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Occupational Exposures to Acid Mists and Gases and Ulcerative Lesions of the Oral Mucosa

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Background *This study examines the hypothesis that acid mist or mixtures of acid mists and acid gases are associated with ulcerative lesions of the oral mucosa.*
Methods *All 665 active male workers of a metal processing factory were the study population. Semi-quantitative measures of exposure were estimated from a job exposure matrix constructed with industrial hygienist scoring and job titles. Ulcerative lesions of the oral mucosa were identified with standardized clinical dental exams.*
Results *Past exposure to acid mists were positively associated with ulcerative lesions of the oral mucosa but only among workers without lip sealing (age- and alcohol consumption-adjusted prevalence ratio (PR), $PR_{adjusted} = 3.40$; 90% CI: 1.48–7.85). Also in this worker group, the mixture of acid mists and acid gases was associated with ulcerative lesions of the oral mucosa limited to exposure in the past ($PR_{adjusted} = 2.83$; 90% CI: 1.12–7.17).*
Conclusions *There is a positive association between acid mist or mixtures of acid mists and acid gases and ulcerative lesions of the oral mucosa only in the absence of lip sealing. The evidence of a chronic rather than acute irritative process suggests a possible step on the etiology of oral malignancies, which needs investigation.* Am. J. Ind. Med. 45:238–245, 2004. © *2004 Wiley-Liss, Inc.*

KEY WORDS: ulcerative lesions; oral mucosa; acid mist exposures; acid gases exposures; sulfuric acid; industrial dentistry; oral epidemiology

INTRODUCTION

Ulcerative lesions of the oral mucosa are characterized by damage of the epithelium and lamina propria with a cratered appearance, resulting from swelling, edema, and proliferation of the surrounding tissue [Scully and Porter, 1998]. Chronic, ulcerative lesions can be common symptoms of early stages of oral cavity cancer [Benner et al., 1995]. In Brazil, it is responsible for the sixth largest number of deaths by neoplasms among male adults [BRASIL, 2001].

Occupational exposure to certain acid products is a known risk factor for oral neoplasms [WHO, 1992]. Although oral mucosal lesions can be easily detected, as in the case of ulcerative lesions, studies focusing on their relations with acid mists are rare. With data from a cross-sectional study, evidence of a dose-response gradient between acid mist exposures and ulcerative lesions of oral

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mucosa were observed, but confounders or effect modifiers were not analyzed [Araújo, 1998]. There are also reports that age, education, duration and intensity of the exposure, lip sealing, saliva flow, oral hygiene, dental care access, and use of dentures may modify the relations of sulfuric acid to other oral health outcomes [Malcom and Paul, 1961; ten Bruggen Cate, 1968; Tuominen and Tuominen, 1992].

In this study, the hypothesis that occupational exposures to acid mists and mixtures of acid mists and acid gases are associated with ulcerative lesions of oral mucosa are examined, taking into consideration sociodemographic, occupational, life style, and dental health-related covariables as potential confounders or effect modifiers.

MATERIALS AND METHODS

This study was carried out with workers who volunteered to participate in an oral health promotion program implemented in a large metal plant in Brazil where inorganic acids are heavily used, particularly sulfuric acid. The eligible study population was comprised of all active workers registered and enlisted in a firm log as of December 1999, when the data collection finished. The oral health program consisted of free periodic dental clinical exams, treatment for simple oral diseases, fluoride therapy, oral health education, and other measures, all of them provided in a dental facility located in the plant.

Data Collection

Dentists working at the plant, in charge of routine care, were trained to perform standardized examinations and recording of clinical findings. Ulcerative lesions of oral mucosa were identified based on their clinical appearance during the dental examination. Also registered was the use of oral prostheses (yes/no) and lip sealing—the individual ability to keep lips closed at rest (yes/no). Absence of lip sealing can express a morphological trait, i.e., shortening of the upper lips, and/or functional changes like acquired occlusive dysfunctions or oral breathing [Moyers, 1991]. Following the exam, in a separate room, workers were interviewed by trained dental students using standardized questionnaires to obtain social, demographic, occupational and health-related data. The following data were registered: age in years, educational level (elementary/high school, technical, college), monthly wage in US dollars, categorized in tertiles (105.00–579.00, 580.00–1,026.00, and 1,027.00–9,500.00); admission time, worksites, job titles and work posts, and time in months spent in each job in the firm; smoking (yes/no) and consumption of alcoholic beverages (yes/no); months after the last dental consultation, and oral hygiene habits, measured as daily frequency of tooth brushing. Clinical examiners were blinded to exposure and interviewers were blinded to oral health status.

Exposure Assessment

Exposure assessment was based on a job exposure matrix that had job titles or locations on one axis, chemical or other physical hazards associated with the job on the other axis. Industrial hygienists who worked in the plant assigned scores, corresponding to the degree of possible exposure to each type of chemical and physical hazard, using four levels of exposure. Because of small numbers, however, individual agents were combined to form two exposure categories: acid mists only, and both acid mists and acid gases. Exposure scores were assigned to each job in a worker's occupational history to develop an individual exposure profile. The four original exposure levels were combined to distinguish workers who were ever and never exposed, as well as those currently exposed and those exposed only in the past. Duration of exposure was estimated as the sum of the years employed in exposed jobs, in three categories: never exposed, exposed less than 5 years, and 5 or more years. These exposure-related variables were defined for acid mists only and for the combination of acid mists and acid gases. Acid mists are composed of sulfuric acid (H_2SO_4), hydrochloric acid (HCl), electrolytic solution of H_2SO_4, and ''acid water,'' that express diluted H_2SO_4; and acid gases by sulfur dioxide (SO_2), sulfur trioxide (SO_3), and mixtures of them.

Data Analysis

The dependent variable was the presence of ulcerative lesions of the oral mucosa. Independent variables of interest were acid mists only, and both acid mists and acid gases. Based on previous research findings candidates for effect modifiers were lip sealing, education and alcohol consumption; and potential confounders were age, education, wage, smoking, alcohol consumption, and oral hygiene.

Ever and never exposed workers were compared by examining frequencies and distributions of the covariates. The associations of ulcerative lesions of oral mucosa with both acid mists only and acid mists and acid gases in combination were evaluated using prevalence ratios (PR), estimated with unconditional logistic regression following the equation $PR = (e^{\beta 0 + \beta 1}/1 + e^{\beta 0 + \beta 1})/(e^{\beta 0}/1 + e^{\beta 0})$ [Hosmer and Lemeshow, 1989]. Statistical inference was based on confidence intervals (CIs) calculated with the Delta Method [Oliveira et al., 1997]. An alpha of 0.10 was utilized because of the small study population and possible interactions to be taken into consideration. Selection of variables for modeling was based on their putative role, previous research findings, and the results obtained in the stratified analysis. Modeling was based on backward procedures, starting with a saturated model containing all candidates for effect modification, their corresponding product terms, and potential confounding variables. Variables whose deletion from the model caused at least a 20.0% change in the point estimate or

CI of the main effect were retained as confounders [Rothman and Greenland, 1998]. Analysis were separately conducted for acid mists only and acid mists and gases combined, considering history of exposure (ever vs. never), experience of exposure (current, past, or no exposure, modeled with two dummy variables); and duration of exposure, also modeled with two dummy variables. Data entry was done with EPI-INFO 6.0 [Dean et al., 1994] and the statistical analysis with SAS 8.1 [SAS Institute Incorporation, 1999/2000]. The research protocol were submitted and approved by a certified Internal Review Board of the Federal University of Bahia, and the results presented to workers and administrative staff of the plant.

RESULTS

From the 870 active workers of the plant, 731 (84.02%) voluntarily participated in the oral health program. Because of their small number and concentration in non-exposed jobs, all 65 women were excluded from the study population. One male worker was also excluded because of incomplete data. Altogether, non-participants comprised 19.4% of the eligible population with equal proportions from both administrative and operational jobs. The final study population was comprised of 665 male individuals, and the estimated crude prevalence of ulcerative lesions was 9.17%.

Characteristics of the Study Population According to the History of Exposure

Workers ever exposed to acid mists only were younger and had less education, lower salaries, and less time in the plant than workers never exposed, with a similar pattern observed for acid mists and gases in combination, except for employment time which did not differ across exposure groups. There were no differences in tobacco or alcohol consumption among ever exposed or never exposed workers. Prevalence of ulcerative lesions of oral mucosa was estimated as 11.60% among ever exposed to acid mists and 7.73% in the never exposed group. Regarding the combination of acid mists and acid gases, the prevalence of ulcerative lesions was 10.22 and 6.98% for ever and never exposed, respectively. The frequency of using oral prostheses and reporting longer time after the last dental appointment were also lower among those ever exposed to acid mists only or combined acid mists and acid gases than among the never exposed. Inadequate oral hygiene did not differ by exposure to acid mists only, but it was more common among workers ever exposed to both acid mists and acid gases than in the reference group. The proportion of workers with lip sealing did not differ across the exposure groups for any of the variables under consideration (Table I).

Acid Mists, Acid Gases, and Ulcerative Lesions of Oral Mucosa

The crude prevalence of ulcerative lesions was increased among workers exposed to acid mists only, particularly among ever exposed (PR = 1.49; 90% CI: 1.00–2.23), past exposed (PR = 1.92; 90% CI: 1.05–3.51), and for those with 5 or more years of exposure as compared to never exposed workers, respectively. This pattern is also shown for acid mists and acid gases combined, but none of the association measures were statistically significant. All age- and alcohol consumption-adjusted PRs for both acid mists only and acid mists and acid gases were also positive but not statistically significant (Table II).

Statistically significant interaction between lip sealing and exposure to acid mists only was found for workers ever exposed ($\chi^2_{2df} = 4.703$ $P < 0.20$) and exposed in the past ($\chi^2_{1df} = 2.86$, $P < 0.20$). Interaction of borderline statistical significance was observed for duration of exposure to acid mists ($\chi^2_{2df} = 3.135$, $P = 0.20$). In the group of workers without lip sealing, a positive association between ever exposed to acid mists and ulcerative lesions was found ($PR_{crude} = 3.05$; 90% CI: 1.33–7.03), which was slightly reduced after adjustment for age- and alcohol consumption ($PR_{adjusted} = 2.70$; 90% CI: 1.14–6.38). Past exposure to acid mists was positively associated with ulcerative lesions [age- and alcohol-adjusted PR was 3.40 (90% CI: 1.48–7.85)]. No statistically significant differences were observed for current exposure in any of the models considered. In the group of workers without lip sealing and 5 or more years of exposure to acid mists, the crude PR was 3.40 (90% CI: 1.14–10.13). No statistically significant effect of exposure duration was found after adjustment for age and alcohol consumption (Table III). Among workers with lip sealing, in contrast, no relevant associations were found.

Regarding exposure to both acid mists and acid gases, point estimates showed positive associations but a statistically significant difference was found only for past exposure among workers without lip sealing ($PR_{adjusted} = 2.83$; 90% CI: 1.12–7.17; Table IV).

DISCUSSION

These findings are suggestive that occupational exposures to acid mists are a risk factor for ulcerative lesions of the oral mucosa, among workers without lip sealing. Prevalence of ulcerative lesions was higher among previously exposed than among currently exposed workers for both acid mists and mixed acid mist and acids gases.

The findings of this study are consistent with the positive, statistically significant prevalence trend of ulcerative lesions with intensity of sulfuric acid mist exposure reported by Vianna and Santana [2001], based on the published data of Araújo [1998]. They also are in accordance with the higher

TABLE I. Socio-Demographic Characteristics of the Study Population and Oral Health-Related Variables According to History of Exposure to Acid Mists Only and Acid Mists Plus Acid Gases (N = 665); Brazil

	Acid mists only				Acid mists and acid gases			
	Ever exposed		Never exposed		Ever exposed		Never exposed	
Variables	**N = 251**	**Percentage**	**N = 414**	**Percentage**	**N = 450**	**Percentage**	**N = 215**	**Percentage**
Age								
18–34	112	44.62	113	27.29	167	37.40	58	26.98
35–44	94	37.45	163	39.37	184	40.89	73	33.95
45–65	45	17.93	138	33.33	99	22.00	84	39.07
Education								
Elem./high school	154	61.35	196	47.34	255	56.67	95	44.19
Technical	72	28.69	140	33.82	153	34.00	59	27.44
College	25	9.96	78	18.84	42	9.33	61	28.37
Monthly wage (in US$)								
105.00–579.00	116	46.22	137	33.09	194	43.11	59	27.44
580.00–1,026.00	67	26.69	131	31.64	130	28.89	68	31.63
1,027.00–9,474.00	68	27.09	146	35.27	126	28.00	88	40.93
Years of employment								
0–9	104	41.43	117	28.26	148	32.89	73	33.95
10–37	147	58.57	297	71.74	302	67.11	142	66.05
Alcohol consumption								
None	42	16.73	80	19.32	83	18.44	39	18.14
Occasionally	127	50.60	215	51.93	240	53.33	102	47.44
2–7 days a week	82	32.67	119	28.74	127	28.22	74	34.42
Cigarettes/day								
None	221	88.05	366	88.83	398	88.84	189	87.91
1–5	8	3.19	18	4.37	14	3.13	12	5.58
6–15	13	5.18	17	4.13	21	4.69	9	4.19
16–25	9	3.59	11	2.67	15	3.35	5	2.33
Lip sealing								
Present	201	80.40	346	83.57	372	82.85	175	81.40
Absent	49	19.60	68	16.43	77	17.15	40	18.60
Oral prostheses								
No	89	35.46	106	25.26	143	31.78	52	24.19
Yes	162	64.54	308	74.40	307	68.22	163	75.81
Time after the last dental appointment								
0–6 months	130	52.00	259	63.33	250	56.18	139	64.95
7–12	64	25.60	81	19.80	106	23.82	39	18.22
Over 12	56	22.40	69	16.87	89	20.00	36	16.82
Oral hygiene								
Non-satisfactory	83	33.07	114	27.54	148	32.89	49	22.79
Regular	95	37.85	181	43.72	173	38.44	103	47.91
Good	73	29.08	119	28.74	129	28.67	63	29.30

prevalence estimated of ulcerative lesions of the oral mucosa observed among metal workers as compared to those of other industries [Zain et al., 1995].

The observed interaction of acid exposure and lip sealing is probably due to the increment in the intensity or exposure time of the oral mucosa among workers without lip sealing. Exposures to these agents can cause oral breathing, which is known to be associated with absence of lip sealing, because they determine chronic inflammatory or allergic manifestations in the upper respiratory tract. The irritant action of acids may therefore force oral respiration, consequently intensifying oral exposure effects [WHO, 1992]. It is noteworthy that

TABLE II. Crude and Adjusted PRs for Ulcerative Lesions of the Oral Mucosa, by Exposure to Acid Mists and Acid Mists Plus Acid Gases (N = 665); Brazil

Exposure variables	N	Prevalence percentage	PR_{crude}[a] 90% CI[b]	$PR_{adj.}$[c] 90% CI
Acid mists only				
History of exposure				
Never exposed	414	7.73	1.0	
Ever exposed	251	11.55	1.49 (1.00–2.23)	1.28 (0.85–1.94)
Experience of exposure				
Never	414	7.73	1.0	
Currently	197	10.66	1.38 (0.89–2.14)	1,20 (0.76–1.88)
Past	54	14.81	1.92 (1.05–3.51)	1.57 (0.83–2.95)
Duration of exposure				
Never	414	7.73	1.0	
Less than 5 years	108	11.11	1.44 (0.85–2.45)	1.02 (0.57–1.82)
5 or more	143	11.89	1.54 (0.96–2.45)	1.49 (0.91–2.44)
Acid mists and acid gases				
History of exposure				
Never exposed	215	6.98	1.0	
Ever exposed	450	10.22	1.47 (0.92–2.34)	1.41 (0.89–2.24)
Experience of exposure				
Never	215	6.98		
Currently	368	9.78	1.40 (0.86–2.28)	1.31 (0.81–2.12)
Past	82	12.20	1.75 (0.92–3.30)	1.66 (0.90–3.06)
Duration of exposure				
Never	215	6.98	1.00	
Less than 5 years	153	11.76	1.69 (0.97–2.91)	1.12 (0.64–1.94)
5 or more	297	9.43	1.35 (0.82–2.24)	1.48 (0.87–2.50)

[a]Crude PR.
[b]Mantel–Haenszel CI.
[c]Age- and alcohol consumption-adjusted PR.

lip sealing has not been considered in studies focusing air pollutant exposures for either external or internal dose assessments. The best known effects of acids on soft tissues are local irritation, followed by inflammatory reactions and/or erosion [Aznar Longares and Nava, 1988; WHO, 1992; Araújo, 1998], but as already mentioned, chronic ulcerative lesions of the oral mucosa are clinically suggestive of malignant neoplasms [Benner et al., 1995]. In addition, it is widely recognized that certain acid products such as sulfuric acid cause cancer of the upper digestive tract [WHO, 1992]. Data from this study, however, did not allow the evaluation of these hypotheses because of its cross-sectional design and the lack of specific diagnostic information.

Some observed differences in the association of ulcerative lesions with acid mists only versus combined acid mists and acid gases may be consequences of physical and chemical characteristics of these exposures. Mists are less volatile than gases and can stay for a long time in the breathing zone, increasing the intensity and duration of the exposure of the oral structures. In addition, the hygroscopic property of H_2SO_4, the principal component of the acid mists analyzed in this study, may contribute to an even greater accumulation of this substance in the oral cavity. It is worth noting that more severe irritant responses have been reported in experimental studies for sulfuric acid as compared to sulfur dioxide, even when the mist particles have the same size and similar acid concentration [Alarie et al., 1975]. This increased severity of H_2SO_4 relative to SO_2 has also been reported by Amdur [1989]. Because SO_2 produces H_2SO_4 when combined with water, the humidity of the respiratory system can also contribute to the increase of acid concentration. However, because this chemical reaction occurs primarily in the lungs, it is possible that this effect is weak in the oral cavity [Finkel et al., 1983].

This is a cross-sectional study, therefore it was not possible to verify the temporal precedence of exposure to acid mists or acid gases in relation to ulcerative lesions of the oral mucosa. Available non-occupational data could be evaluated, suggesting a synergism between lip sealing and acid exposure, a hypothesis not yet verified. Also, it was

TABLE III. PRs and 90% CIs (Estimated by Logistic Regression) for the Association of Exposure to Acid Mists and Ulcerative Lesions of the Oral Mucosa, According to Lip Sealing (n = 664), Brazil

	Lip sealing			
	Present (n = 547)		Absent (n = 117)	
Models	**PR**	**90% CI[a]**	**PR**	**90% CI[a]**
History of Exposure				
Model 1				
Never	1.00	(— —)	1.00	(— —)
Ever	1.15	(0.71–1.86)	3.05	(1.33–7.03)
Model 2 (age[b] and alcohol consumption[c])				
Never	1.00	(— —)	1.00	(— —)
Ever	1.03	(0.63–1.69)	2.70	(1.14–6.38)
Experience of exposure				
Model 1				
No	1.00	(— —)	1.00	(— —)
Currently	1.02	(0.55–1.89)	1.81	(0.73–4.47)
Past	1.36	(0.57–3.29)	3.17	(1.13–8.89)
Model 2 (age and alcohol consumption)				
No	1.00	(— —)	1.00	(— —)
Currently	1.00	(0.53–1.89)	1.52	(0.65–3.54)
Past	1.65	(0.69–3.91)	3.40	(1.48–7.85)
Duration of exposure in years				
Model 1				
No	1.00	(— —)	1.00	(— —)
Less than 5	1.09	(0.49–2.42)	2.62	(0.82–8.30)
Equal or over 5	1.17	(0.60–2.29)	3.40	(1.14–10.13)
Model 2 (age and alcohol consumption)				
No	1.00	(— —)	1.00	(— —)
Less than 5	1.05	(0.49–2.23)	1.72	(0.60–4.96)
Equal or over 5	1.25	(0.63–2.48)	2.35	(0.79–6.98)

[a]90% CI using Delta Method.
[b]Age coded as 1, 18–34 years; 2, 35–44 years; and 3, >44 years.
[c]Alcohol consumption coded as 0, non drinker; 1, occasionally; and 2, 2–7 days a week.

possible to control for important confounding variables. Semiquantitative exposure measurements by means of a job exposure matrix, as utilized in this study, have been reported as reasonable approximations of environmental quantitative exposure data [Boliej et al., 1995]. By knowing the chemical components of the exposures of interest, it was possible to identify epidemiological differences concerning acid mists and acid mists plus acid gases, which are consistent with its toxicology. However, ulcerative lesions of oral mucosa comprise a heterogeneous group of oral pathologies, which can lead to classification bias. The finding of a statistically significant positive association of acid mists and ulcerative lesions suggests that this possible bias was not strong enough to compromise inferences from this study. Calibration of the diagnosis of clinical examiners performed in a pilot study showed a high proportion of agreement for ulcerative lesions (98.0%).

Selection bias towards the null hypothesis are common in occupational studies limited to active workers, as exemplified by the so-called healthy worker effect [Choi, 1992]. In this study, the population was comprised of workers previously selected through pre-employment screenings, who remained as active employees until these data were collected. However, as widely known, when workers develop work-related health problems, they may be moved to worksites free of the putative risks or leave the industry entirely. This termination of exposure at the onset of the disease may lead to biased negative results. However, ulcerative lesions of oral mucosa are rarely checked in routine medical exams and are not recognized as severe enough to

TABLE IV. PRs and 90% CIs (Estimated by Logistic Regression) for the Association of Ulcerative Lesions of the Oral Mucosa With Exposure to Acid Mists and Acid Gases With, According to Lip Sealing (n = 664), Brazil

	Lip sealing			
	Present (n = 547)		Absent (n = 117)	
Models	**PR**	**90% CI[a]**	**PR**	**90% CI[a]**
History of Exposure				
Model 1				
Never	1.00	(— —)	1.00	(— —)
Ever	1.29	(0.76–2.21)	2.25	(0.82–6.16)
Model 2 (age[b] and alcohol consumption[c])				
Never	1.00	(— —)	1.00	(— —)
Ever	1.22	(0.70–2.10)	2.10	(0.75–5.89)
Experience of exposure				
Model 1				
No	1.00	(— —)	1.00	(— —)
Currently	1.20	(0.68–2.13)	1.05	(0.42–2.63)
Past	1.07	(0.47–2.43)	2.69	(1.02–7.13)
Model 2 (age and alcohol consumption)				
No	1.00	(— —)	1.00	(— —)
Currently	1.17	(0.64–2.15)	0.98	(0.42–2.31)
Past	1.71	(0.78–3.76)	2.83	(1.12–7.17)
Duration of exposure in years				
Model 1				
No	1.00	(— —)	1.00	(— —)
Less than 5	1.37	(0.63–3.00)	2.59	(0.72–9.28)
Equal or over 5	1.25	(0.64–2.47)	1.90	(0.51–7.11)
Model 2 (age and alcohol consumption)				
Non	1.00	(— —)	1.00	(— —)
Less than 5	1.00	(0.47–2.14)	1.57	(0.52–4.77)
Equal or over 5	1.08	(0.51–2.28)	1.53	(0.47–5.04)

[a]90% CI using Delta Method.
[b]Age coded as 1, 18–34 years; 2, 35–44 years; 3, >44 years.
[c]Alcohol consumption coded as 0, non drinker; 1, occasionally; 2, 2–7 days a week.

require workers' firing or withdrawal from exposed worksites. Notwithstanding, respiratory symptoms caused by acid exposures can easily be identified as a consequence of these irritants and cause workers dismissal. In addition, refusals were evenly distributed across worksites, therefore bias caused by these losses are not plausible.

In sum, these results point out the need for the evaluation of ulcerative lesions as a marker or an early sign of severe oral diseases, including oral neoplasms. It is also necessary to develop a better understanding of the role of lip sealing in the association under consideration, as well as its relationship with effectiveness of personal protective equipments by workers, such as masks. The possible synergism with lip sealing brings to light a sensitive ethical problem of taking a biological trait for workers' selection into the labor force, which is used despite recommendations that preventive strategies should rely on engineering controls, rather than selective screening. It is particularly relevant when the absence of lip sealing is under consideration, because it can also be a consequence of the acid mist exposure itself.

Although social inequities, common in less developed countries, are reproduced inside the firms themselves, determining that less qualified workers with low education and salaries are also more commonly assigned to ''dirty'' jobs with higher exposure levels, as shown in this study. This represents a perverse simultaneous co-occurrence of poor life conditions and occupational hazards that compose a scenario unfavorable for health and wellbeing [Santana, 1996].

This study revealed the potential damage of acid mists to oral health, thus reaffirming the need to set up control

programs, already in effect in several countries. The need for consideration of lip sealing when inhalable exposures are assessed is also supported by the results of this study.

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