

# Burning Issues

Tobacco's Hottest Topics Online



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## Burning Issues

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University of California  
Office of the President  
300 Lakeside Drive, 6th FL.  
Oakland, CA 94612-3550  
Phone: (510) 987-9870  
Fax: (510) 835-4740  
e-mail: trdrp@ucop.edu  
www.trdrp.org

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## Message from the Editor



### *A Sacrificial Lamb?*

Colleagues,

#### *Menthol Moves Center Stage*

In this edition, Burning Issues zeroes in on Menthol. In the lead article we examine the significance of menthol for African American smokers, the uproar surrounding the exemption given to menthol initially in the proposed FDA oversight legislation and the nationwide fight and outcry that culminated in menthol moving to the top of the FDA's agenda.

#### *Health Hazards of Chewing Acera Nut, Betel-Quid and Gutkha, part-2*

In the first part of this article Drs. Asotra and Sharan discussed the history and explained the use of areca nut in India and other parts of Asia. The first article also discussed the good pharmacological properties associated with this substance, whether as a digestive aid, or for relief from headaches and arthritis. On the other hand, in this second installment, the ugly side of areca nut use and addiction is explored.

#### *TRDRP: Still Relevant after 20 years*

Interim Director George Lemp looks back over the 20 years of TRDRP's existence and highlights some of our accomplishments and identifies that even though there have been bumps in the road, the future is bright for tobacco related disease research in California.

**Major Changes to TRDRP award mechanism**

This short announcement by the TRDRP Senior Staff is just one of many reminders of the changes to TRDRP award mechanisms; we have dropped our Research Awards and IDEA Awards and replaced them with Exploratory and Developmental Awards and California specific Awards.

*Phillip Gardiner, Dr.P.H.  
Editor*

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## Menthol Moves Center Stage



### *A Sacrificial Lamb?*

By: Phil Gardiner, Dr. P.H.

**O**n a vote of 326 to 102, the United States House of Representatives voted overwhelmingly to pass the Waxman/Warner bill (HR 1108) and give the Food and Drug Administration (FDA) authority to regulate tobacco products. At the same time, the original language, which had exempted menthol from the list of prohibited additives, was modified to mandate that an FDA scientific advisory committee study the effects of menthol flavoring and issue a recommendation within one year. FDA also would have to produce an action plan on the advertising and promotion of menthol and other cigarettes to young people, particularly those in minority communities (1). Behind this last-minute change is a series of developments that propelled menthol, in the course of a two-month period, to the center of the national debate around FDA regulation. Below, we explore why menthol is an issue, what happened to make it a national issue and what is the road ahead.

### **Menthol: The African American Cigarette of 'choice'**

Why is menthol an issue? Mentholated cigarettes comprise about 25% of the overall tobacco market, making it by far the leading additive marketed in cigarettes and other tobacco products (2). Menthol, when added to tobacco masks the harshness of the tobacco smoke, and many scientists speculate that this allows for the deeper inhalation of the poisonous products in cigarette smoke (3). Not only is menthol a mild

analgesic, but functions as a bronchodilator, expanding the airways to the lungs to ensure the maximum entry of tobacco smoke (4). It should be noted that all cigarette and tobacco products have menthol in them, 0.003% for non-mentholated cigarettes; 0.1 - 0.45% for mentholated smokes (5). This is also true of pipe tobacco and “roll your own” tobacco. And while these scientific facts are salient in and of themselves, it is the politics of menthol that has made it an issue.

Overwhelmingly, menthol cigarettes are the brand of choice of African Americans. And this choice was created by the tobacco industry itself.

“Today, over 70% of African American smokers prefer menthol cigarettes, compared with 30% of White smokers. This unique social phenomenon was principally occasioned by the tobacco industry’s masterful manipulation of the burgeoning Black, urban, segregated, consumer market in the 1960s. Through the use of television and other advertising media, coupled with culturally tailored images and messages, the tobacco industry ”African-Americanized” menthol cigarettes. The tobacco industry successfully positioned mentholated products, especially Kool, as young, hip, new, and healthy. During the time that menthols were gaining a large market share in the African American community, the tobacco industry donated funds to African American organizations hoping to blunt the attack on their products. . . .Unfortunately, the long-term impact of the industry’s practice in this community may be partly responsible for the disproportionately high tobacco-related disease and mortality among African Americans generally and African American males in particular” (6).

*The disproportionately high mortality from tobacco related diseases was captured succinctly in the 1998 Report of the Surgeon General (7):*  
(CHD = Coronary Heart Disease; CVD = Cerebrovascular Disease)

Age Adjusted Death Rates per 100,000 (Males, 1992-1994) (RSG, 1998)					
	AA	AIAN	AAPI	W	Hispanic
Oral Cancer	7.7	2.6	3.3	3.0	2.4
Esophagus	11.4	3.2	2.7	4.4	2.8
Lung Cancer	81.6	33.5	27.9	54.9	23.1
CHD	138.3	100.4	71.7	132.5	82.7
CVD	53.1	23.9	29.3	26.3	22.7

Across the board, African Americans are dying at disproportionate rates from tobacco related diseases compared to other racial and ethnic groups. Let’s be clear, even though these figures are from a decade ago, the situation has not changed one bit. American Cancer Society data from 2007 shows the same disparity (8):

## Age Adjusted Mortality Rates

(All sites and Lung)  
per 100,000 (Females and Males, ACS 2007)

	AA	AIAN	AAPI	Whites	Hispanic
All Sites					
M	331.0	153.4	144.9	239.2	166.4
F	192.4	111.6	98.8	163.4	108.8
Lung Cancer					
M	98.4	42.9	38.8	73.8	37.2
F	39.8	27.0	18.8	42.0	14.7

Today, even though Kool has receded in prominence and Newport has ascended as the main menthol brand, still African Americans disproportionately smoke menthols. Here in lies the politics of the question. The tobacco industry does not want to potentially disrupt African American consumption of its product by agreeing to remove menthol from cigarettes. And with the organized African American tobacco-control and research community not being part of the negotiations on FDA oversight, this issue was not central to the deliberations. However, in a series of unexpected and stunning developments, menthol not only made the front pages of the leading papers around the country, but became a discussion on the floor of the House of Representatives.

### The Gathering Storm

The harbinger that menthol was on the national agenda was a May 13th article on the front page of The New York Times: “Cigarette Bill Treats Menthol with Leniency” (9). Stephanie Saul’s article, in which she interviewed key members of the African American tobacco-control movement, exposed for the first time this burning issue to a larger public that menthol was getting a free pass. Unlike cloves, cinnamon, etc, being banned, which MF Bowen reported on in a previous Burning Issues article, *FDA at the Crossroads*, menthol would be exempt (10). Make no mistake, the tobacco industry understood full well why they wanted menthol exempt: Menthol cigarettes are by far the most popular cigarettes among African Americans. To outlaw the use of this additive would seriously undermined big-tobacco market share among this key tobacco-consuming group.

Robert G. Robinson captured the matter succinctly: “I think we can say definitively that menthol induces smoking in the African-American community and subsequently serves as a direct link to African-American death and disease,” said Robinson, who retired two years ago as an associate director in the Office on Smoking and Health at the Centers for Disease Control and Prevention (CDC) (9).

Following *The New York Times’* article, a flurry of activity surrounded this issue, much of it spearheaded by the National African American Tobacco Network and its Executive Director Bill Robinson. One result was an unprecedented move by seven former U.S. Secretaries of Health, Education, and Welfare to pen an open letter to the Congress, strongly urging the Senators and House members to ban menthol from cigarettes (11). Some of the language was quite pointed, and I quote it at length:

“The bill bans the use of all artificial or natural flavors in cigarettes—except menthol. Since menthol is by far the most popular “flavor” for cigarettes, that’s a loophole big enough for a herd of wild animals to romp through and trample the health of African Americans.”



“ . . . by failing to ban menthol, the bill caves to the financial interests of tobacco companies and discriminates against African Americans—the segment of our population at greatest risk for the killing and crippling smoking-related diseases. It sends a message that African American youngsters are valued less than white youngsters.

“To make the pending tobacco legislation truly effective, menthol cigarettes should be treated the same as other flavored cigarettes. Menthol should be banned so that it no longer serves as a product the tobacco companies can use to lure African American children.

“We do everything we can to protect our children in America, especially our white children. It’s time to do the same for all children.”

This letter really got the ball rolling and forced the hand of the Congressional Black Caucus (CBC). By late June, representatives of the 43 members CBC along with Louis Sullivan and Joseph Califano were in negotiations with Representative Waxman to alter the FDA oversight bill to include language that would give the FDA authority to ban menthol (11). Clearly, not all in the CBC were for not exempting menthol, but evidently those favoring a ban won the day.

Independent of the political struggle in Washington, Harvard researchers, publishing in the *American Journal of Public Health*, documented that the tobacco industry has been manipulating the dose of menthol in cigarettes to ensure the uptake and continued use, especially by the young people and other vulnerable populations for many years (12).

Taken together the national news coverage; the letter from the seven former Secretaries’ of Health; the work of the NAATN; the involvement of the Congressional Black Caucus; and the release of the Harvard study forced a major amendment to the FDA oversight Bill.

### **The Next Step**

Many would argue that a menthol ban should have been part of the legislation from the beginning. African American tobacco-control activists have asserted that since Black people were not at the negotiating table, this issue did not move to the center of discussions. On the other hand, the Campaign for Tobacco Free Kids, one of the main tobacco-control proponents at the table with Philip Morris, felt that the tobacco industry would back away from any deal for FDA oversight that included a ban on menthol in cigarettes and other tobacco products. In any event, the compromise brokered on Capital Hill sets the agenda for all players on this issue in the immediate next period.

As was stated at the outset, whether the Bill passes the Senate this session or next and assuming House and Senate conferees leave the compromise in place, it will mean that tobacco control activists will have at least a year to get menthol banned from cigarettes. Who will make up the FDA scientific advisory committee is still to be determined. The political gamesmanship exhibited by the letters from the past Secretaries of Health will have to be repeated several-fold to ensure that the issue of menthol remains an important and controversial topic.

Tobacco researchers and advocates have already set their sights on a national conference to summarize the scientific and the political issues surrounding this thorny topic. Preparations are underway to convene this gathering at Howard University in Washington D.C. in the fall of 2009. It was felt that holding such a gathering at a historic Black college campus was appropriate, given the disproportionate carnage faced by African American from tobacco-related diseases.

The next few years will be crucial in determining the use of menthol in cigarettes in the United States. The conclusion to this story is not yet written; we can all play a role in determining the outcome.

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## Health Hazards of Chewing Areca Nut, Betel-Quid, and Gutkha (Part 2)

*This is the second part of a two part article that the authors prepared for Burning Issues. The addictive practices of people world wide often do and don't include tobacco products. With the steady growth of peoples from the Indian sub-continent and other parts of the world, it behooves tobacco control researchers and advocates to familiarize themselves with their tobacco and other addictive practices. (PG) [part #1](#)*

*By Kamlesh Asotra, Ph.D and Rajesh N. Sharan, Ph.D.*

### **The Bad...**

Habitual and regular chewing of betel nut produces several adverse effects on the oral and upper digestive tract, including inflammation and development of white or gray patch on the tongue and inside of cheeks (leukoplakia), fibrosis, and oral cancers. Frequent use turns the lips red and the mouth and teeth black. Betel leaf contains large proportion of a carcinogen Safrole, which is readily metabolized and excreted in urine as dihydroxychavicol and eugenol (17). Safrole used to be the ingredient in original root beer; because of its cancer-causing properties, the formula for root beer was later reformulated without this key flavor ingredient.

Areca nut contains cancer-causing alkaloids (0.25% of sun-dried Areca nut by weight), predominantly arecoline (0.15%) and Arecaidine (0.10%) and trace amounts of guvacine, guvacoline, and arecolinidine. Arecaidine is reportedly more toxic than arecoline, but both have similar pharmacokinetic properties (17). When oxidized in the presence of lime, the compounds extracted by chewing of Areca nut give a characteristic red coloration to saliva, teeth, tongue, and lips. Gallotannic acid is the predominant tannin in betel nut, with minor components as gallic acid, D-catechol, and phioatannin. The Areca alkaloids are cholinergic agonists, which affect the nervous system's functions via acetylcholine and result in a stimulant action that increases capacity to work and has euphoric effects with heightened alertness. Arecoline, a mildly toxic agent, interacts preferentially with the muscarinic receptors, rather than the nicotinic receptors that mediate the action of nicotine. If excessive amounts of betel nut are used, the symptoms of Amanita poisoning occur such as intense discharges, including production of saliva, tears, sweat, diarrhea, vomiting, and stomach cramps. Urinary incontinence, fever, flushing, confusion, difficulty in walking, memory lapse, and anxiety may also result from intake of large quantities of Areca nut. Metabolomic technologies have recently been developed to identify the metabolic products of Areca nut alkaloids Arecaidine and arecoline in urine samples of animals, and soon this technology may be useful in human studies (18).

Heavy use of Areca nut produces a wide spectrum of adverse health effects including cardiovascular disease (19, 20), heart attacks (21), arrhythmia (22), metabolic syndrome (23), and diabetes (24, 25).

### **...and the Ugly**

Areca nut and betel-quin chewing leads to oral submucous fibrosis (OSF)— a painful, disabling and potentially precancerous condition of the oral mucosa (Figure 4). The elasticity of the inner lining of the



cheeks and mouth becomes reduced, and fibrous bands develop in people who chew Areca nut, betel-quin, paan masala, gutkha, and tobacco (26, 27). If not diagnosed and treated early, OSF can lead to dysplasia and oral squamous cell carcinoma. Oral cancer represents only 2–4% of the malignancies in the Western world, but accounts for nearly 40% of all cancers in the Indian subcontinent (28, 29).

The carcinogenic agents in the betel quid are thought to be at least three of the constituents: arecoline, Arecaidine, and safrole. Arecoline and Arecaidine from the Areca nut may be promoters for other carcinogens (especially the N-nitroso compounds with which they can combine); the Areca alkaloids also contribute to changes in the oral mucosa that lead to the detrimental oral effects, including oral cancer.



*Figure 4. Left panel: Oral submucous fibrosis of the lower lip in a patient. Notice the white coloration of the affected area. Right panel: Toluidine blue stained area showing dysplasia of the lower lip and dark-stained teeth because of betel-quin chewing. (Courtesy, Mehrotra et al., 2006; reference 29).*

Some studies suggest that the combined use of betel-quin with tobacco and tobacco-containing gutkha is much more damaging to the chewer's health, perhaps because of greater combinatorial dose of nitrosamines from Areca nut and tobacco. However, the absence of tobacco in the Taiwanese quids helps avoid the objection that it is inclusion of tobacco in the chewing material that is causing oral cancers. In addition, it is suspected, though not proven, that regular chewing of betel nut also increases the occurrence of other cancers besides those of the mouth.

#### Cytotoxic, Genotoxic, Mutagenic, and Teratogenic Effects

Sufficient and compelling evidence shows that constituents of Areca nut, betel leaf, betel-quin, and catechu cause, both independently and synergistically, several cytotoxic, genotoxic, and mutagenic effects on mammals. For example, these products enhance chromatid breaks and exchanges in the range of 12–37% in human cells in vitro (30) and in DNA strand breaks in mouse kidney cells or human buccal epithelial cells (31–34). Shirname and colleagues (35) were the first group to show that betel-quin caused gene mutations. Their findings have been confirmed and replicated in other human and mammalian cell types by others (2, 36). Cytotoxic, genotoxic, and mutagenic effects of Areca nut saliva extract due to nitrosamines derived from alkaloids, are widely implicated in oral cancers (37, 38).

Teratogenic effects of Areca nut and arecoline have been reported in mice and rats including death, enhanced resorption, and reduced weight of the fetus (39). A study on six babies of Asian women who habitually chewed Areca nut reported abnormalities of the fetoplacental circulation such as those seen with nicotine or cocaine addiction, but the authors could not make a definitive conclusion regarding the correlation between prenatal exposure to arecoline and birth outcomes (40). Perhaps, a larger study would shed more light on the possible teratogenic effects of Areca nut in humans.

#### **Induction of Carcinogenesis by Areca Nut Alkaloids**

It is believed that Areca-nut-specific N-nitroso compounds converted from alkaloids are the causal agents in oral and esophageal cancer (reviewed in 2, 3). The major cancer-causing agents from tobacco are also N-

nitroso compounds. Recent studies have demonstrated the molecular mechanisms by which Areca nut and betel-quid cause esophageal cancer (41-43). Induction of esophageal cancer in Areca nut and betel-quid chewers in India was found to be associated with up-regulation of genes of four different molecular pathways and down-regulation of genes of six different molecular pathways (43). The significantly over-expressed pathways included the genes for mitogen-activated protein kinase signaling cascade, G-protein coupled receptor, and cation transporter. The down-regulated pathways included the cytoskeletal genes, the ribosomal genes, and genes that regulate the antioxidant activity. The ribosomal proteins may function as cell-cycle checkpoints and play a role in cellular transformation, tumor growth, and metastasis. Thus, Areca nut alkaloids cause cancer at molecular level by modulating the expression of a number of genes (Chattopadhyay et al., 2007). An important step in Areca nut-induced carcinogenesis is catalyzed by the process of poly-ADP-ribosylation of chromosomal proteins, which alters chromosomal superstructure and, consequently, the functional status of chromosomes (44, 45).

### **Efforts to Control Use of Areca nut, Betel-quid, and Gutkha**

In recognition of the health hazards due to chewing Areca nut, betel-quid, and the tobacco-containing gutkha preparation, policy makers in many countries have enacted laws banning the chewing of these masticatories in public places, with threat of stiff fines for violators. Since 2001, India and Taiwan have been particularly aggressive in such control measures. Several states and cities in India such as Pune and Mumbai in Maharashtra State, Lucknow in Uttar Pradesh and the city of Hyderabad, among others have embraced these policies to discourage the use of gutkha and paan masala. The most effective implementation of control efforts was observed in the state of Tamil Nadu. However, enforcement of ban on the sale of these masticatories in the Indian states of Goa, Gujrat, Andhra Pradesh, and Kerala has not met with much success (46). Interestingly, when the ban on sale and use of gutkha and paan masala was enforced in the city of Hyderabad in India, the sales of fresh betel-quid increased by 50% (47). Even after the imposition of a ban on open sale of gutkha and paan masala in Patna city of Bihar, these were available “under the counter” in almost every betel shop in the city (48). The restrictions imposed on gutkha and paan masala in India have been challenged by the manufacturers in the State High Courts and The Supreme Court of India (49). The battle between the health policy makers and the suppliers of Areca nut, betel-quid, and gutkha continues. One can only hope that by educating general public about the health hazards of these masticatories, the younger generations can be dissuaded from taking up the habit and help the current users quit. Enforcement of ban, the will of governments, and cooperation of courts must be in place to combat the public health hazards due to the practice of Areca nut, betel-quid, and gutkha chewing in the Asian and Pacific Rim countries.

### **Future Research Needs**

California has a large population of immigrant Asians and Pacific Islanders, who may have traditionally practiced chewing Areca nut and betel-quid, with or without tobacco. Since paan masala is freely available in Asian stores, one would assume that it is consumed by Californians. Although Areca nut and betel-quid are on the State of California’s list of materials that cause cancer, there is no information available about the use of these harmful masticatories. TRDRP encourages and welcomes research grant applications from investigators in California proposing to investigate the statewide use and health effects of Areca nut, betel-quid, and gutkha.

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*\*Dedication: This article is dedicated to the loving memory of Mrs. Kamini Grover, who passed away on February 16, 2008 in Winnipeg, Canada, after a battle with stomach cancer diagnosed at a very advanced stage. Kamini was best known for her remarkable cheer, grit, and helping nature. All family members and friends will dearly miss Kamini.*

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# Burning Issues

Tobacco's Hottest Topics Online

Tobacco-Related Disease Research Program Newsletter

Volume 10, Number 2

October 2008

## **TRDRP UPDATE**

*by George Lemp, Dr. P.H.*

### **TRDRP: Still Relevant After 20 Years**

**A**s the Tobacco-Related Disease Research Program approaches its 20th anniversary, there is much to celebrate and, at the same time, there are reasons for concern. Since the passage of Proposition 99, the Tobacco Control Section (TCS), the Tobacco Use Prevention Program (TUPE), and the TRDRP have all worked to create a smoke-free California. The efforts of these three programs, spearheaded by the TCS, to change social norms regarding smoking in California, have led to a dramatic reduction in smoking rates and have set the standard, worldwide, for the creation and implementation of smoking-related policies that safeguard the public's health.

Since its inception in 1989, TRDRP has awarded 1,260 grants to over 900 investigators at 81 California institutions for a total of over \$393 million. These funds have supported a broad research portfolio ranging from studies of molecular cellular processes disrupted by tobacco smoking to studies that evaluate the impact of smoking on California's burgeoning multiracial and multiethnic populations. Our research efforts have played an important role in crafting tobacco-control efforts, which have resulted in the striking reduction in California's smoking rate and corresponding decline in the health care costs associated with tobacco-related disease. A recent study found that during the period from 1989 to 2004, an estimated \$86 billion in savings on health care expenditures can be attributed to the tobacco control and research efforts in California (1). Indeed, this same study showed that 3.6 billion fewer packs of cigarettes were sold in California between Fiscal years 1989-90 and 2003-04. This represents a loss of \$9.2 billion to the tobacco industry in pre-tax cigarette sales (1).

Of course, as anyone who is either familiar with tobacco-related public health issues or the tobacco industry knows, the battle is far from over. For example, while lung cancer mortality rates have declined, it continues to be a leading cause of death in California and the nation. Lung cancer is still the leading cause of cancer death in the U.S. (one in three cancer deaths are attributable to lung cancer), and the majority of people diagnosed with the disease die within a year. Despite these grim statistics, less than 5% of the National Cancer Institute's budget is devoted to lung cancer. TRDRP has stepped into this breach and has made lung cancer one of its top research priorities.

Another need for expanded research is in the area of tobacco control policy and strategy. The tobacco industry continues to have a significant impact on the political process as demonstrated by its recent involvement in the defeat of CA Prop. 86 (2,3) as well as its role in manipulating federal legislation that would on the one hand give the Food and Drug Administration (FDA) jurisdiction over tobacco products, while at the same time prevent the removal of menthol from those products (see article in this current issue; Menthol Moves Center Stage by P. Gardiner). Since California represents the largest tobacco market in the country, it is unlikely that the industry will willingly reduce its inroads to



the state's political process or voluntarily modify its marketing strategies in a way that would cut into profits. Previous TRDRP-sponsored research has revealed how the industry operates and pointed the way to more effective strategies to counter one of the most profitable and deadly industries in the world (4). In addition, ironically, cigarette sales have been shown to increase during times of economic uncertainty; the tobacco-related product market is therefore considered recession-proof (5). New research is needed to guide tobacco-control efforts and strategy, including assessing the cost-benefit of various tobacco-control efforts, evaluating existing and improved interventions and strategies, and developing new models for social marketing and control efforts in disenfranchised and highly impacted populations within the state.

### **The Challenging Road Ahead**

Despite the current state of fiscal crisis in California and the nation, the challenge remains to invest in effective efforts to prevent and curtail tobacco use in addition to improving detection and treatment of tobacco-related diseases. The Prop. 99-based research, control, and education funds are vital resources needed to have an impact on one of the most significant public health issues in this state, and must be safeguarded to ensure the improved health and well-being of current and future citizens. This makes TRDRP's mission just as vital and relevant today as it was 20 years ago.

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# Burning Issues

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## Major Changes in 2009 TRDRP Award Mechanisms

*by Kamlesh Asotra, M.F. Bowen, Phillip Gardiner, and Teresa Johnson*

At the completion of a two-year-long strategic planning effort, with support from stakeholders and the TRDRP's scientific advisory committee, major changes in three grant award mechanisms will be instituted beginning the 2009 funding cycle. These decisions have been dictated, in large part, by diminishing tobacco surtax and hence continuously decreasing research budget of TRDRP. The good news is that there has been a significant decrease in California smokers, now hovering around 14% (1). On the other hand, if TRDRP is to continue to fund research that can make a significant impact on tobacco control and blunt the human and economic costs of tobacco-related diseases, then change is the order of the day.

Specifically, the Research Grant Awards (RTs) and the IDEA Research Awards (ITs) have been discontinued. California Research Awards and Exploratory/Development Research Awards will now replace these. The California Research Award (capped at \$170,000 each year for three years in direct costs; \$140,000 without human subjects) will be open to applicants who can demonstrate that their proposed research would be specifically relevant to tobacco use in California. There will be only a limited number of the California Awards funded; we expect to fund between up to, but not more than 6 of these awards.

The Exploratory/Development Research Awards —akin to the NIH R-21 Awards —will be capped at \$250,000 in direct costs for two years. With these smaller awards, we hope that the number of research grants will increase and correspondingly the number of scientists receiving awards. TRDRP envisions that these awards will serve as seed money toward larger research grants from the TRDRP, federal and other nonprofit funding agencies.

These major changes, hopefully, will not only allow opportunities of continued scientific excellence in tobacco control and tobacco-related disease research, but also sustain the leadership of California research enterprise in global public health arena. These funding-mechanism changes are both a challenge and an opportunity; although many awardees will have to retool current research endeavors, these changes will ensure continued research funding to hopefully larger number of California scientists.

Potential applicants should review the new [Call for Applications](#), which was released on September 2, 2008. [Webinars](#) are planned for the *15th and 21st of October* to describe the new TRDRP award mechanisms, and we welcome all queries from interested applicants. The exact dates and times for such webinars will be communicated to the applicants via e-mail. Please contact TRDRP research administrators for any and all questions you have concerning these new award mechanisms.

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