"*

**543 Subjects respond "yes"**

*Asked "..like to purchase the medicine today"*

**339 Subjects respond "yes"**

**262 Subjects actually purchase**

**237 Subjects use and provide  
follow-up data**

# Orlistat for weight loss – key behaviors of interest

- Would orlistat be used with meals as required for efficacy? - *>95% used with meals*
- Would consumers exceed the maximal daily dose? - *< 3% exceeded the maximal label dose*
- Would consumers adhere to chronic therapy? – *46% of consumers still on orlistat after 90 days*

# Orlistat for weight loss – key behaviors of interest

- Would consumers use a multi-vitamin as directed? - *< 50% used a multivitamin per label*
- Would drug interactions be avoided? – *One of two participants on cyclosporine elected to use orlistat*
- Would non-overweight consumers abuse the weight loss product? – *8% BMI < 25*

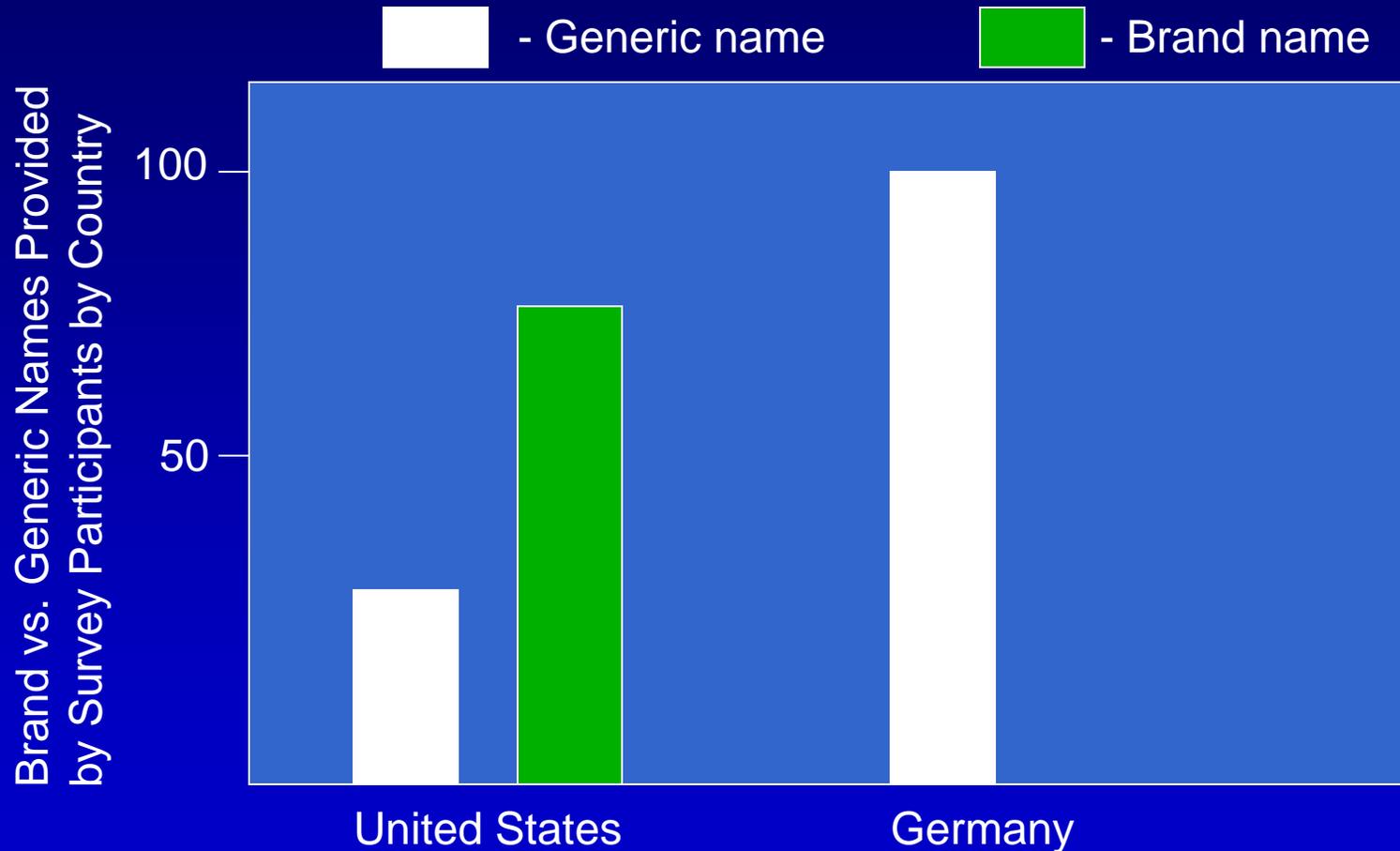
# Orlistat for weight loss – key behaviors of interest

- Would adolescents abuse the weight loss drug?
  - Consumers less than 18 years old excluded from main Actual Use Study
  - Addressing issues required a separate study focused on behavior of adolescents

# Can knowledge and attitudes of young consumers be modified?

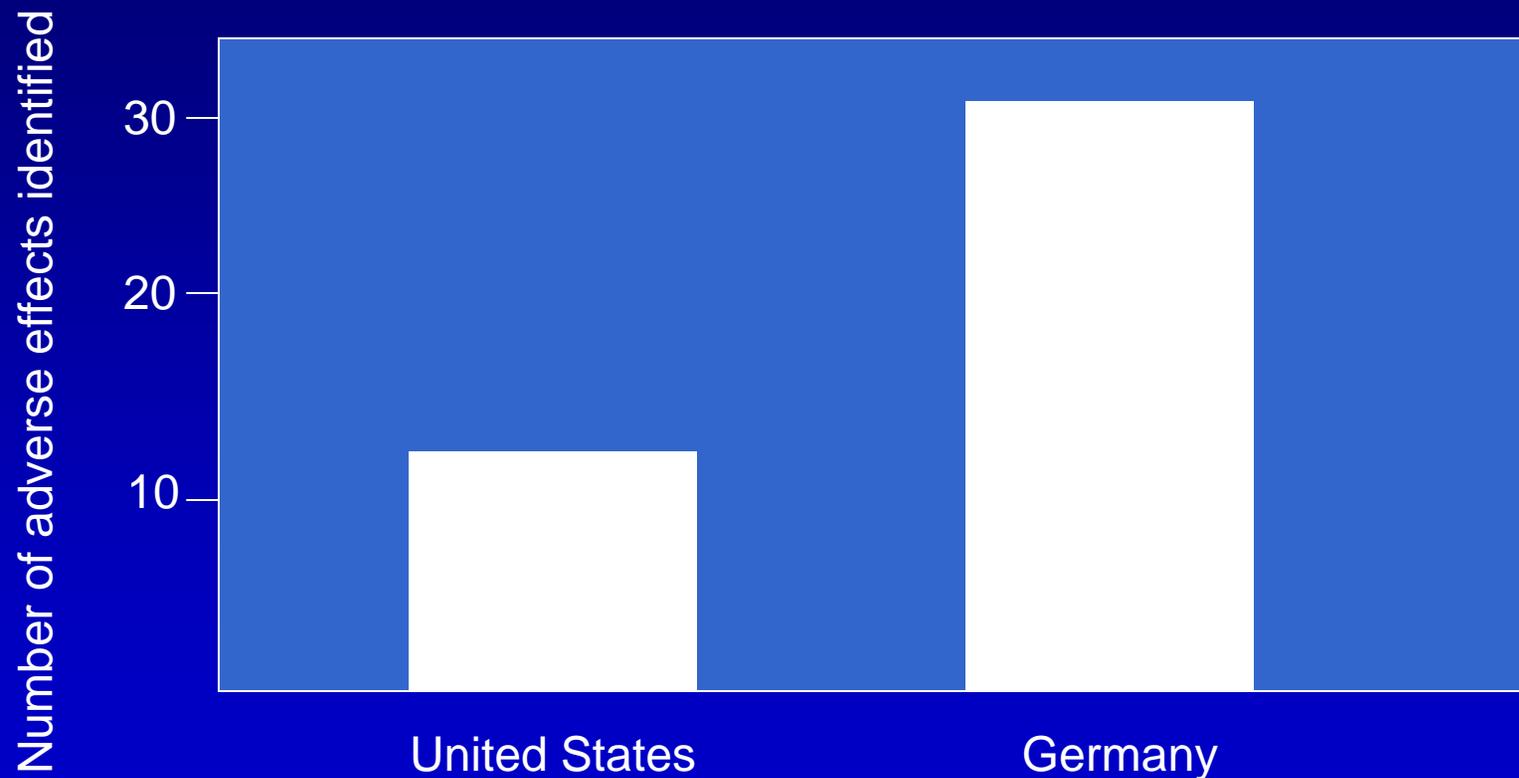
- Pilot study of college students in United States (n=58) and Germany (n=50) using survey
- Many limitations:
  - Non-random, non-representative convenience sample
  - Many factors may influence responses of the two cohorts

# How do consumers identify the analgesics they use?



*Hanoch et al Health Psychology 26:802, 2007*

# Are consumers familiar with adverse effects of OTC analgesics?



*Hanoch et al Health Psychology 26:802, 2007*

# Closing thoughts - Research status and needs

- Continued evolution of research methodologies for conduct of OTC trials
  - NDAC September 2006
    - Pre-specify objectives/hypotheses
    - Pre-define benchmarks of adequate comprehension/behavior rates
    - Robust statistical approaches
  - Specific questions about a specific switch necessitate specific trial designs
  - Concerns about a specific population require studying that population

# Closing thoughts - Research status and needs

- Need for validation by bridging to post-marketing research of OTC drugs
  - Are current trials predictive of behavior?
  - Identify types of non-heeding to design remediation
- Recognize influences not incorporated into trial design
  - Advertising
  - Peer pressure
  - Mis-information and rumors about a drug's effects

# Clinical research informs OTC regulatory decision making

