EVALUATING POTENTIAL REDUCED-RISK TOBACCO PRODUCTS

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Purpose

The purpose of the Reduced Risk Review Project (RRRP) is to develop a science-based process to evaluate and assess the risk-reduction characteristics of potential reduced-risk tobacco products (PRRTP).

Goals

- Identify the scientific information needed to assess risk reduction
- Establish criteria to evaluate the scientific information, including specification of comparison benchmarks
- Define a process to review the scientific information

Context

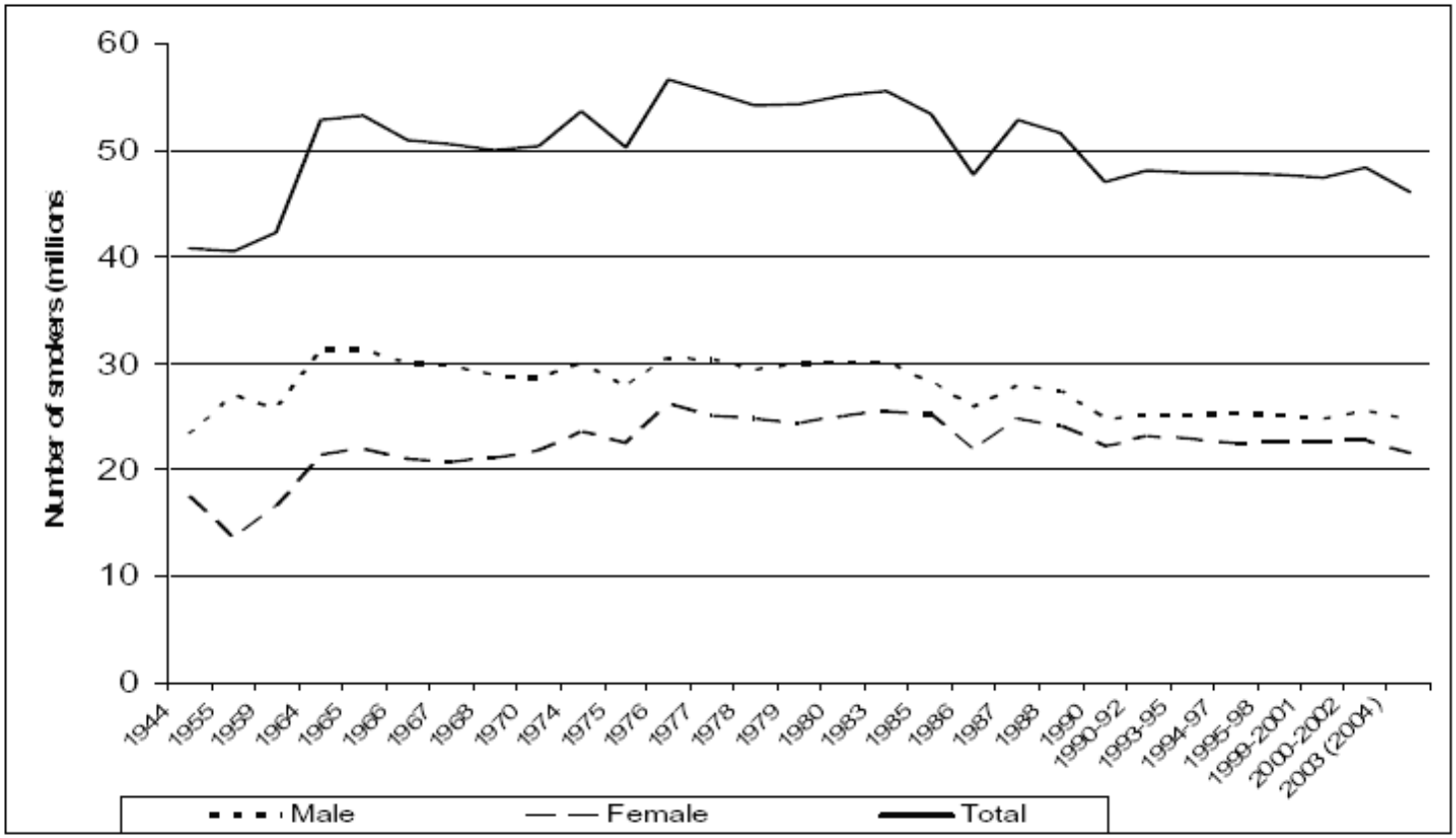
- *Public health*: Cigarette smoking is the number one preventable cause of death and disease in the United States. One out of every five adults smokes cigarettes.

Context

- *Public policy*: Reducing adverse health impacts in smokers who will not or can not abstain from the use of tobacco products through the use of reduced-risk tobacco products is highly controversial.

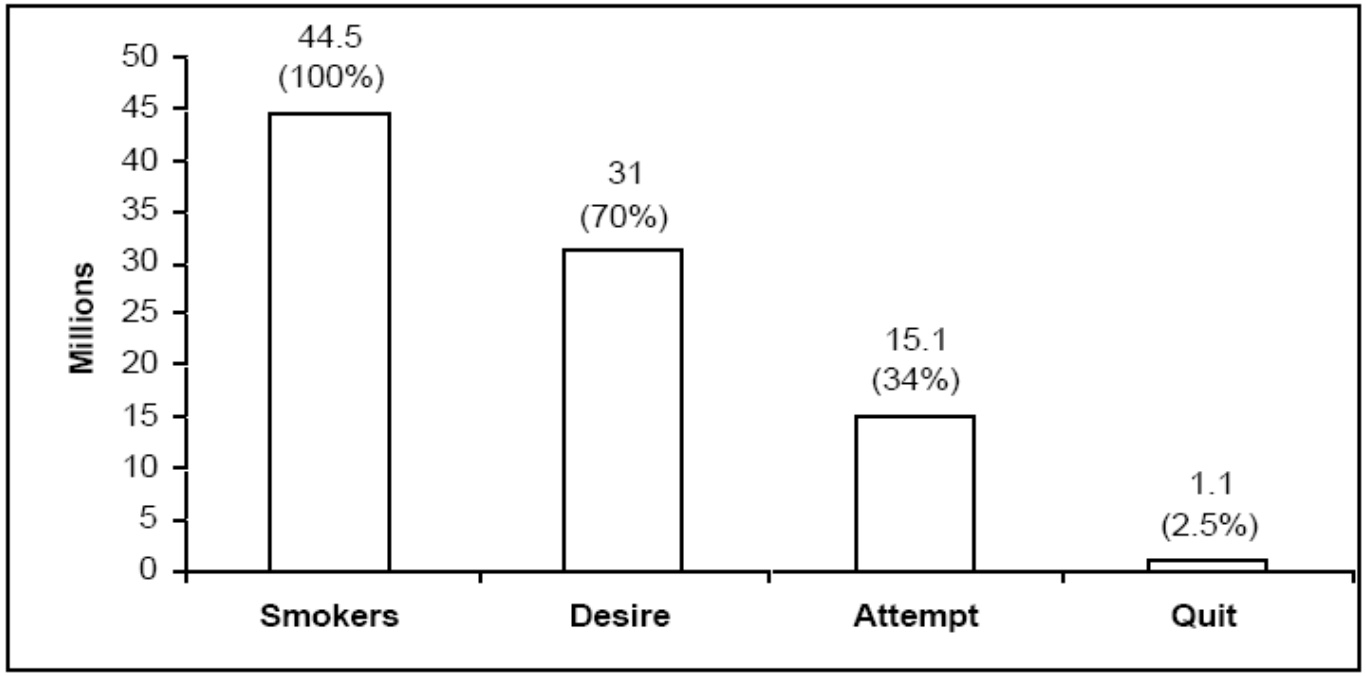
Trends in Smoking

Figure 1. Number of U.S. Smokers (1944-2004)



Cessation Statistics

Figure 2. Cessation Statistics



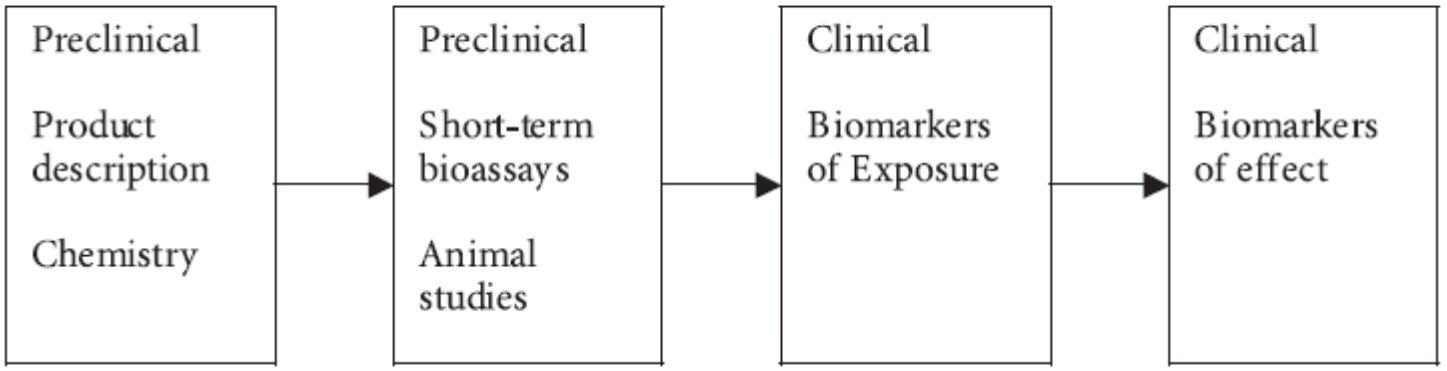
[2] Defined as abstinence from smoking of at least six months (Stead & Lancaster, 2005a; Stead & Lancaster, 2005b).

Tobacco Control Concerns

- Distrust of the industry coupled with the absence of comprehensive regulatory oversight
- Scientific uncertainty
- Adverse population effects
- Detracts from abstinence message

Testing Sequence

Figure 3: Testing Sequence



Hatsukami *et al.*

- Chemistry: identify toxins in product and smoke; machine-generated smoke chemistry yields
- Preclinical: Cell culture studies, preclinical animal trials of exposure to product and toxins

Hatsukami *et al.*

- Comprehensive clinical trials for exposure reduction, patterns of use, health effects (biomarkers relevant to carcinogen uptake, cardiovascular and lung function using comprehensive panel of biomarkers)
- Studies of consumer perceptions, market research on consumer perceptions

Differences

- Abuse liability testing
- Potential population effects: behavioral studies, surveys, and evaluation of marketing and advertising messages (to assess perceptions and demand for product)

Clearing the Smoke

The inherent tension facing the scientific and public health communities—

There is an urgent need to evaluate products/claims, but the science base is incomplete.

Risk Assessment

- Risk assessment methods are used to guide public health policy decision making when the science base is incomplete and/or uncertain
- Use of a risk assessment approach for the evaluation of PRRTPs provides a framework for the systematic evaluation of scientific evidence and uncertainties

Science and Judgment in Risk Assessment

Uncertainties are addressed by

- Scientific assumptions (based on what is most likely to be correct)
- Risk assessment policy (insufficient information to develop a ‘best guess’ so most health-protective scientific assumption is used)

Examples of Information Gaps

Information Gap	Assumption
The relationship between exposure to specific smoke constituents and development of disease has not been established	Reduction in one or more toxicants may indicate the potential for reduced exposure and reduced risk of disease

Examples of Information Gaps

Information gap	Assumption
Currently available animal models are limited in their relevance to human disease	Evidence of reduced toxicity in animals is an indication that adverse effects in humans may be reduced

Examples of Information Gaps

Information gap	Assumption
The degree of exposure reduction needed to reduce disease risk has not been established	As exposure is reduced, risk is also likely to be reduced

Examples of Information Gaps

Information gap	Assumption
The role of currently available biomarkers of effect in the development of disease has not been established	Biomarkers of effect are acceptable indicators of biological processes associated with the development of disease

Science and Judgment in Risk Assessment

- Clarity and credibility of a risk assessment are significantly increased when scientific facts (actual data) are clearly distinguished from assumptions based on ‘best guess’ or ‘most health-conservative’

Research and Risk Assessment Elements

Preclinical: Short-term biological assays; animal studies	**Biological Effects Assessment (BEA):** What is the evidence that use of the PRRTP instead of conventional cigarettes results in biological changes that indicate reduced risk?
Clinical: Biomarkers of effect studies	

Research and Risk Assessment Elements

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Weight of Evidence

- A process that assigns levels of importance (“weights) to evidence based on a number of factors such as type of study, quality of study, relevance to outcome of interest
- Sequence of testing coincides with increasing weight

Sufficiency of Evidence

Source	Claim	Evidence Required
Hatsukami and Hecht, 2005	Reduced exposure	Clinical trials of toxin exposure, patterns of use
	[Reduced toxicity]	Clinical trials of health effects of toxicity and abuse liability studies
	Reduced harm	Post marketing testing, longitudinal studies, epidemiologic studies

Sufficiency of Evidence

Source	Claim	Evidence Required
IOM, 2001	Reduced exposure	Consistent finding of reduced exposure in human biomarker studies and evidence of reduced toxicity in clinical studies
	Reduced risk	Consistently reduced toxicity/biomarkers of potential harm and decreased abuse liability
	Reduced harm	Epidemiologic studies show reduced disease incidence/mortality

Sufficiency of Evidence

Source	Claim	Evidence Required
WHO, 2003	Smoke composition	Emissions data
	Reduced exposure	Adequate studies in fully characterized subpopulations
	Reduced risk potential	Measures of injury using validated biomarkers show reduced toxicity; measures of addiction potential show no increase
	Reduced harm	Epidemiologic studies show reduced disease incidence/mortality

Sufficiency of Evidence

Source	Claim	Evidence Required
Philip Morris USA	Reduced exposure	Human biomarker studies show consistent reduction
	Reduced risk	Human health effect biomarkers show reduction
	Reduced harm	Epidemiologic data show reduced harm

Decision Making: Science + Policy

- “Science” is the PRRTP risk assessment describing the relative risk of the PRRTP compared to conventional cigarettes
- “Policy” includes all other relevant considerations, e.g. regulatory/legal, ethical, social, economic, political…

Framing the Decision

- Is the scientific evidence sufficient to conclude that a PRRTP is likely to reduce risk?

The focus is on relative risk and the potential to reduce risk of disease in smokers who cannot or will not quit(continuing smokers)

Framing the Decision

- <u>Is the evidence sufficient to conclude that a PRRTP is safe?</u>
  - The focus is on safety (definition? benefits outweigh risks?) not relative risk
  - Because tobacco products are known to cause certain diseases, a PRRTP will never be deemed to be ‘safe’
  - This focus is a deal breaker

Framing the Decision

- Will the use of a PRRTP contribute to or detract from abstinence from tobacco use/nicotine addiction?
  - Also a deal breaker
  - CSH observation—Many tobacco control professionals reject any form of harm reduction including PRRTPs and NRTs on this basis

Framing the Decision

- Is there sufficient evidence to conclude that population risk will not increase due to the availability of a PRRTP?
  - Also a deal breaker
  - Scientific methods to assess potential population impacts are woefully inadequate (pre- and postmarketing)

Smokeless Tobacco (ST)

Scientific consensus: Smokeless tobacco (of the type used in Western cultures) has been demonstrated to be a reduced-harm tobacco product. Evidence for significant reductions in harm is strongest for low-nitrosamine products such as snus.

ST and WHO

- There is no evidence to recommend that any smokeless tobacco product should be used as part of a harm reduction strategy
- The designation of ST as harm-reducing agents may promote a false perception of safety. Risk reduction is achieved by reducing smoking incidence and not substituting another form of tobacco use.

ST and the Surgeon General

- The SG cannot recommend as a quitting aid the use of a product that causes disease and death
- We do not have enough scientific evidence to endorse any tobacco product, including ST, as a means of reducing the risks of cigarette smoking
- At this time, ST cannot be recommended as a safer substitute for smoking—to do so would be premature and dangerous

Summary

- Scientific approaches recommended to assess PRRTPs are generally consistent
- The devil is in the details—we believe that the LSRO report will provide sufficient detail to stimulate scientific dialogue
- TC/PH opposition to marketing reduced-risk tobacco products (with claims) in the absence of gov't regulation is especially strong