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## *Harm Reduction*

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Jack E. Henningfield  
Institute for Global Tobacco Control



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## *Section A*

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Harm Reduction

- Provide a product or behavior to someone in order to reduce the potential of causing harm
- Find a way to help people reduce death and disease

- Potential strategy to reduce death and disease with certain analogies to other medical practices, seatbelts, needle-exchange programs, condoms, and malaria control
- Potential indication for current and new drugs
- Currently “owned” by tobacco companies who seek to expand the claim and marketability

- Potential to undermine cessation and prevention
- Implies either a massive five- to ten-year effort or “fast-track” approaches relying upon surrogate markers and intense surveillance

- Toxicity of product
  
- Actual use
  - How is each unit used?
  - How much per day?
  - How many years?
  
- Toxin exposure could be greatly reduced per unit but could lead to more units and more toxins per day

- Toxin exposure could be reduced per day but could be accompanied by more years of use
- Thus, actual use may be more important in harm risk than product toxicity or exposure



KG4

Judith, do you think we can eliminate this slide?

Kathy Gresh, 10/13/2003

- Reduce tobacco attributable morbidity and mortality
  
- Strategies
  - Prevention of initiation of tobacco use
  - Treatment of existing and future users
  - Reduction of use and toxin exposure (PREPS)—  
modified tobacco products, cigarette substitutes,  
pharmaceutical-enabled reduction

- Industry owns tobacco product knowledge
  - Need pipeline of non-industry scientists
- Vector of disease spread (marketing) is difficult to control because of protected status of product
- No meaningful regulatory oversight to minimize toxicity or addictiveness

## *Due to Contaminated Drug Delivery Systems*

- Cigarettes—lung cancer, emphysema
- Smokeless tobacco—oral cancer due to “avoidable” nitrosamines
- Moonshine—lead contaminated alcohol
- Shared drug syringes—HIV and hepatitis

## *In the “Old” Days Things Were Relatively Simple*

- 90% of tobacco smoked as cigarettes
- Single product use dominant
- Major toxins documented
- Dose-response relationships between use and disease risk relatively well documented

- The line between smoked and smokeless is becoming the only easy one to draw . . .

## **Cigarettes:**

Unfiltered, Filtered Regular,  
Light, Ultralight

## **Engineered Cigarette Devices:**

Eclipse, Accord, Premier

## **Modified Cigarettes:**

Advance, Omni,  
Omni Free

## **Cigars and Pipes**

# Continuum of Products

## **Conventional SLT:**

Skoal, Copenhagen

## **Modified SLT:**

Stonewall

## **NRT:**

Nicorette, NicoDermCQ

## **Novel SLT:**

Exalt, Revel

## **Hard SLT:** Ariva

## **Quasi-NRT:**

Vasatek Vector nicotine gum

*The Virus Is Mutating—Is Tobacco Control Keeping Up?*

Eclipse

Lights

Exalt

Accord

Advance

Stonewall

Omni / Quest

Ariva

SCOR

Ariva — Higher Dose?

Revel

- Claim—1/3 usual nitrosamines, reduced risk
- A charcoal filter cigarette containing “Star-cured” low tobacco specific nitrosamines (TSNA) tobacco containing no stems (U.S. marketing since spring 2000)
- Dosing—full nicotine, lower CO, and other?
- Biomarkers—cigarette type but dose response relationships unknown



- Omni is a low TSNA, palladium filter cigarette—U.S. marketing Nov. 2001
- Claims—“reduced cancer causing chemicals,” “virtually free” of TSNA, and “significant reduction” of PAHs
- Dosing—new chemical cocktail (full nicotine, “reduced carcinogens?”)
- Questions
  - Addition of palladium, other substances?
  - Actual use?

# QUEST

*Step your way to Nicotine Free!*

- 1. Low nicotine*
- 2. Extra low nicotine*
- 3. Nicotine free*

- No addiction warning, no proven method of stepping down, no standard for “nicotine free,” no effort to prevent use for initiation, maintenance, or relapse, does not use “vaunted” Vector Omni “reduced toxin” technology . . .

## Quest “Nicotine Free!” (Vector)

- Uses transgenic “virtually nicotine free” tobacco (U.S. marketing planned 2003)
- Claims—“can help smokers quit” vs. “not for quitting” vs. “step your way to nicotine free”
- Guidance for reduction or cessation or how to minimize risks
- Dosing—low to moderate nicotine, other?
- Questions—safety “claims,” actual use, guidance for use

# The Best Choice for Smokers Who Worry about Their Health Is to Quit.

*Reduces secondhand  
smoke by 80%*

*... may present less  
risk of cancer*

## Here's The Next Best Choice.

*No messy ashes*



- Charcoal-tipped device made to look like a cigarette that volatilizes glycerin and nicotine, which the user inhales (marketed in U.S., Japan, Sweden, Germany)
- Claims—reduced delivery of toxins and reduced risk of cancer and lung disease
- Dosing—full nicotine, high CO, other?
- Biomarkers—nicotine, CO, acrolein, glass fibers, other, dose response?

- Hand-held computer chip based system that loaded with cigarette-like dosing cartridges (cartridges can't be used like cigarette and cigarettes can't be used in system)—test market in U.S. since 2000
- Claims—reduced toxins
- Dosing—full nicotine, reduced CO, and other chemicals?
- Biomarkers—nicotine, other, dose response?

- Hard tobacco/nicotine lozenge (cigarette) that is designed to dissolve in mouth (test marketed in the U.S., Nov. 2001)
- Claims—for when you can't smoke, reduced cancer causing chemicals?
- Dosing—1 mg nicotine, other
- Biomarkers—nicotine, other, dose response?

- Dry and moist snuff that is taken orally and made with Star Cured low nitrosamine tobacco (test marketed in U.S. Oct. 2001?)
- Claims—lower cancer causing nitrosamines than Skoal
- Dosing—full nicotine, other?
- Biomarkers—nicotine, other, dose response?



- Spitless, moist low TSNA snuff sachet that is placed between the lip and gum (test marketed in U.S. since mid-2001)
- Claims—"Gothiaterk" processed tobacco—low cancer causing chemicals, for when you can't smoke"
- Dosage—full nicotine, other?
- Biomarkers—nicotine, other, dose response?

# REVEL

Anytime. Anywhere.

Introducing Revel, a fresh new way to enjoy tobacco when you can't smoke.

New Revel – discreet, easy-to-use packs that contain a perfect blend of mild tobaccos and fresh mint flavor. Simply place one anywhere in your mouth where its comfortable, and enjoy full tobacco satisfaction that's yours and yours alone. Revel's cleaner and neater tobacco experience is available in two flavors – Regular and Mild.

# *Nicotine Lollipops, "Gummy Bears," and Lip Balm*

- Formulated in pharmacies to maximize the effect of cigarettes (i.e., the most addictive form of nicotine known)
- Flavored to be attractive, not just acceptable to motivated users (i.e., cherry, grape, root beer, tequila sunrise)
- Non-FDA approved nicotine forms (i.e., nicotine salicylate)

# *Nicotine Lollipops, "Gummy Bears," and Lip Balm*

- No scientifically developed guidance for how to use to maximize benefit and minimize risk—claimed quitting “as easy as having a lollipop!”
- Were sold by Internet and in drug stores 2001 until April 2002 when FDA banned the practice

## *Nicotine Water (from Ken Warner)*

- The goal of Nicotine Water is to give cigarette users an alternative source of nicotine that is free of the severe health risks of tar and smoke
- But what good is an alternative if it does not come in a form or taste that is appealing to the consumer?
- That is where Nicotine Water has no equal
- As a result of careful development and attention to detail, with Nicotine Water, all you will taste is the water

- Selective Constituent Reduction (SCOR)
- Anticipate profile with broader range of toxin reductions than Omni or Eclipse
- PM would be in the position of advocating its cigarettes as the new standard for FDA regulation and would be a step closer toward “owning” the market



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## *Section B*

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Implications for Standards and Regulations

- No standards for labeling, warnings, age restrictions, or special population restrictions
- No standards for directions for use to minimize adverse effects (e.g., overdose, use during pregnancy) or to maximize theoretical beneficial effects (e.g., reduce or quit smoking)
- No standards for other substances in product



- No requirements for pharmacokinetic studies to determine actual dosing capacity or determinants of bioavailability
- No standards for labeling dosing capability
- No standards for controlling inappropriate use

- No standards for minimizing appeal to youth, maximizing addictive sensory or pharmacological profile (e.g., the lollipop makers boasted of great taste and faster, stronger nicotine effects)
- No requirements for surveillance to detect and report harm

# *Multi-Product Use May Become Dominant*

- Preference for cigarettes
- Fear of cigarettes
- Products promoted for “dual” use
- Products designed for “dual” use
- Regulatory prohibitions against dual use nicotine replacement therapies (NRT) but not against new devices from tobacco companies

- Collateral damage not measured
  - Undermine prevention/cessation
  - Gateway to cigarettes and other drugs
  - Prevent treatment development
  - “Safe Harbor” for smokers
  - Promote relapse in former users
- Misleading reassurance by marketing focus

## *Science Needs to be the Supportive Companion of Regulation*

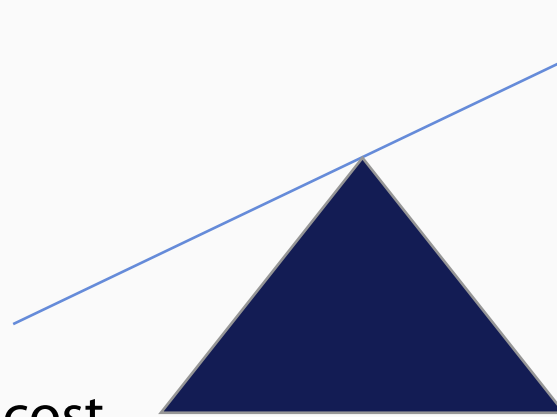
- The virus is mutating!
- Is our research keeping pace?
- Are regulatory efforts keeping pace?

- Present regulatory approaches foster the situation in which it is easy to develop and market tobacco products (and foster disease) and much more difficult to develop treatments and prevent disease

## Medicines

- Prior approval
- Proof for claims
- GMP
- Less access
- Higher purchase cost
- Low intrinsic appeal
- Low dependence potential by design

## Tobacco



## Regulatory Framework

- PREPS—Potential Reduced Risk Products
  - Modified tobacco (e.g., low nitrosamine)
  - Cigarette like (e.g., Eclipse)
  - Pharmaceutical (e.g., NRT to reduce smoking)
  
- Disease reduction through toxin reduction is plausible, viable, and should be encouraged BUT with [FDA] regulation as precondition



- Presently available NRT is safe and effective for cessation, not approved for reduction
- Presently marketed reduction tobacco products (e.g., lights and Eclipse) have not been proven to be less harmful

- Conventional tobacco products with actual reduced toxin delivery—unlike “light” cigs
- A new category of novel tobacco-based nicotine delivery devices (e.g., Eclipse, Accord)
- Pharmaceuticals (e.g., nicotine gum or bupropion) with exposure reduction indications
- Each raises challenges for clinical trials, regulation, and public health

- Decrease access to tobacco
- Decrease appeal of products
- Decrease exposure in users and nonusers
- Increase tobacco costs
- Reduce product toxicity
- Increase treatment access
- Regulate products

## *Public Health Challenge to Exposure Reduction Efforts*

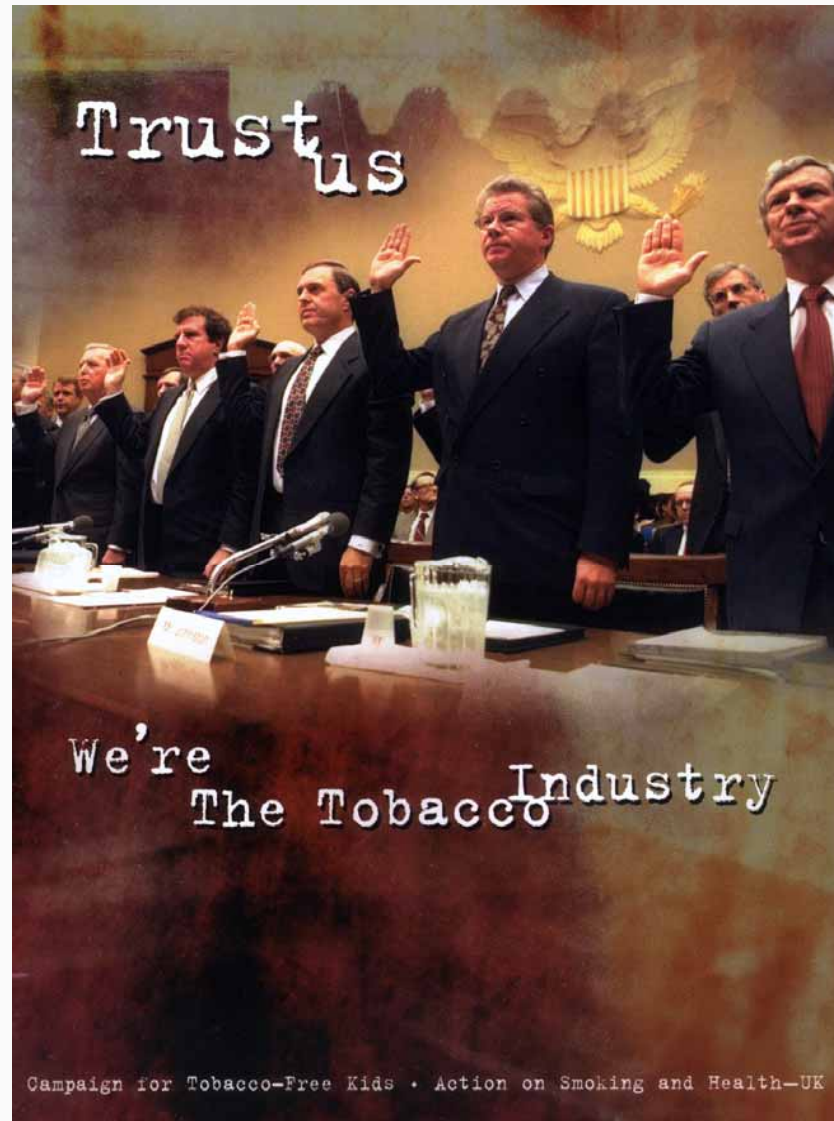
- Devise and implement strategies to reduce death and disease in continuing tobacco users WITHOUT undermining prevention and treatment efforts—otherwise the public health benefits from the reduction of risk in continuing users could be offset by increased prevalence

- "... [T]he effect of switching to low tar cigarettes may be to increase, not decrease, the risks of smoking."

- Products are more toxic and more addictive than need be
  - No standards for meaningful reductions exist but claims are made
- Products are marketed and advertised with claims that imply safety, yet are intended to keep people using tobacco, and effectively delay quitting—this is deadly

- New products are proliferating which push the bounds of tobacco products and which are making new claims to hook the young and keep users using

# Why Regulation Is Needed





# *Co-Regulation of Tobacco and Nicotine Medicines*

- A common standard for tobacco and drugs may not be possible due to the toxicity of tobacco products; however, co-regulation is critical to level the regulatory playing field between tobacco products and medications

## *Co-Regulation of Tobacco and Nicotine Medicines*

- If tobacco products make health claims (e.g., “light” or “reduced”), tobacco manufacturers should be held to the same standards of proof and monitoring as drug products
- FDA “full” regulation is essential

## *Considerations for Regulatory Strategies for Reduction*

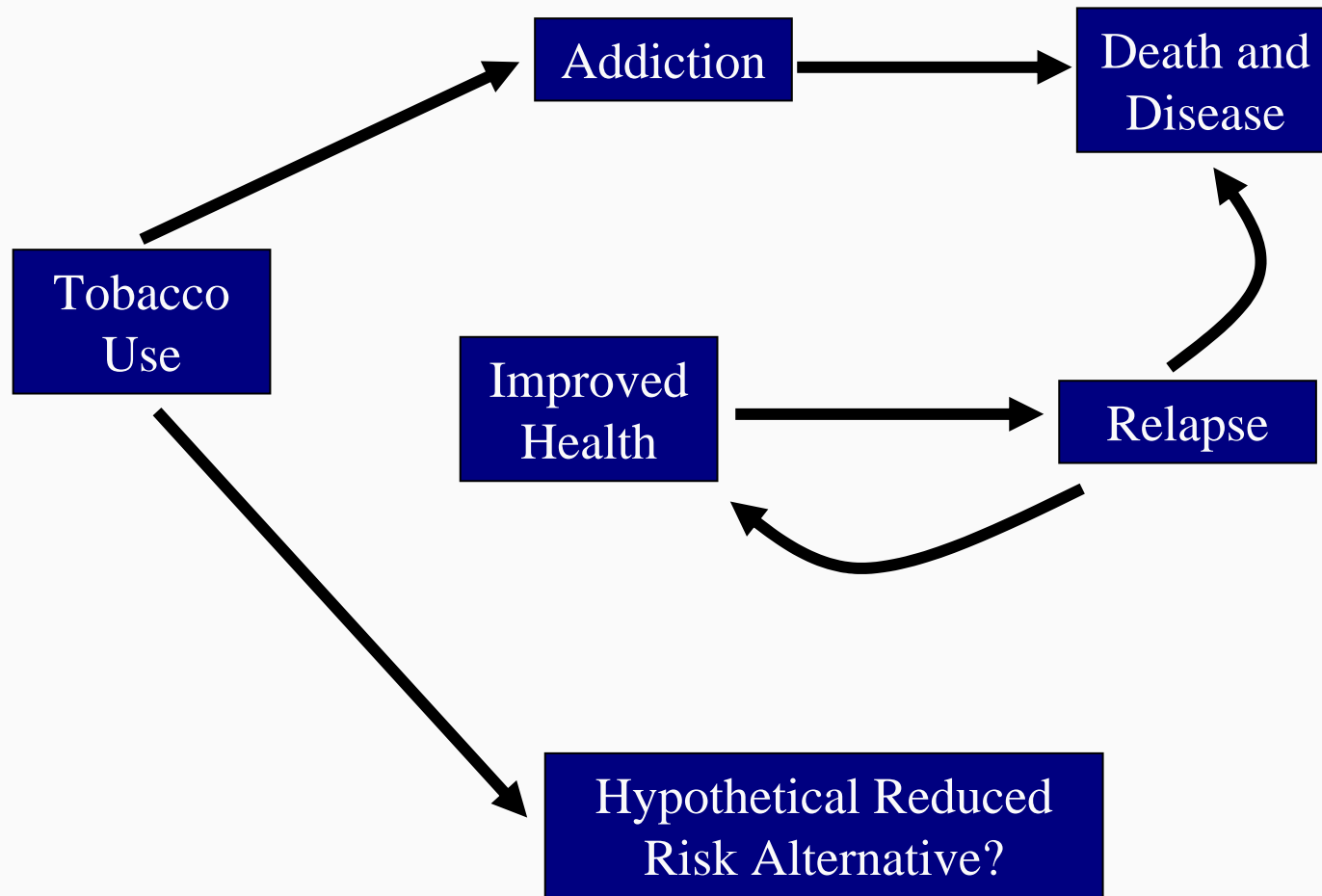
- Strategies should not undermine prevention of initiation (at any age)
- Strategies should not undermine cessation/treatment efforts
- Strategies should foster product labeling and innovations that reduce disease in continuing tobacco users

- Experience
  - Drug dosing measurement and communication
  - Toxicity measurement and communication
  - Addictive drug regulation experience
  - Marketing guidance
  - Precedents for regulatory actions
  
- Resources
  - Human
  - Fiscal

- With steps towards effective tobacco control
  - Most youth (including those who try tobacco) do not develop dependence
  - Adults increasingly attempt cessation and it appears that more than half of lifetime smokers will achieve non-tobacco using status

- If reduced risk tobacco products (or dual tobacco product use) leads to dependence in persons who would not have achieved dependence and perpetuates smoking in persons who would otherwise have quit, the reduced risk product might increase overall disease
- There is no validated means of predicting trajectory in individuals though various risk factors exist

# Trajectory of Tobacco Use



- Does it introduce a new chemical cocktail?
- Are toxins reduced in actual use?
- Are reduced concerns met with more units used per day?
- Is it designed to undermine cessation or prevention (e.g., by facilitating initiation)?
- Will marketing undermine prevention or cessation (e.g., by promoting dual use to enable continued smoking)?



- Are new claims introduced (e.g., nicotine free, reduced carcinogens, reduced nitrosamines)?
- Standards exist for terms such as “free,” “reduced,” and “light” for foods but none have been set for tobacco—should any such terms be allowed for tobacco products before standards are set?
- Could reduced concerns delay quitting?

- Decrease access to tobacco
- Decrease appeal of products
- Decrease exposure in users and nonusers
- Increase tobacco costs
- Reduce product toxicity
- Increase treatment access
- Regulate products