Supplemental Materials

This appendix was provided by the authors to give readers additional information about this manuscript.

Ambient Melamine Exposure and Urinary Biomarkers of Early Renal Injury

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METHODS

Questionnaire

All eligible exposed and non-exposed workers were interviewed by well-trained researchers using a structured questionnaire face-to-face to collect detailed information about demographic characteristics, medical history, family history, their uses of substances (cigarette, alcohol, and betel quid), and occupational history. Body weight (kg) and body height (cm) were measured by professional examiners while participants stood in light street clothes. Body mass index (BMI (kg/m^2)) was calculated with body weight divided by the square of body height. Family history of renal calculi or other kidney-related disease were considered to be present if any first-degree relative had a history of urolithiasis or other kidney-related disease.

Subjects were defined as alcohol drinkers, cigarette smokers or betel quid chewers if they had regularly consumed any alcoholic beverage ≥1 times per week, smoked ≥10 cigarettes per week, or chewed ≥1 betel quid per day for at least 6 months.[1] These three variables of substance uses from questionnaire have been validated by using different biomarkers in our previous study.[2] Occupational history, including job title, job duration, past working history, and use of personal protective equipment (e.g., dust masks), were also collected.

Quantification and method validation of melamine in air, urine, and serum samples

For the measurement of melamine in air sample, we modified the analytical method from Yassine *et al*.[3] After weighing, all filters were placed in glass extraction vials and spiked with melamine isotopically labeled standards before extraction. Glass fibers were wetted by using 20 μl isopropanol and then were sonicated for 30 min with the mixture of 1 ml 2% (v/v) formic acid/acetonitrile (ACN). Subsequently, the extract was filtered through a 0.22 μm polyvinylidene fluoride (PVDF) syringeless filter device with polypropylene housing (Mini-Uniprep™ Syringeless Filter; Whatman, Florham Park, NJ, USA). The analysis of melamine in blank samples followed the same procedure. Finally, the filtered samples were transferred into certified liquid chromatography (LC) vials for analysis by the method of liquid chromatography-electrospray ionization-tandem mass spectrometry (LC-ESI-MS/MS) (Supplemental Figure 1).[4]

To extract melamine from serum samples, $^{13}C_3{}^{15}N_3$-melamine was added as an internal standard to an aliquot of 300 μl serum samples. Then, 900 μl 2% phosphoric acid was added to the mixture and vortexed, and the mixture was centrifuged at 3,500 rpm for 10 minutes under room temperature. The aqueous supernatant was introduced into the solid-phase-extraction (SPE) cartridge (Bond Elut Plexa PCX 60 μm, 1ml, 30 mg) for analysis (Supplemental Figure 2).[4] For the measurement of melamine and creatinine in urine samples, the detailed methods are described elsewhere.[4,5] Briefly, the elute of 1 ml urine sample collected from an Oasis® MCX SPE cartridge (Waters Corp., Malford, MA, USA) was dried under nitrogen gas. Then, the residues were reconstituted in 200 μl mobile phase and subjected into LC-MS/MS for analysis. The method of detection limit (MDL) in urine was 0.8 ng/ml (ppb), with any measurement below MDL treated as 0.4 ng/ml.[4,5] Urinary creatinine was determined using spectrophotometry (U-2000; Hitachi, Tokyo, Japan) at a wavelength of 520 nm to measure the creatinine–picrate reaction. Urinary melamine concentration were expressed either ng/ml or μg/mmole creatinine. In the present study, urinary melamine levels were detectable in all 39 (100%) urinary samples in 39 melamine workers and 39 (92.9%) out of 42 urinary samples in the non-exposed workers.

The method validations for air and serum samples are summarized in Table S2. The MDL was determined using a blank glass fiber sample or blank serum sample spiked with standards. For air samples, the MDL was 50 ng/ml; thus, MDL of air melamine concentration was converted to unit at ng/m^3 as 46.30 ng/m^3. For serum samples, the MDL was 1.33 ng/ml in serum.

Quantification and method validation of formaldehyde in air samples

The analytical method of formaldehyde was adopted from previous studies.[6,7] Air samples were extracted with ACN and analyzed by the method of high-performance liquid chromatography with UV detection (HPLC-UV) (Jasco PU-2809, Japan/Varian UV-Vis detector, USA) in a gradient mode from 40% acetonitrile/60% water to 90% acetonitrile /10% water at a wavelength of 360 nm. The MDL was 0.23 μg/m^3 (Supplemental Table 2).

Analyses of renal injury biomarkers in urine

The quantitation of urinary microalbumin, NAG, and β2-microglobulin have been described in detail elsewhere.[5] The assay kits included microalbumin kit/ALB-TIA "SEIKEN" X1 (Denka Seiken, Tokyo, Japan), NAG assay kit (Diazyme Laboratory, Poway, CA), and N Latex β2-microglobulin assay (Siemens Healthcare Diagnostics, Marburg, Germany). The MDLs were 0.96 ng/ml for microalbumin and 0.206 mg/l for β2-microglobulin.[5]

Analysis of serum biochemistry and other examinations

All routine biochemistries such as liver function, cardiometabolic function, and renal function (BUN, creatinine, and uric acid) were measured in the central clinical laboratory of KMHKH. Both exposed and non-exposed workers underwent renal echo, whereas only exposed workers (melamine workers) had KUB radiography (Kidney, ureter, bladder X-ray) to detect any urolithiasis. All task forces were performed by health staff members who were blinded to this study design from KMHKH.

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Legends

Supplemental Figure 1. **Flowchart of study subjects.**

Supplemental Figure 2. **Signals of ion chromatograms for ambient melamine.** a) Blank glass fibers; b) Glass fibers fortified with 1.0 ng of melamine standard; c) Melamine in air samples with the concentration of 6.09 ng/m^3. (Upper and middle panels of chromatograms are melamine standard and lower panel of chromatogram is $^{13}C_3{}^{15}N_3$-melamine internal standard (IS)).

Supplemental Figure 3. **Signals of ion chromatograms for serum melamine.** a) Negative control serum without fortified melamine standard; b) Control serum with fortified 2.0 ng/ml of melamine standard; c) Melamine in one serum sample of melamine worker. The melamine level from this sample was calculated to be 10.54 ng/ml. (Upper and middle panels of chromatograms are melamine standard and lower panel of chromatogram is $^{13}C_3{}^{15}N_3$-melamine internal standard (IS)).

Supplemental Figure 4. **The ambient distribution of different dust particle sizes (particulate matter (PM) 10, 2.5, and 1.0 μm) in a real-time status (one measurement every one minute) by portable laser aerosol spectrometers and dust monitors in one melamine manufacturing company (Factory A) during work from Monday to Friday.** a) Monday; b) Tuesday; c) Wednesday; d) Thursday; e) Friday. (arrow indicates one worker smoked cigarettes close to the area dust monitor).

Supplemental Figure 5. Predicted temporal change of urinary melamine concentrations by work sites. a) Predicted daily mean (± SE) difference of post-shift and pre-shift of urinary melamine concentration by work sites from Monday to Friday; b) Predicted daily mean (± SE) urinary melamine concentrations in the morning by work sites from Monday, weekend, to the following Monday.

Supplemental Figure 6. **Relationship between urinary melamine concentrations and early renal tubular injury markers in urine by work sites.** a) Urinary melamine concentrations and NAG levels (n = 81); b) Urinary melamine concentrations and microalbumin levels (n = 81). Abbreviation: Cr = cratinine; NAG = N-acetyl β-D-glucosaminidase.

Supplemental Table 1. **STROBE Statement—checklist of items that should be included in reports of observational studies**

Supplemental Table 2. Accuracy and precision of melamine validation solutions spiked in air and serum samples (n = 5 each), and formaldehyde validation solutions spiked in air samples (n = 5).

Supplemental Table 3. Daily averaged preshift and postshift urinary melamine concentration in melamine workers by work sites.

Supplemental Table 4. Daily averaged ambient personal and area melamine and formaldehyde concentrations ($\mu g/m^3$) in melamine workers by work sites.

Supplemental Table 5. Daily averaged ambient concentrations of different dust particle sizes (particulate matter (PM) 10, 2.5, and 1.0 μm) by portable laser aerosol spectrometers and dust monitors in one melamine manufacturing company (Factory A) during work.

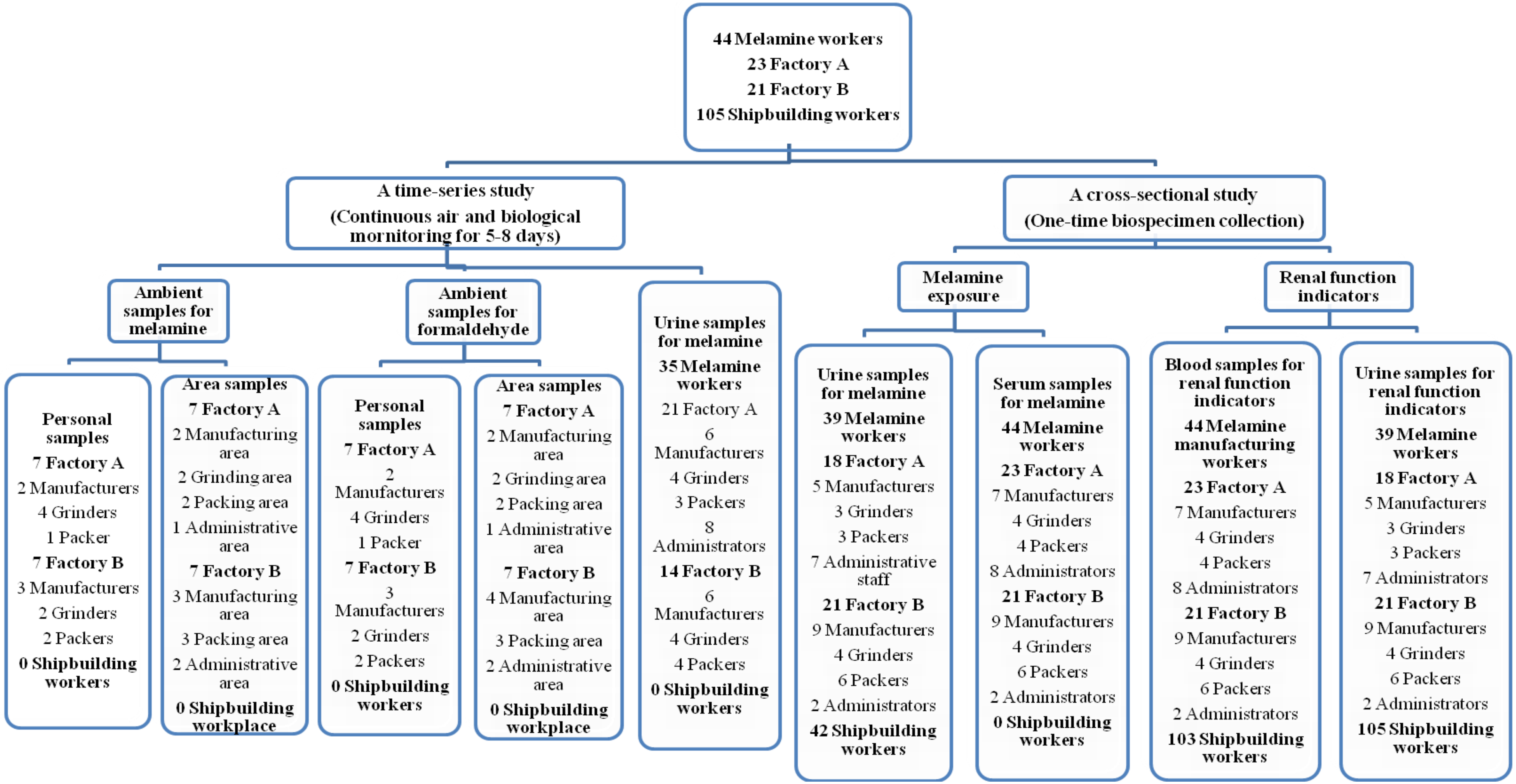
Supplemental Table 6. Daily variations of preshift and postshift urinary melamine concentrations concentrations in generalized linear mixed models.[a]

Supplemental Table 7. Other clinical and laboratory data in melamine tableware manufacturing workers by work sites and their comparison group.

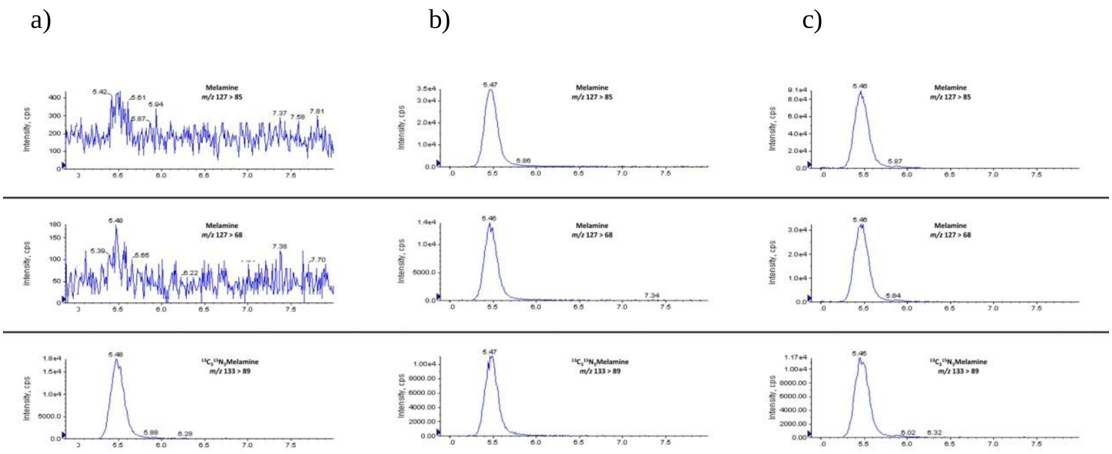
Supplemental Table 8. Relationship of urinary biomarkers of renal injury with urinary melamine levels or work sites after adjusting for hypertension in multiple linear regression models.

Supplemental Table 9. Summary of literature data about industry of melamine-formaldehyde resin related to occupational melamine exposure.

Supplemental Table 10. Summary of urinary melamine concentration variations in different populations from the literature.



Supplemental Figure 1. Flowchart of study



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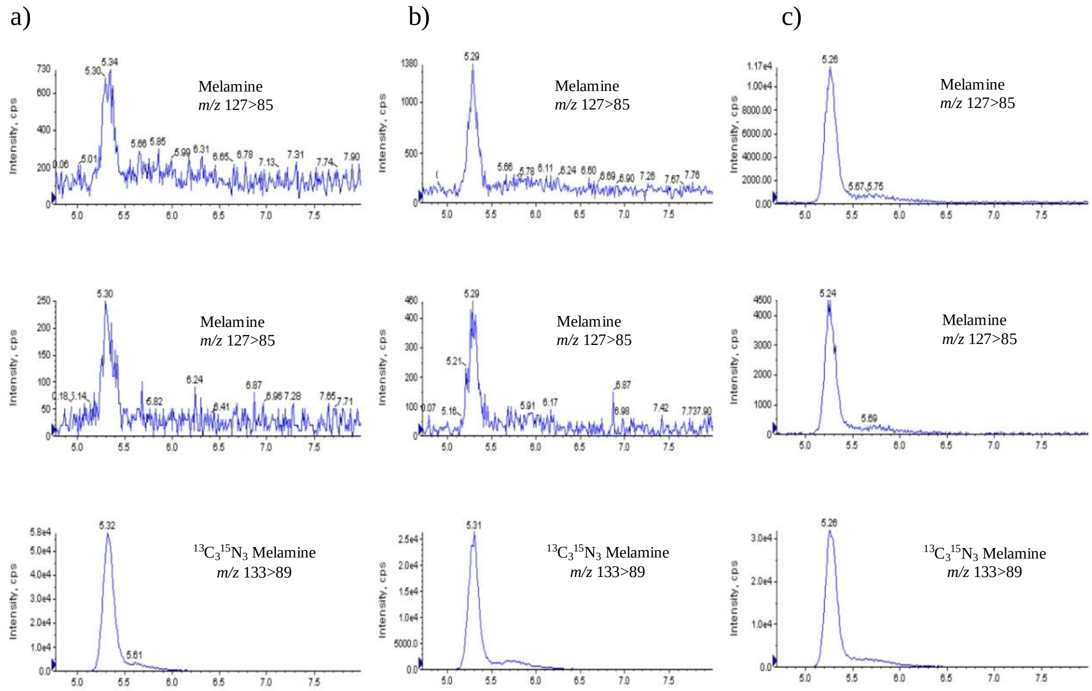

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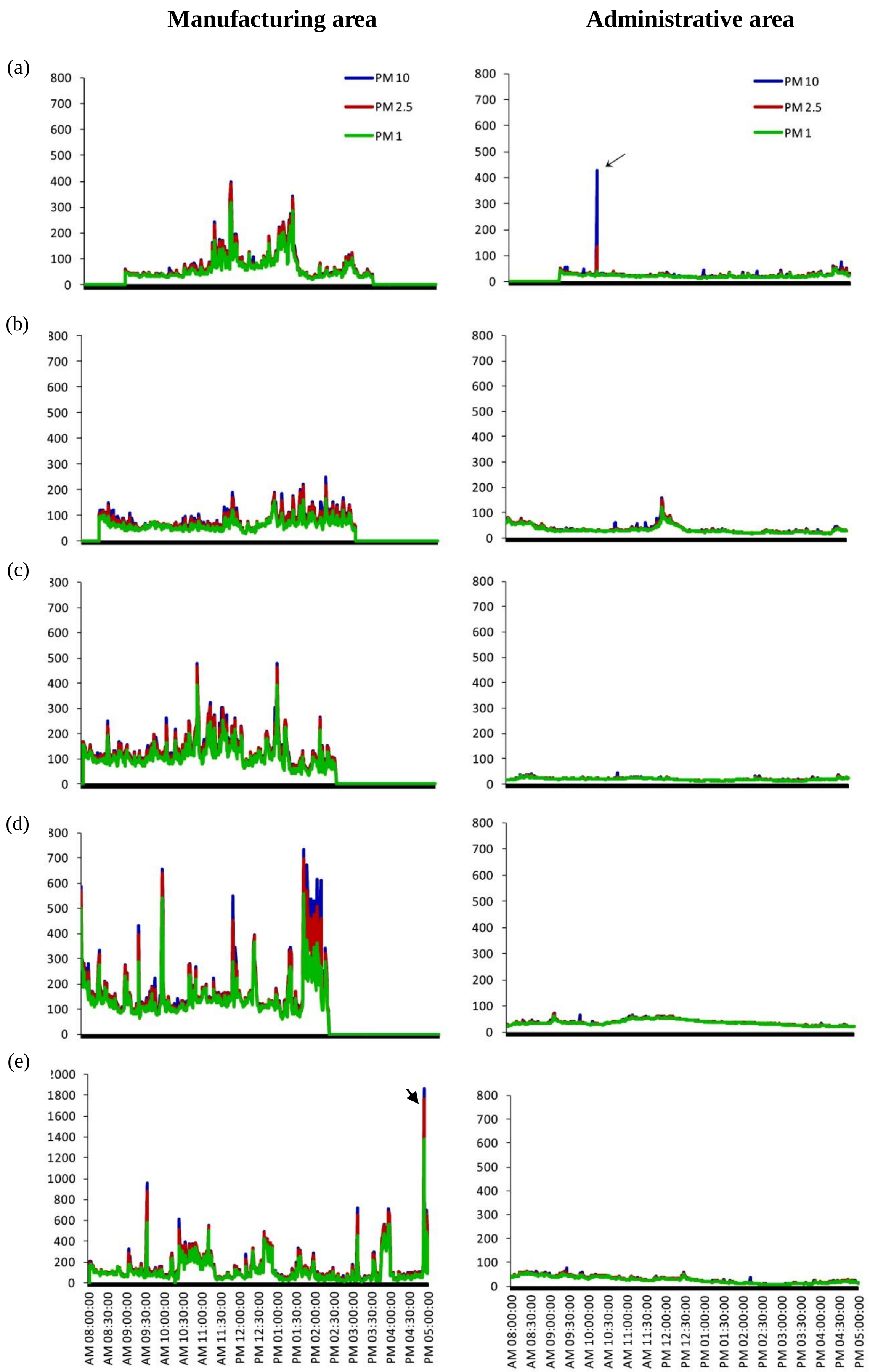
Manufacturing area
Administrative area
(a)
(b)
(c)
(d)
(e)
PM 10
PM 2.5
PM 1
AM 08:00:00
AM 08:30:00
AM 09:00:00
AM 09:30:00
AM 10:00:00
AM 10:30:00
AM 11:00:00
AM 11:30:00
PM 12:00:00
PM 12:30:00
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PM 02:00:00
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PM 03:30:00
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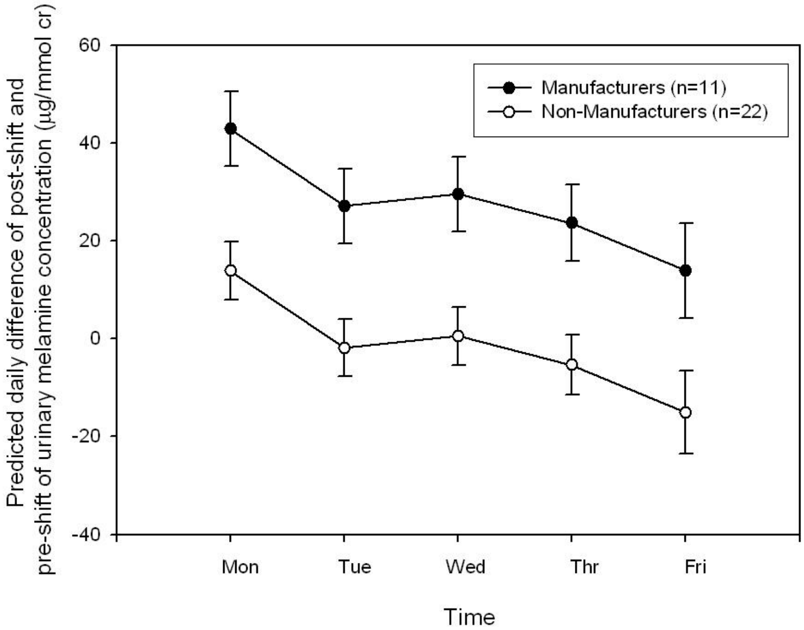
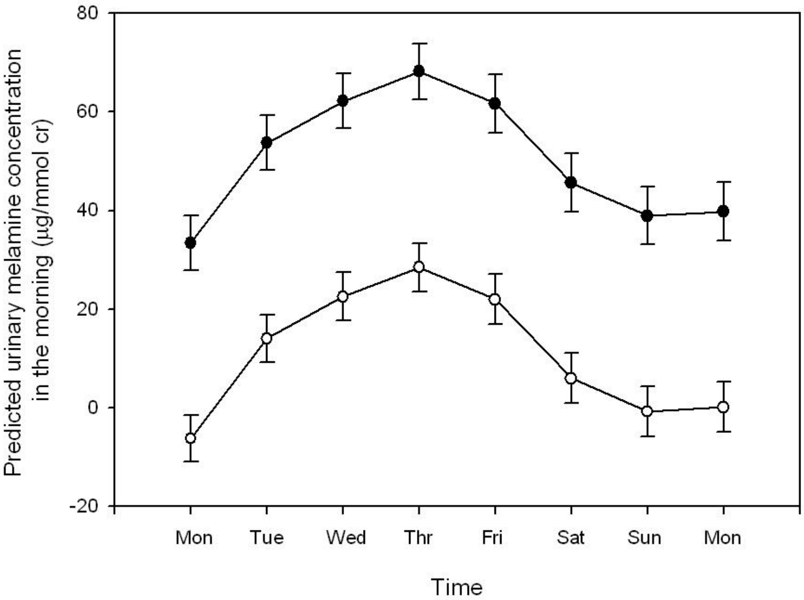
Supplemental Figure 4. The ambient distribution of different dust particle sizes (particulate matter (PM) 10, 2.5, and 1.0 μm) in a real-time status (one measurement every one minute) by portable laser aerosol spectrometers and dust monitors in one melamine manufacturing company (Factory A) during work from Monday to Friday. a) Monday; b) Tuesday; c) Wednesday; d) Thursday; e) Friday. (arrow indicates one worker smoked cigarettes close to the area dust monitor; arrow head indicates the highest ambient concentrations of PM 10 μm (1861.8 $\mu g/m^3$), PM 2.5 μm (1761.1 $\mu g/m^3$) and PM 1.0 μm (1384.1 $\mu g/m^3$))

a)



b)



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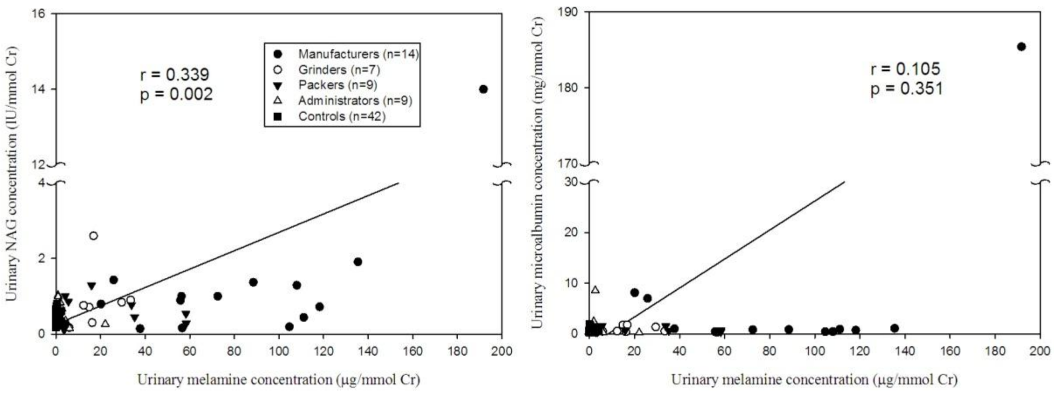
a) b)



Supplemental Figure 6. Spearman correlation between urinary melamine concentrations and early renal tubular injury markers in urine by work sites. a) Urinary melamine concentrations and NAG levels (n = 81); b) Urinary melamine concentrations and microalbumin levels (n = 81). Abbreviation: Cr = cratinine; NAG = N-acetyl β-D-glucosaminidase.

Supplemental Table 1. STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Checklist
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Yes
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Yes
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Yes
Objectives	3	State specific objectives, including any prespecified hypotheses	Yes
Methods			
Study design	4	Present key elements of study design early in the paper	Yes
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Yes
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	Yes
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Yes
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Yes
Bias	9	Describe any efforts to address potential sources of bias	Yes
Study size	10	Explain how the study size was arrived at	Yes
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Yes
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Yes
		(*b*) Describe any methods used to examine subgroups and interactions	Yes
		(*c*) Explain how missing data were addressed	Yes
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	Yes
		(*e*) Describe any sensitivity analyses	N/A
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes
		(b) Give reasons for non-participation at each stage	Yes
		(c) Consider use of a flow diagram	Yes
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes
		(b) Indicate number of participants with missing data for each variable of interest	Yes
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	N/A
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	N/A
		Cross-sectional study—Report numbers of outcome events or summary measures	Yes
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Yes
		(*b*) Report category boundaries when continuous variables were categorized	Yes
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Yes
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Yes
Discussion			
Key results	18	Summarise key results with reference to study objectives	Yes
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Yes
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Yes
Generalisability	21	Discuss the generalisability (external validity) of the study results	Yes
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Yes

Supplemental Table 2. Accuracy and precision of melamine validation solutions spiked in air and serum samples (n = 5 each), and formaldehyde validation solutions spiked in air samples (n = 5).

Spiked concentration (ng/ml)	Day 1		Day 2		Interday difference (%)[c]	LOQ	MDL
	Accuracy (%)[a]	RSD (%)[b]	Accuracy (%)	RSD (%)			
Melamine							
In serum							
2	100.4	3.8	102.5	6.2	1.99	2.00	1.33
5	91.8	2.5	91.0	2.6	0.87		
10	101.8	3.9	107.7	0.5	5.80		
In air						0.50	50.00
5	99.7	8.2	101.9	2.3	2.21		
50	100.2	7.3	101.0	2.0	0.76		
500	98.4	4.2	98.6	2.9	0.21		
Formaldehyde							
In air						2.9	8.0
15	90.4	3.1	92.5	2.0	2.36		
60	94.1	0.2	91.6	0.2	2.66		
300	95.9	0.3	99.5	0.3	3.75		

Abbreviation: LOQ = Limit of quantitation; MDL = method of detection limit; RSD = relative standard deviation or precision; SD = standard deviation.

[a]Accuracy = (mean observed concentration/standard concentration) $\times$ 100

[b]RSD = (SD/mean) $\times$ 100.

[c]Interday difference =[(mean of Day 2 – mean of Day 1) / mean of Day 1] $\times$ 100

Supplemental Table 3. Daily averaged preshift and postshift urinary melamine concentration in melamine workers by work sites.

Mean ± SE	Monday				Tuesday				Wednesday				Thursday				Friday				Saturday		Sunday		Monday	
	N	AM	N	PM	N	AM	N	PM	N	AM	N	PM	N	AM	N	PM	N	AM	N	PM	N	AM	N	AM	N	AM
Without creatinine correction (ng/ml)																										
Manufacturers	12	112.2 ± 25.1	11	1321.3 ± 547.6	12	739.3 ± 175.8	12	1065.5 ± 318.7	12	802.9 ± 197.6	12	1116.2 ± 247.6	11	753.2 ± 118.8	10	793.1 ± 209.7	11	752.2 ± 178.2	5	534.2 ± 196.0	11	404.7 ± 104.8	11	181.9 ± 37.6	11	245.4 ± 83.9
Grinders	8	111.4 ± 41.2	8	159.8 ± 44.4	8	105.0 ± 28.7	8	174.3 ± 40.9	8	205.0 ± 81.1	8	290.7 ± 71.6	7	190.9 ± 41.2	7	258.7 ± 60.5	7	160.8 ± 37.8	2	236.9 ± 47.3	6	110.3 ± 50.5	6	65.8 ± 20.0	6	49.2 ± 8.5
Packers	7	36.4 ± 13.4	7	134.0 ± 31.6	7	175.1 ± 89.3	7	310.0 ± 99.6	6	432.8 ± 229.4	7	267.6 ± 78.9	7	381.5 ± 205.2	7	310.5 ± 94.7	5	104.3 ± 44.4	3	90.8 ± 20.4	6	77.6 ± 21.6	6	130.3 ± 108.6	6	46.1 ± 13.1
Administrators	8	18.5 ± 5.9	8	69.4 ± 29.2	8	34.3 ± 10.6	8	66.0 ± 24.2	8	44.3 ± 11.6	8	41.2 ± 13.8	8	39.5 ± 12.7	7	38.9 ± 12.7	7	23.7 ± 6.5	5	20.4 ± 7.0	7	43.1 ± 20.4	7	80.4 ± 43.0	7	88.3 ± 34.3
With creatinine correction (µg/mmol)																										
Manufacturers	12	11.5 ± 2.0	11	74.6 ± 17.2	12	61.3 ± 9.8	12	80.0 ± 10.9	12	65.1 ± 8.3	12	97.0 ± 17.6	11	89.0 ± 15.3	10	112.7 ± 18.0	11	83.8 ± 16.5	5	51.9 ± 11.7	11	44.9 ± 11.1	11	19.0 ± 3.5	11	27.5 ± 9.3
Grinders	8	8.9 ± 1.8	8	14.0 ± 1.6	8	11.5 ± 1.7	8	15.3 ± 3.3	8	21.5 ± 6.9	8	25.6 ± 3.3	7	25.0 ± 7.1	7	18.6 ± 2.6	7	16.3 ± 3.1	2	16.0 ± 1.7	6	9.5 ± 2.3	6	8.2 ± 1.6	6	6.9 ± 1.9
Packers	7	3.8 ± 0.6	7	7.8 ± 1.8	7	15.2 ± 5.7	7	16.7 ± 4.0	6	42.7 ± 19.5	7	30.0 ± 14.0	7	27.2 ± 14.6	7	21.9 ± 6.3	5	12.3 ± 3.8	3	6.1 ± 0.8	6	8.4 ± 2.1	6	16.3 ± 12.4	6	5.8 ± 0.9
Administratiors	8	1.7 ± 0.8	8	4.9 ± 2.0	8	3.0 ± 0.7	8	5.7 ± 2.3	8	3.0 ± 0.6	8	3.6 ± 0.6	8	3.1 ± 0.7	7	4.1 ± 1.2	7	1.9 ± 0.5	5	2.4 ± 0.9	7	3.4 ± 0.9	7	9.7 ± 6.9	7	10.3 ± 4.8

Abbreviation: SE = Standard error; AM = morning (preshift); PM = afternoon (postshift).

Supplemental Table 4. Daily averaged ambient personal and area melamine and formaldehyde concentrations (µg/m^3) in melamine workers by work sites.

	Monday		Tuesday		Wednesday		Thursday		Friday		Five days	
	N	Mean ± SE	N	Mean ± SE	N	Mean ± SE	N	Mean ± SE	N	Mean ± SE	N	Mean ± SE
Melamine												
Personal samplers												
Manufacturers	5	131.6 ± 64.5	3	15.1 ± 4.5	4	39.1 ± 30.3	5	93.2 ± 54.5	1	426.4	18	97.3 ± 31.4
Grinders	6	14.4 ± 8.4	5	9.1 ± 5.1	5	48.5 ± 57.8	6	115.5 ± 51.0	4	32.6 ± 13.5	26	46.1 ± 14.6
Packers	3	12.0 ± 7.9	3	12.3 ± 5.3	0		3	4.2 ± 1.6	1	2.3	10	8.8 ± 2.9
Area samplers												
Manufacturing area	5	23.2 ± 10.2	4	2.7 ± 1.4	5	21.0 ± 13.0	4	16.1 ± 13.8	0		18	16.5 ± 5.4
Grinding area	1	2.7	1	12.5	2	10.1 ± 5.9	0		0		4	8.9 ± 3.2
Packing area	4	2.7 ± 2.2	5	1.6 ± 0.6	4	1.1 ± 0.4	3	1.3 ± 0.2	1	2.6	17	1.8 ± 0.5
Administrative area	2	0.3 ± 0.1	2	0.3 ± 0.0	2	1.2 ± 0.9	1	0.4	1	0.5	8	0.6 ± 0.2
Formaldehyde												
Personal samplers												
Manufacturers	5	229.0 ± 18.5	3	184.6 ± 20.7	5	193.5 ± 11.5	5	212.3 ± 5.3	1	208.8	19	207.2 ± 7.2
Grinders	6	139.3 ± 37.0	5	144.9 ± 32.4	5	113.7 ± 31.6	6	159.3 ± 33.4	4	141.1 ± 20.6	26	140.3 ± 13.9
Packers	2	74.6 ± 34.7	3	44.2 ± 12.7	0	-	3	82.4 ± 52.3	1	21.6	9	61.2 ± 18.2
Area samplers												
Manufacturing area	5	81.2 ± 14.5	4	71.9 ± 18.0	5	109.7 ± 31.1	4	171.5 ± 34.3	0		18	107.1 ± 14.7
Grinding area	1	76.1	1	77.0	2	55.2 ± 2.6	0	-	0		4	65.9 ± 6.3
Packing area	5	31.3 ± 12.7	5	36.5 ± 9.2	5	40.6 ± 6.8	3	45.8 ± 2.1	1	27.6	19	37.2 ± 4.3
Administrative area	2	24.4 ± 18.0	3	30.6 ± 9.6	2	14.7 ± 2.5	1	26.8	1	16.5	9	23.7 ± 4.7

Abbreviation: SE = Standard error.

Supplemental Table 5. Daily averaged ambient concentrations of different dust particle sizes (particulate matter (PM) 10, 2.5, and 1.0 μm) by portable laser aerosol spectrometers and dust monitors in one melamine manufacturing company (Factory A) during work.

Dust size ($\mu g/m^3$)	Manufacturing area					Administrative area					p-value
	N	≤ 100	>100-≤ 200	> 200	Mean±SD (Min, Median, Max)	N	≤ 100	>100-≤ 200	> 200	Mean±SD (Min, Median, Max)	
Monday											
PM 10	381	300	67	14	75.5±53.5 (23.9, 55.6, 398.5)	476	475	0	1	25.7±20.1 (12.9, 23.2, 426.6)	< 0.0001
PM 2.5		304	63	14	73.9±52.2 (23.8, 54.4, 391.3)		475	0	1	24.4±8.7 (12.9, 22.6, 134.9)	< 0.0001
PM 1.0		324	50	7	65.1 ± 44.0 (20.5, 47.4, 320.5)		476	0	0	22.5±5.9 (12.6, 21.5, 51.5)	< 0.0001
Tuesday											
PM 10	389	303	83	3	81.0±32.7 (31.6, 72.4, 248.7)	569	566	3	0	35.5±16.6 (18.4, 30.2, 156.7)	< 0.0001
PM 2.5		316	71	2	77.4±30.0 (31.6, 70.6, 217.1)		566	3	0	34.8±15.6 (18.4, 29.9, 150.5)	< 0.0001
PM 1.0		359	30	0	65.5±22.1 (30.9, 61.1, 164.8)		567	2	0	32.5±13.9 (17.5, 28.4, 122.2)	< 0.0001
Wednesday											
PM 10	386	110	237	39	132.8±60.1 (39.7, 118.6, 479.2)	576	576	0	0	20.2±5.0 (12.6, 19.9, 67.5)	< 0.0001
PM 2.5		119	228	39	128.7±57.0 (39.1, 116.0, 466.4)		576	0	0	19.9±4.4 (12.6, 19.8, 36.9)	<0.0001
PM 1.0		176	190	20	112.4±47.1 (34.5, 103.6, 394.8)		576	0	0	19.0±4.0 (12.0, 19.1, 32.2)	< 0.0001
Thursday											
PM 10	389	41	258	90	180.5±112.7 (62.5, 138.4, 732.2)	570	570	0	0	36.6±10.9 (12.0, 35.4, 73.9)	< 0.0001
PM 2.5		51	251	87	172.6±100.6 (62.2, 134.4, 695.5)		570	0	0	36.3±10.7 (12.0, 35.2, 70.4)	< 0.0001
PM 1.0		92	226	71	149.7±75.8 (59.1, 126.3, 556.7)		570	0	0	34.9±10.3 (11.8, 33.8, 59.6)	< 0.0001
Friday											
PM 10	541	303	132	106	136.7±146.8 (15.8, 91.7, 1861.8)	574	574	0	0	28.6±14.7 (6.8, 27.2, 75.3)	< 0.0001
PM 2.5		312	128	101	131.9±140.2 (14.5, 88.4, 1761.1)		574	0	0	28.2±14.4 (6.8, 26.9, 63.0)	< 0.0001
PM 1.0		348	111	82	112.6±114.6 (11.5, 77.4, 1384.1)		574	0	0	26.2±13.3 (6.5, 25.7, 58.5)	< 0.0001
Five days											
PM 10	2086	1057	777	252	121.1±102.2 (15.8, 98.3, 1861.8)	2765	2761	3	1	29.6±15.6 (6.8, 26.4, 426.6)	< 0.0001
PM 2.5		1102	741	243	116.7±95.9 (14.5, 95.4, 1761.1)		2761	3	1	29.0±13.2 (6.8, 26.2, 150.5)	< 0.0001
PM 1.0		1299	607	180	100.6±77.4 (11.5, 84.4, 1384.1)		2763	2	0	27.3±12.0 (6.5, 24.7, 122.2)	< 0.0001

Abbreviation: SD = Standard deviation.

Supplemental Table 6. Daily variations of preshift and postshift urinary melamine concentrations concentrations in generalized linear mixed models.[a]

Variables	β	SE	95% CI	p-value
a) Model 1[b]				
Work sites				
Non- manufacturers	1	-	-	-
Manufacturers	28.99	8.51	12.31~45.66	0.001
Sampling day				
Mon	1	-	-	-
Tue	-15.73	6.56	-28.58 ~ -2.87	0.016
Wed	-13.27	6.61	-26.2 ~ -0.31	0.045
Thu	-19.22	6.79	-32.54 ~ -5.90	0.005
Fri	-28.91	9.02	-46.59 ~ -11.22	0.001
b) Model 2[b]				
Air melamine (μg/m^3)	0.09	0.04	0.01 ~ 0.17	0.034
Sampling day				
Mon	1	-	-	-
Tue	-9.40	5.15	-19.48 ~ 0.69	0.068
Wed	-0.23	5.51	-11.03 ~ 10.56	0.966
Thu	-12.60	4.96	-22.32 ~ -2.87	0.011
Fri	-22.03	8.84	-39.36 ~ -4.70	0.013
c) Model 3[b]				
Air formaldehyde (μg/m^3)	0.03	0.06	-0.10 ~ 0.15	0.658
Sampling day				
Mon	1	-	-	-
Tue	-13.63	6.33	-26.03 ~ -1.22	0.031
Wed	-6.59	6.51	-19.35 ~ 6.16	0.311
Thu	-15.37	6.14	-27.40 ~ -3.34	0.012
Fri	-20.04	10.53	-40.69 ~ 0.60	0.057
d) Model 4[c]				
Work sites				
Non-manufacturers	1	-	-	-
Manufacturers	39.66	5.47	28.93 ~ 50.38	< 0.001
Day				
Mon	1	-	-	-

Tue	20.25	5.92	8.65 ~ 31.86	0.001
Wed	28.75	5.97	17.06 ~ 40.45	< 0.001
Thu	34.68	6.02	22.89 ~ 46.48	< 0.001
Fri	28.19	6.18	16.07 ~ 40.31	< 0.001
Sat	12.15	6.18	0.03 ~ 24.26	0.049
Sun	5.47	6.18	-6.65 ~ 17.58	0.377
Mon	6.33	6.18	-5.79 ~ 18.44	0.306

Abbreviation: CI = Confidence interval; SE = standard error;

[a]Adjusting for age, sex, educational level, BMI, smoking status, and serum uric acid.

[b]Dependent variable: Daily difference of preshift and postshift urinary melamine concentrations (postshift - preshift).

[c]Dependent variable: Daily preshift urinary melamine concentrations.

Supplemental Table 7. Other clinical and laboratory data in melamine tableware manufacturing workers by work sites and their comparison group.

Variables	Exposed workers (N = 44)				Non-exposed workers	*p*-value[a] (Overall)	*p*-value[b] (Manufacturers *vs.* controls)
	Manufacturers	Grinders	Packers	Administrators	Controls		
N	16	8	10	10	105		
				Mean ± SD (Median, IQR)			
Height (cm)	166.2 ± 7.2	162.3 ± 6.5	156.0 ± 9.5	167.0 ± 10.6	168.1 ± 6.6	0.010	0.307
	(165.0, 159.6-171.4)	(161.0, 158.3-167.8)	(157.0, 153.6-165.3)	(164.0, 160.3-175.5)	(168.6, 163.3-172.9)		
Weight (kg)	63.9 ± 13.1	59.2 ± 6.5	57. 8 ± 9.7	72.4 ± 28.2	67.2 ± 9.5	0.022	0.665
	(67.9, 51.9-72.3)	(59.4, 54.4-64.8)	(56.9, 50.1-65.9)	(62, 53.6-84.8)	(67.6, 60.2-73.6)		
Waist (cm)	79.2 ± 9.8	75.4 ± 5.6	76.2 ± 5.5	84.9 ± 18.5	81.5 ± 11.3	0.011	0.411
	(81.5, 76.3-85.8)	(75.5, 70.3-80.3)	(77.0, 70.8-80.8)	(78.0, 75.3-92.3)	(82.0, 78.0-88.0)		
Hip (cm)	92.1 ± 6.7	93.5 ± 6.4	92.3 ± 5.0	98.3 ± 10.4	93.5 ± 14.0	0.141	0.092
	(93.5, 89.0-96.5)	(92.5, 90.5-93.8)	(93.5, 87.3-96.3)	(95.0, 91.0-102.0)	(95.0, 92.0-99.0)		
Blood Pressure (mmHg)							
Systolic blood pressure	124.3 ± 16.3	117.0 ± 18.0	109.7 ± 10.0	120.5 ± 12.5	132.5 ± 14.2	<0.0001	0.073
	(123.0, 112.8-138.3)	(115.0, 106.3-120.5)	(110.5, 101.8-119.3)	(119.5, 109.8-132.8)	(132.0, 123.0-139.0)		
Diastolic blood pressure	74.6 ± 11.2	68.8 ± 12.1	67.2 ± 8.5	77.0 ± 11.4	84.6 ± 11.8	<0.0001	0.003
	(72.0, 63.0-84.0)	(64.5, 60.3-76.8)	(69.5, 58.8-74.3)	(74.0, 67.3-85.8)	(86.0, 74.5-92.0)		
				N (%)			
Hypertension (> 140/90 mmHg)						0.094	0.231
Abnormal	2 (12.5)	1 (12.5)	0	1 (10.0)	32 (30.5)		
Normal	14 (87.5)	7 (87.5)	10 (100.0)	9 (90.0)	73 (69.5)		
Liver function							

GOT (IU/L)	23.7 ± 6.1	38.8 ± 43.2	21.0 ± 5.6	25.3 ± 10.1	26.4 ± 9.5	0.505	0.402
	(23.5, 18.5-27.0)	(24.0, 19.5-31.3)	(22.5, 17.3-25.5)	(22.5, 18.8-28.0)	(25.0, 20.0-30.0)		
GPT (IU/L)	21.8 ± 12.4	33.6 ± 36.1	17.3 ± 7.0	22.5 ± 18.5	28.2 ± 17.6	0.088	0.131
	(20.5, 14.5-25.5)	(22.0, 15.0-32.8)	(15.5, 11.8-23.0)	(18.5, 9.8-24.8)	(24.0, 16.0-36.0)		
r-GT (IU/L)	36.2 ± 23.2	98.9 ± 187.8	18.6 ± 4.0	30.3 ± 21.5	35.4 ± 32.4	0.046	0.640
	(31.0, 18.8-45.8)	(25.5, 17.5-80.0)	(20.5, 16.5-21.0)	(18.5, 13.0-56.5)	(28.0, 20.0-38.3)		
Cadiometabolic indicators							
Glu(Ac) (mg/dL)	106.9 ± 61.7	84.1 ± 4.9	84.3 ± 10.7	90.5 ± 15.9	100.5 ± 34.3	0.006	0.717
	(89.0, 87.3-97.8)	(84.5, 80.5-88.3)	(82.0, 79.0-88.0)	(90.0, 78.3-96.3)	(93.0, 85.0-101.0)		
T-cholesterol (mg/dL)	187.4 ± 44.9	162.8 ± 20.0	194.0 ± 35.8	183.2 ± 25.8	204.8 ± 36.4	0.004	0.068
	(180.5, 154.5-216.5)	(158.5, 150.5-183.3)	(196.0, 168.0-221.0)	(186.0, 164.5-201.8)	(204.0, 182.0-227.0)		
Triglyceride (mg/dL)	120.1 ± 109.8	120.0 ± 140.2	90.0 ± 42.5	123.1 ± 106.6	119.1 ± 68.3	0.253	0.330
	(90.0, 58.3-141.3)	(76.5, 52.3-101.8)	(82.0, 56.0-108.5)	(72.0, 56.0-167.5)	(102.0, 80.0-147.0)		
Fibrinogen (mg/dL)	258.4 ± 41.4	286.6 ± 75.4	281.6 ± 58.1	281.3 ± 41.7	293.0 ± 62.5	0.300	0.033
	(266.2, 221.6-292.5)	(285.9, 212.0-352.2)	(263.8, 246.5-306.5)	(288.4, 262.6-299.7)	(293.8, 246.5-323.9)		
HSCRP (mg/dL)	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	<0.0001	<0.0001
	(0.1, 0.0-0.1)	(0.1, 0.0-0.1)	(0.1, 0.0-0.1)	(0.1, 0.0-0.2)	(0.1, 0.0-0.1)		
Lung function							
FVC (L)	2.9 ± 0.5	2.8 ± 0.8	2.8 ± 1.1	3.0 ± 0.7	3.5 ± 0.6	<0.0001	0.001
	(2.9, 2.6-3.4)	(2.7, 2.2-3.5)	(2.4, 2.2-3.1)	(2.9, 2.5-3.3)	(3.4, 3.0-3.9)		
FVC (%)	78.8 ± 14.9	81.1 ± 19.6	80.3 ± 10.8	74.6 ± 9.0	89.8 ± 12.6	<0.0001	0.002
	(78.5, 68.2-82.7)	(80.0, 73.9-83.8)	(81.2, 70.0-91.3)	(77.4, 69.4-81.4)	(87.0, 81.5-99.2)		
FEV1 (L)	2.8 ± 0.5	2.6 ± 0.8	2.7 ± 1.1	2.7 ± 0.7	3.3 ± 0.6	<0.0001	0.007
	(2.8, 2.5-3.4)	(2.7, 1.7-3.2)	(2.3, 2.1-2.9)	(2.7, 2.3-2.9)	(3.2, 2.9-3.5)		

FEV1/FVC (%)	96.1 ± 5.4	92.1 ± 7.6	95.8 ± 4.4	92.9 ± 9.3	93.2 ± 5.7	0.195	0.032
	(98.8, 92.0-100.0)	(92.5, 86.1-99.7)	(96.7, 92.4-100.0)	(96.9, 87.8-100.0)	(94.0, 89.5-97.8)		
Blood routine WBC							
WBC (10^3/uL)	6.4 ± 1.6	6.5 ± 1.5	7.0 ± 2.1	7.6 ± 2.0	6.1 ± 1.4	0.094	0.742
	(6.0, 5.3-6.5)	(6.1, 5.1-7.9)	(6.7, 5.1-8.5)	(7.0, 6.4-8.8)	(5.8, 5.2-6.9)		
RBC (10^6/uL)	4.9 ± 0.5	4.6 ± 0.4	4.9 ± 0.5	5.0 ± 0.7	5.2 ± 0.5	0.005	0.032
	(4.8, 4.7-5.4)	(4.6, 4.2-5.0)	(4.8, 4.5-5.4)	(5.0, 4.5-5.6)	(5.2, 4.9-5.4)		
HGB (g/dL)	14.9 ± 1.5	13.8 ± 1.3	13.7 ± 1.5	14.4 ± 1.3	15.2 ± 1.2	0.001	0.402
	(14.8, 13.9-16.3)	(13.6, 13.1-15.3)	(13.8, 12.2-14.5)	(14.1, 13.5-15.6)	(15.4, 14.4-16.0)		
HCT (%)	44.0 ± 4.2	41.6 ± 3.7	41.0 ± 3.4	43.3 ± 3.7	45.2 ± 3.0	<0.0001	0.174
	(43.7, 40.7-47.7)	(41.3, 38.8-45.3)	(40.7, 39.0-42.9)	(42.9, 40.8-45.6)	(45.8, 43.6-47.2)		
MCHC (g/dL)	33.8 ± 0.7	33.3 ± 0.7	33.2 ± 1.2	33.3 ± 0.9	33.6 ± 1.0	0.433	0.415
	(33.8, 33.3-34.3)	(33.4, 32.5-33.9)	(33.4, 32.15-34.33)	(33.0, 32.7-34.1)	(33.6, 33.1-34.2)		
MCH (pg)	30.4 ± 2.4	29.9 ± 1.4	28.1 ± 3.6	28.9 ± 3.0	29.3 ± 2.9	0.121	0.044
	(30.7, 30.1-31.5)	(29.8, 28.5-31.4)	(29.8, 26.9-30.1)	(30.0, 28.4-30.5)	(30.1, 28.9-30.9)		
MCV (fl)	89.7 ± 6.5	89.9 ± 3 .2	84.4 ± 9.2	86.6 ± 8.3	87.2 ± 7.6	0.199	0.049
	(91.7, 89.1-92.8)	(89.3, 86.7-93.3)	(89.2, 80.2-90.0)	(89.8, 82.8-92.3)	(88.6, 85.5-91.4)		
PLT (10^3/uL)	212.1 ± 46.0	221.1 ± 47.5	276.9 ± 67.7	250.3 ± 70.4	233.0 ± 48.8	0.055	0.131
	(206.0, 182.0-248.5)	(205.5, 179.8-262.5)	(289.0, 234.5-318.5)	(249.0, 196.8-273.3)	(232.0, 196.5-268.5)		
				N (%)			
Abdominal echo							
Nephrectomy	0	0	0	1 (10.0)	1 (1.0)	-	-
Gall stone	0	0	0	0	9 (9.0)	-	-
Renal stone	0	1 (12.5)	0	1 (10.0)	10 (10.0)	-	-
Urine routine							

Strip-GLU						0.826	0.546
Normal	13 (81.3)	7 (87.5)	9 (90.0)	9 (90.0)	97 (92.4)		
Abnormal	1 (6.3)	0	0	0	5 (4.8)		
Miss	2 (12.5)	1 (12.5)	1 (10.0)	1 (10.0)	3 (2.9)		
Strip-BIL						0.005	-
Normal	14 (87.5)	7 (87.5)	8 (80.0)	9 (90.0)	102 (97.1)		
Abnormal	0	0	1 (10.0)	0	0		
Miss	2 (12.5)	1 (12.5)	1 (10.0)	1 (10.0)	3 (2.9)		
Strip-KET						0.542	0.346
Normal	12 (75.0)	7 (87.5)	9 (90.0)	9 (90.0)	94 (89.5)		
Abnormal	2 (12.5)	0	0	0	8 (7.6)		
Miss	2 (12.5)	1 (12.5)	1 (10.0)	1 (10.0)	3 (2.9)		
Strip-SG						0.399	0.248
Normal	12 (75.0)	6 (75.0)	8 (80.0)	7 (70.0)	96 (91.4)		
Abnormal	2 (12.5)	1 (12.5)	1 (10.0)	2 (20.0)	6 (5.7)		
Miss	2 (12.5)	1 (12.5)	1 (10.0)	1 (10.0)	3 (2.9)		
Strip-OB						0.830	0.637
Normal	12 (75.0)	6 (75.0)	8 (80.0)	7 (70.0)	92 (87.6)		
Abnormal	2 (12.5)	1 (12.5)	1 (10.0)	2 (20.0)	10 (9.5)		
Miss	2 (12.5)	1 (12.5)	1 (10.0)	1 (10.0)	3 (2.9)		
Strip-PH						-	-
Normal	14 (87.5)	7 (87.5)	9 (90.0)	9 (90.0)	102 (97.1)		
Abnormal	0	0	0	0	0		
Miss	2 (12.5)	1 (12.5)	1 (10.0)	1 (10.0)	3 (2.9)		
Strip-PRO						0.538	0.302

Normal	9 (56.3)	6 (75.0)	8 (80.0)	8 (80.0)	81 (77.1)		
Abnormal	5 (31.3)	1 (12.5)	1 (10.0)	1 (10.0)	21 (21.0)		
Miss	2 (12.5)	1 (12.5)	1 (10.0)	1 (10.0)	3 (2.9)		
Strip-URO						0.883	1
Normal	14 (87.5)	7 (87.5)	9 (90.0)	9 (90.0)	99 (94.3)		
Abnormal	0	0	0	0	3 (2.9)		
Miss	2 (12.5)	1 (12.5)	1 (10.0)	1 (10.0)	3 (2.9)		
Strip-NIT						0.005	-
Normal	14 (87.5)	7 (87.5)	9 (90.0)	8 (80.0)	102 (97.1)		
Abnormal	0	0	0	1 (10.0)	0		
Miss	2 (12.5)	1 (12.5)	1 (10.0)	1 (10.0)	3 (2.9)		
Strip-WBC						<0.0001	1
Normal	14 (87.5)	5 (62.5)	5 (50.0)	5 (50.0)	99 (94.3)		
Abnormal	0	2 (25.0)	4 (40.0)	4 (40.0)	3 (2.9)		
Miss	2 (12.5)	1 (12.5)	1 (10.0)	1 (10.0)	3 (2.9)		

Abbreviation: SD = Standard deviation; IQR = interquarter range.

[a]Kruskal-Wallis test or Chi-square test.
[b]Wilcoxon rank sum test or Fisher's exact test.

Supplemental Table 8. Relationship of urinary biomarkers of renal injury with urinary melamine levels or work sites after adjusting for hypertension in multiple linear regression models.

				Adjusted[c]	
Log_{10} NAG[a]	**N**	**Mean ± SD**	**Median, IQR**	**β (SE)**	**p-value**
Model1					
Urinary melamine (μg/mmol Cr)	81	0.7 ± 1.5	0.5, 0.3-0.8	0.004 (0.001)	0.0003
Hypertension (mmHg)					
Normal	61	0.6 ± 0.4	0.5, 0.3-0.8	1	-
Abnormal (>140/90)	20	1.2 ± 3.0	0.5, 0.4-0.7	0.169 (0.076)	0.029
Model2[d]					
Non-exposed workers	105	0.4 ± 0.2	0.4, 0.3-0.5	1	-
Administrators	9	0.6 ± 0.3	0.6, 0.4-0.8	0.162 (0.103)	0.119
Grinders & packers	16	0.7 ± 0.6	0.7, 0.3-0.9	0.103 (0.093)	0.272
Manufacturers	14	1.8 ± 3.5	0.9, 0.4-1.4	0.234 (0.102)	0.023[e]
Hypertension (mmHg)					
Normal	108	0.5 ± 0.4	0.4, 0.3-0.7	1	-
Abnormal (>140/90)	36	0.9 ± 2.3	0.5, 0.3-0.6	0.157 (0.054)	0.004
Log_{10} Microalbumin[a]					
Model1					
Urinary melamine (μg/mmol Cr)	81	3.3 ± 20.5	0.5, 0.4-1.0	0.003 (0.001)	0.063
Hypertension (mmHg)					
Normal	61	0.9 ± 1.4	0.5, 0.4-0.8	1	-
Abnormal (>140/90)	20	10.3 ± 41.2	0.6, 0.4-1.3	0.273 (0.110)	0.016
Model2					
Non-exposed workers	105	1.9 ± 6.8	0.6, 0.4-0.9	1	-
Administrators	9	1.5 ± 2.7	0.4, 0.3-0.6	-0.153 (0.178)	0.389
Grinders & packers	16	0.9 ± 0.5	0.6, 0.4-1.5	-0.161 (0.161)	0.320
Manufacturers	14	14.8 ± 49.2	0.8, 0.4-1.1	0.048 (0.176)	0.784
Hypertension (mmHg)					
Normal	108	0.9 ± 1.4	0.6, 0.4-0.9	1	-
Abnormal (>140/90)	36	9.4 ± 32.2	0.6, 0.5-1.6	0.304 (0.093)	0.001

β2-Microglobulin[a]	**N**	**Normal N (%)**	**Abnormal N (%)**	**Adjusted OR (95%CI)[c]**
Model1				
Urinary melamine (μg/mmol Cr)	81	75 (92.6)	6 (7.4)	1.03 (1.01-1.06)
Hypertension (mmHg)				
Normal	61	56 (74.7)	5 (83.3)	1
Abnormal (>140/90)	20	19 (25.3)	1 (16.7)	0.24 (0.01-8.20)
Model2[d]				
Non-exposed workers	105	101 (96.2)	4 (3.8)	1
Administrators	9	9 (100.0)	0	-
Grinders & packers	16	15 (93.8)	1 (6.2)	0.73 (0.04-15.27)
Manufacturers	14	10 (71.4)	4 (28.6)	26.39 (1.09-636.79)
Hypertension (mmHg)				
Normal	108	101 (74.8)	7 (77.8)	1
Abnormal (>140/90)	36	34 (25.2)	2 (22.2)	0.87 (0.82-1.52)

Abbreviation: BMI = Body mass index; Cr = creatinine; NAG = N-acetyl-beta-D-glucosaminidase; OR = odds ratio.
[a]Multiple linear regression or logistic regression.
[c]Adjusting for age, sex, BMI, educational level, cigarette smoking, and serum uric acid.
[d]Missing data, N = 1 for office staff, 2 for grinders & packers, and 2 for manufacturers.

Supplemental Table 9. Summary of literature data about industry of melamine-formaldehyde resin related to occupational melamine exposure.

Study	Subjects/Source	Exposure assessment	Ambient F/M[a]	Main results
Case report or case series				
Srivastava et al., 1992 [India][8]	Six male workers who were employed for 3-10 years in the preparation of melamine resin from melamine formaldehyde in a paper mill.	Measure urinary formic acid, one metabolite of formaldehyde	-/-	1. Range of urinary formic acid was 13.5-173.0 mg/1 (n = 6). 2. 4/6 of the subjects had low values of hemoglobin (< 14g%) and 3/6 had raised total lymphocyte counts (>3200).
Aalto-Korte et al., 2003 [Finland][9]	1. Plywood industry (A 26-year-old man) 2. Production of melamine-laminated chipboard (A 38-year-old female) 3. Laboratory of analysis and production of resins (A 38-year-old female)	-	-/-	Allergic contact dermatitis (Formaldehyde-negative)
Garcia Gavin et al., 2008 [Spain][10]	Plywood worker in the melamine paper impregnation line (A 28-year-old female)	-	-/-	Contact allergic dermatitis (patch-test: positive to melamine formaldehyde resins but negative to formaldehyde)
Epidemiologic study				
Niemela & Vainio, 1981 [Finland][11]	Melamine-formaldehyde plastic in electrical machinery Urea and melamine resins in particle board plants	Monitor ambient formaldehyde concentrations in workplaces	+/-	Formaldehyde concentrations in air: $0.25\text{-}0.63\ mg/m^3$ (n = 8) $0.13\text{-}6.13\ mg/m^3$ (n = 220)
Marsh et al., 1992 [PA, USA][12]	Study 20,067 white male workers exposed to formaldehyde in the presence of 12 selected co-exposures, including melamine exposure	Questionnaire	-/-	Lung cancer mortality Significant positive associations were found between the risk of lung cancer and cumulative exposure to formaldehyde in the presence of several co-exposures, including melamine (estimated RR=1.59 with over 1.5ppm-yr, p=0.04).
Isaksson et al., 1999 [Sweden][13]	88 workers, employed for 4-6 years, worked in the composite production with the use of cellulose fibers and melamine-formaldehyde resins	Questionnaire	-/-	Occupational dermatoses 1. 10.2% (9/88) diagnosed with occupational dermatoses 2. 5 workers had contact allergy to melamine-formaldehyde resin
Lazarov. 2004 [Israel][14]	644 contact dermatitis patients suspected exposed to textile	-	-/-	83 (12.9%) had an allergic reaction to textile dyes and melamine formaldehyde resins.
Neghab et al., 2011 [Iran][15]	70 workers employed for 13.2±7.8 years, and 24 controls employed for 14.5±8.1 years in a melamine-formaldehyde resin producing plant	Monitor ambient formaldehyde concentrations in workplaces	+/-	Respiratory morbidity 1. Area formaldehyde: 0.78±0.4 ppm[b] for 7 workshops and ND for 1 office areas 2. Exposed group had higher frequency of respiratory symptoms. 3. Pulmonary function was significant decrements in preshift and postshift of exposed group.
Wu et al., 2014 [Taiwan in our study]	44 exposed workers in melamine tableware manufacturing factories and 105 controls	1. Monitor ambient formaldehyde concentrations in workplaces 2. Monitor	+/+	Renal function impairment 1. Area formaldehyde: $107.1\pm14.7\mu g/m^3$ in manufacturing area (n=18) and $23.7\pm4.7\mu g/m^3$ in office area (n=9) Area melamine: $16.5\pm5.4\mu g/m^3$ in manufacturing area (n=18) and $0.6\pm0.2\mu g/m^3$ in office area (n=8)

		personal formaldehyde concentrations in workplaces	2. Personal formaldehyde: 207.2±7.2μg/m^3 in manufacturing area (n=19) Personal melamine: 97.3±31.4μg/m^3 in manufacturing area (n=18) 3. Manufacturers had the highest NAG levels and the highest detectable β2-MG than controls, but not found in urinary microalbumin.

[a]F: ambient formaldehyde measurement; M: ambient melamine measurement
[b]Exceeded current permissible levels (0.3ppm) in Iran, 1ppm=1.2 mg/m^3.

Supplemental Table 10. Summary of urinary melamine concentration variations in different populations from the literature.

Study / study time	Subjects	Analytic methods	Markers for renal damages in urine	Results				
				Study groups	Melamine concentrations without creatinine correction (ng/ml)	Melamine concentrations with creatinine correction (µg/mmol Cr)	% of < LOQ/MDL	Outcome of renal injuries
Affected children from 2008 melamine incident								
Lam et al., 2009 [Hong Kong, China][16] 2008/9	14 cases (urinary stones) 20 controls (non-stones) (Aged < 3 yrs) All with a confirmed history of consuming melamine-tainted milk	LC-MS/MS (SPE) MDL: not available	Protein, microalbumin, β2-MG	Cases	-	21[a] (0.87-2002)	0	2/11 cases and no controls with detectable β2-MG
				Controls	-	6.6[a] (0.08-37)	0	
Cheng et al., 2009 [Taipei, Taiwan][17] 2008/9	10 nephrolithiasis 20 matched-controls (Aged 2-9 yrs)	UPLC-MS/MS (SPE) LOQ: 10 ppb MDL: 6 ppb	-	Cases	- (30-300)	- (9-71)[b]	70	-
				Controls	- (20)	- (2.3-2.6)[b]	90	
Zhang et al., 2010 [Shanghai, China][18] After 2008/9	86 children suspected to have ingested melamine-tainted powdered formula (Aged 0-8 yrs)	LC-MS/MS (LLE) LOQ: 10 ppb	-		< 10 (17.4%) **10-100 (46.5%)** 100-1000 (17.4%) 1000-10000 (16.3%) > 10000 (2.3%)	-	-	-
Gao et al., 2011 [Shanghai, china][19]	96 children with melamine-tainted milk associated urolithiasis: Baseline & follow-up at 6 months (Aged ≤ 6 yrs)	-	Microalbumin, immunoglobulin G, NAG		-	-	-	Detection rate of abnormal urinary microprotein excretion: 54.2% in children with persistent stones, *vs.* 38.2% in children who passed their stones
Urolithiasis in adults								
Wu et al., 2010 [Kaoshiung, Taiwan][4] 2003-2007	11 uric acid stones 21 calcium stones 22 matched-controls (Aged 36-69 yrs)	LC-MS/MS (SPE) LOQ: 2 ppb MDL: 0.4 ppb	-	Uric acid stones	3.5	0.5	36.4	-
				Calcium stones	1.02	0.14	38.1	
				Controls	0.4	0.06	68.2	

Liu et al., 2011 [Kaohsiung, Taiwan][20] 2003-2007	211 calcium stones 211 matched-controls (Aged 22-85 yrs)	LC-MS/MS (SPE) LOQ: 1 ppb MDL: 0.2 ppb	-	Calcium stones	0.9	0.21	37.9	-
				Controls	0.2	0.02	79.6	
General population								
Zhang et al., 2010 [Shanghai, China][18] After 2008/9	110 adults (Aged 25-75 yrs) for health examination after the 2008 melamine incident	LC-MS/MS (LLE) LOQ: 10 ppb	-		< 10 (12.7%) **10-100 (69.1%)** 100-1000 (13.6%) 1000-10000 (4.5%) > 10000 (0%)	-	-	-
Kong et al., 2011 [Hong Kong, China][21] 2007-2008	502 school children (Aged 6-20 yrs)	LC-MS/MS LOQ: 5 ppb	Albumin		-	0.8 (ND-1467)	42.0	High melamine exposure (> 7.1 μg/mmol Cr) not associated with high excretion of albumin in urine
Panuwet et al., 2012 [Georgia, USA][22] Not available	492 general US adults	LC-MS/MS (SPE) Method LOD: 0.66 ppb	-		GM 2.37 (ND-161)	-	24.0	-
Lin et al., 2013 [Kaohsiung, Taiwan][5] 2011	22 school children (median age 8.0 yrs) and their parents (n = 44, median age 40 yrs)	LC-MS/MS (SPE) LOQ: 2 ppb MDL: 0.4 ppb	NAG, β2-MG, microalbumin	Children	7.20-9.42	0.93-1.73	0	No associations between melamine exposure and urinary NAG and microalbumin
				Mothers Fathers	4.49-6.53 4.91-5.11	0.87-1.21 0.84-0.87	2.9	
Wu et al., 2013 [Kaohsiung, Taiwan][23] 2011/12	12 volunteers (Aged 20-27 yrs) Cross-over study design 6/6 melamine tableware 6/6 ceramic tableware		-	Melamine 0 hr	9.41	0.98	0	-
				6 hr	26.89	5.59		
				Ceramic 0 hr	11.40	1.02	33.0	
				6 hr	1.26	0.25		
Occupational workers								
Our study [Kaohsiung, Taiwan] 2012/8-12	Two melamine tableware manufacturing factories (Aged 25-57 yrs) 44 exposed workers, including 16 manufacturers 8 grinders	LC-MS/MS (SPE) LOQ: 2 ppb MDL: 0.4 ppb	NAG, β2-MG, microalbumin	Manufacturers	943.0	80.5	0	Urinary melamine levels were **significantly and positively** associated with NAG levels and the detectable rate of β2-MG.
				Grinders	206.3	16.2	0	
				Packers	252.6	15.9	0	

10 packers 10 administrators 105 non-exposed workers from one shipbuilding company as controls (Aged 21-63 yrs)	Administr ators	18.2	1.9	0
	Controls	4.3	0.3	7.1

Value represent as Median (range).

Abbreviation: Cr = Creatinine; LOQ = the lower limit of quantitation; MDL = the method detection limit; LC-MS/MS = liquid chromatography tandem mass spectrometry; SPE = solid-phase extraction; UPLC-MS/MS = ultra performance liquid chromatography tandem mass spectrometry; LLE = liquid-liquid extraction; β2-MG = beta 2-microglobulin; NAG = N-acetyl-β-glucosaminidase; ND = non detectable; GM = geometric mean.

[a]Urine samples collected at least 10 days of stopping the consumption of melamine-tainted milk products (Lam et al., 2009)[16].

[b]Urine samples collected at first visit or 1 week later (Cheng et al., 2009).[17]