

# Tobacco use as an Exemplar of What can be Accomplished with Behavior Change: Challenges Ahead



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I consult to GlaxoSmithKline on smoking cessation and consult to other pharmaceutical companies on abuse liability, post marketing surveillance and risk management. I serve as an expert witness against the tobacco industry, and I share an interest in patents on a potential oral nicotine delivery system  
(University of VT Center on Behavior and Health Policy, Burlington, September 9, 2013)

# Congratulations Steve Higgins & UVT TEAM

## First Cohort FDA/NIH TCORS

*Funded by the Family Smoking Prevention  
And Tobacco Control Act*



# Joe Brady's Philosophy: *"Its All About Behavior"*

(Title of the 50<sup>th</sup> Anniversary IBR Conference, 2011)

- Behavior is the interface between tobacco and disease
- Altering tobacco products to reduce the number and quantity of toxicants measured by machines is relatively simple but easily undermined by how they are used
- The tobacco industry extensively researched product modifications to promote addiction and hence harm
- FDA Family Smoking Prevention and Tobacco Control Law & the WHO Framework Convention both include behavioral targets for research and policy, e.g., abuse liability, addiction, initiation, and cessation



What makes tobacco control such  
a complicated problem --  
on top of historical legacy, economic and  
political factors

It's the behavioral factors:

Addiction

Harm Reduction

Compensation

Initiation

Relapse

2<sup>nd</sup> Hand Smoke

Use patterns & rates

Ethnic differences

TOBACCO  
RELATED  
DEATHS



S I D E  
E F F E C T S

***“Smoke for nicotine –  
Die from smoke”***

***Michael A.H. Russell***

# Tobacco Caused Death & Disease:

Behavioral research from laboratory to population level is:

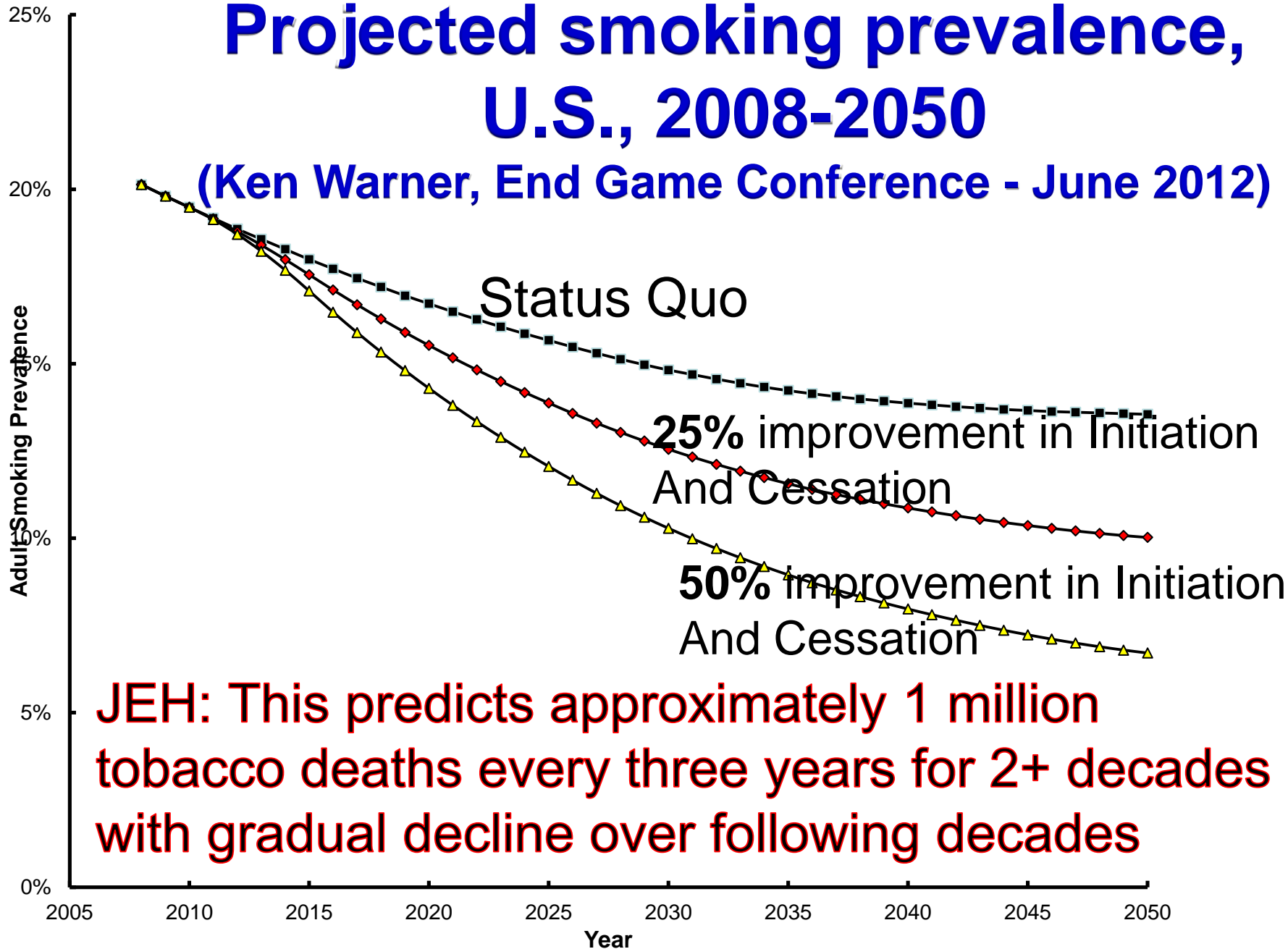
- (1) Helping understand the problem
- (2) Guiding policy formation and implementation
- (3) Guiding further research
- (4) Funded by Tobacco Control Act

Examples of Trends in Behavior  
and Challenges to Research,  
Regulation, and Policy that are  
behaviorally based



# Projected smoking prevalence, U.S., 2008-2050

(Ken Warner, End Game Conference - June 2012)

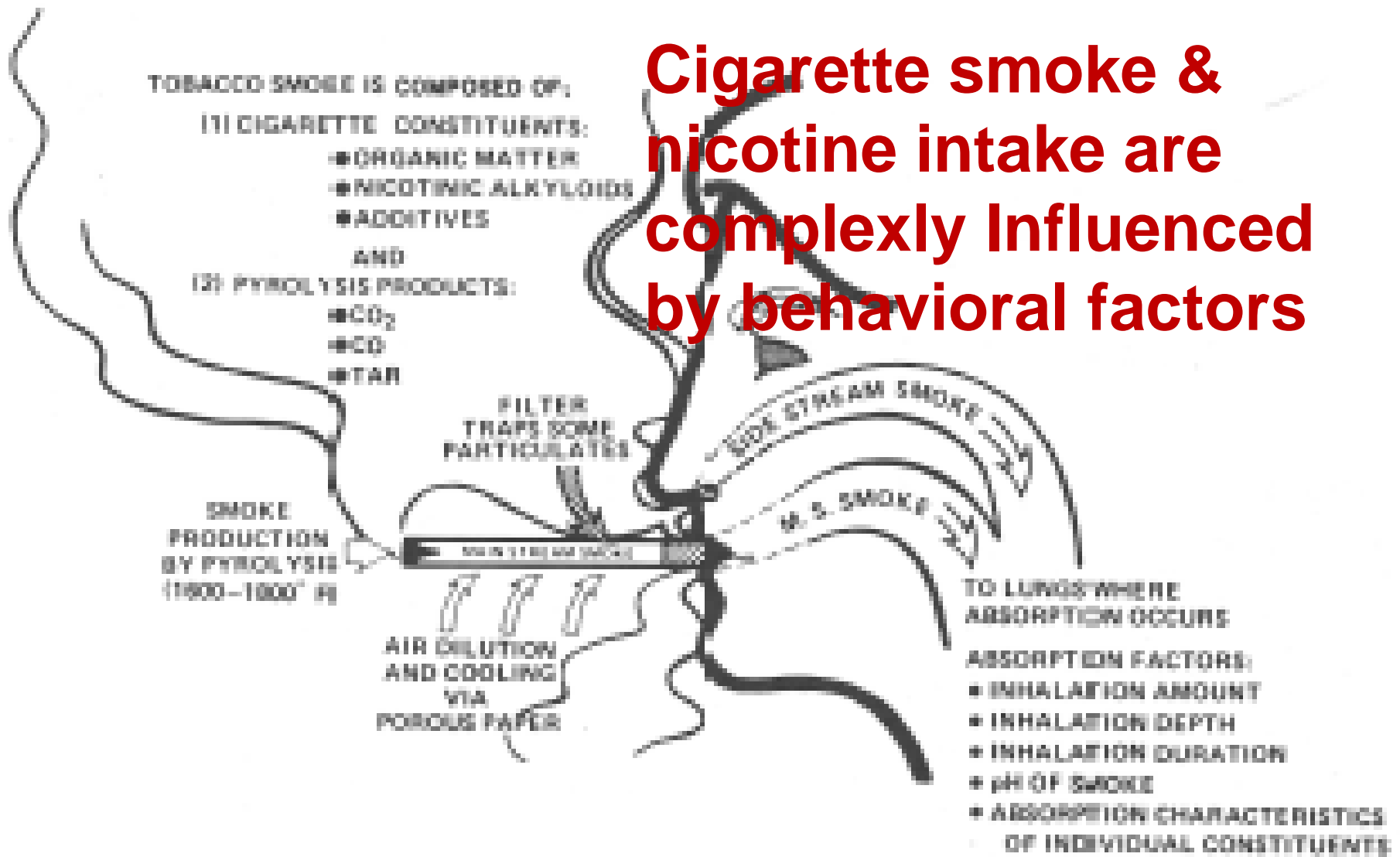


**JEH: This predicts approximately 1 million tobacco deaths every three years for 2+ decades with gradual decline over following decades**

# Many Special Population Challenges to Research and Policy



# Cigarette smoke & nicotine intake are complexly influenced by behavioral factors



**John Grabowsky, 1980s: “can’t have an APA Div 28 Mtg w/o this Slide”**

Henningfield, Behavioral Pharmacology of Cigarette Smoking in T. Thompson, P.B. Dews and J.E. Barrett (eds), *Advances in Behavioral Pharmacology*, 1984

# Brown & Williamson Internal Document, 1979

Low tar cigarettes--

“Provide smokers with a choice and a reason not to quit.”

*Filter ventilation: main Industry approach to “low tar” claims. It provides the ILLUSION of Low Tar & Nicotine while actually delivering full tar & nicoti*



# Filter Ventilation led to plummeting machine tested tar & nicotine since the 1960s while enabling full addictive nicotine dosing to cigarette smokers

- The tobacco Industry researched designs by the 1960s to promote larger, deeper puffs and allow finger blocking – NCI Mono 13 & Kozlowski et al: vents are a designed defect promoting high smoke intake, compensation, addiction and disease
- Ads: “you don’t need to give up satisfaction” [or tar & nicotine]
- Should vents be banned?



# Tobacco product A.L. diversely manipulated



## Additives

- Sugars
- Cocoa
- Acetaldehyde
- Ammonia
- Levulinic acid
- Menthol

## Airways & Lungs

- Smoke chemistry & particle size affect ease and depth of lung inhalation



## Sensory Stimuli

- Taste
- Smell
- Sight
- Feel

## Nicotine

- Dose
- Speed of delivery
  - Ammonia
  - pH
  - Ventilation

# FDA Tobacco Investigation And Litigation Discoveries & Implications

- From documents and insiders: The tobacco industry has been using many pharmacological and pharmaceutical techniques to *increase* addiction promoting effects (e.g., increasing inhalability of smoke)
- Control of nicotine dose and delivery speed are major addiction promoting design parameters
- If such parameters can be manipulated to increase addictiveness and addiction risk, they could also be constrained to reduce addictiveness

RECEPTORS



**Nicotine receptor modulation produces cascading effects via neurohormones**





**Increased receptors associated with tolerance and dependence**

# Consideration of Menthol Ban By FDA

## It's All About Behavior

### FDA TPSAC Report, 2011

- Overall Conclusions: (1) “adverse impact on public health” & (2) no public health benefits **ADDITIONALLY:**
- Menthol increases addiction in youth.
- Menthol lowers smoking cessation success in African Americans.
- Menthol increases experimentation and regular smoking... particularly in African Americans
- **DID NOT CONCLUDE THAT Menthol Smokers inhale more smoke or tobacco toxins**

# Electronic Nicotine Delivery Systems (ENDS), Smokeless Tobacco, Dissolving Strips, Oh My! The Promise and The Peril

- **Promise:** Progress toward “a future world where almost no one uses a combustible tobacco product” (Mitch Zeller and the Strategic Dialog, 2009)
- **Peril:** Delay cessation (“use when you can’t smoke”), encourage initiation, invite relapse, opened door to very successful mid 20<sup>th</sup> century tobacco marketing



Might ENDS and other noncombustible products contribute to mass migration from cigarettes?

Could such products (with appropriate regulation) make the idea of removing nicotine from cigarettes viable policy?



# FDA Regulation – by Law – Must Consider Key Behavioral Factors in Tobacco Product Regulation

- Will the new product or constituent:
  - -- increase or decrease initiation?
  - -- increase or decrease dependence [level or risk]?
  - -- increase or decrease cessation [difficulty or rates]?
  - -- must consider diverse populations and particular population risks [e.g., youth, pregnant women, ethnic minorities, etc.]

Spring, 1994: David Kessler asked Henningfield then Benowitz: What is the threshold for the addictive dose of nicotine in cigarettes? This led to:

- “Benningfield” Proposed limit nicotine to levels that would not be likely to cause and sustain addiction (NEJM, July 14, 2004: “*Establishing a Nicotine Dose Threshold for Addiction*”)
- And “*A Proposal to Develop Meaningful Labeling for Cigarettes*” by Henningfield, Kozlowski and Benowitz (JAMA, July 27, 2004)
- Aug. 3: FDA Drug Abuse Advisory Committee considered the proposal and concluded: *The theory makes sense but more research is needed on behavioral issues*

# Ron Davis, John Slade & AMA Endorsement 1998

## NIH, CDC and FDA now Researching Idea

- *Ron Davis, John Slade and others thought the idea merited consideration for implementation. AMA commissioned a report by Henningfield, Benowitz, John Slade, Tom Houston, Ron Davis and Scott Deitchman: Reducing the Addictiveness of Cigarettes, Tobacco Control, 1998.*
- *The AMA Council on Scientific Affairs, and the House of Delegates endorsed the main recommendations in 1998*
- *NIH, FDA and CDC are now developing the science base and considering potential public health approaches and behavioral endpoints impact*

# Reducing Addictiveness is not “All or Nothing”

As we consider Nicotine Reduction, we could reduce addiction promoting designs and ingredients

- Limit maximum nicotine contents and deliveries
- Prohibit sugar (#1 Marlboro additive) and other, flavorings and addiction promoting substances including menthol
- Prohibit ventilation holes that promote larger puffs and free-base nicotine formation, fool the body, AND may be blocked to drastically increase smoke intake

**It is not pie in the sky  
we can control the addiction  
promoting effects of opioids**



**stimulants, nicotine  
replacement products, and  
other CNS drugs**

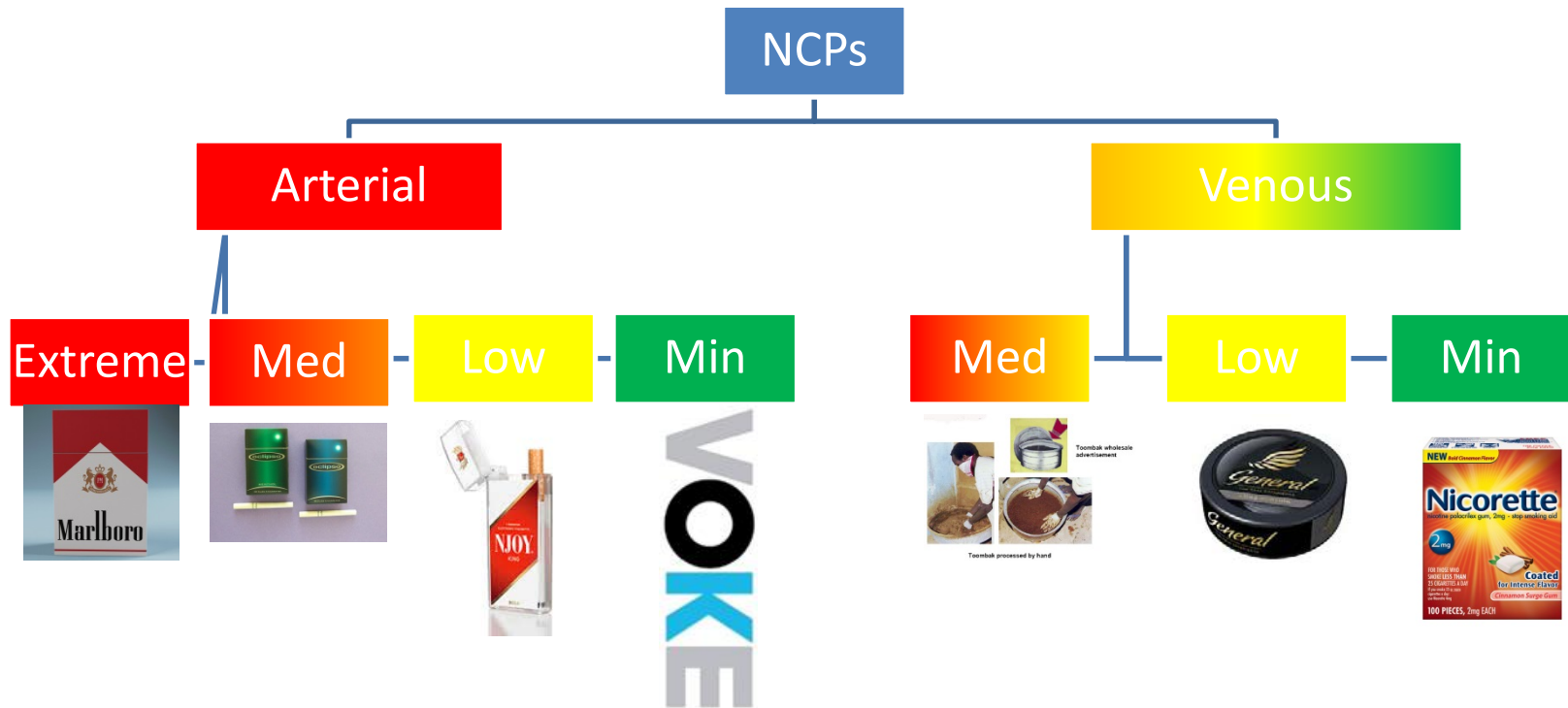
**We can do it for tobacco!**



FDA's goal for opioids & other addictive drugs:  
Drugs without "abuse deterrent" designs go the  
way of cars without seat belts and shatter-  
resistant windshields – An incremental process



# As we reduce tobacco product addictiveness we need to consider the place of potential “escape” products to manage behavior (Gitchell et al. Proposed Taxonomy)



# Fang by Fang

Reducing the addictiveness of cigarettes is like de-fanging an untamed killer beast fang by fang





*To good that  
to many  
of good*

# the KOOP de grâce



STATSKAL