Visual and ocular changes associated with exposure to two tertiary amines

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BACKGROUND
Facility and process description
This label printing plant is one of the largest flexographic printing operations for consumer product labelling in the United States. Flexography printing is a form of rotary web letter press that uses flexible rubber plates mounted to a printing cylinder. The production facility opened in 1995. The facility operates two 10-hour shifts on Monday to Thursday, and not on weekends when production had not been able to associate these visual changes with any particular substance in use. The symptoms were reported only by employees in the line division of the plant, only on Mondays to Thursdays, and not on weekends when production was lower.

Aims: To determine if exposure to dimethylisopropanolamine (DMIPA) and dimethylaminoethanol (DMAE) in a label printing plant was associated with visual disturbances and/or ocular changes.

Methods: Questionnaires, eye examinations (visual acuity, contrast sensitivity at 2.5% and 1.25% contrast, slit lamp biomicroscopy, and pachymetry), and industrial hygiene monitoring for DMIPA and DMAE were performed over a two week period.

Results: Eighty nine per cent of line workers reported having experienced blurry vision while at work in the past 12 months, compared to 12.5% of prime workers. A total of 108 full shift personal breathing zone (PBZ) air samples for the amines were collected. The mean time weighted average (TWA) concentration of DMIPA was significantly higher in the line division than in the prime division, as was the mean TWA concentration for total amines. The mean TWA concentration of DMAE was higher in the prime division than the line division. Higher levels of total amines were associated with increased risk of reporting blurry vision, halo vision, and blue-grey vision. The risk of corneal opacity rose with increasing exposure to total amines. The prevalence of corneal opacity also increased with increasing concentration of total amines. Median corneal thickness increased with increasing grades of corneal opacity. There was a statistically significant relation between total amine concentration and increased risk of reduced bilateral visual acuity and 2.5% contrast sensitivity.

Conclusions: Exposure to tertiary amines was associated with blurry, halo, and blue-grey vision, corneal opacity, and decrements in visual acuity and contrast sensitivity at 2.5% contrast.

Main messages
- Exposure to DMIPA and DMAE can cause corneal opacity, with resultant decrements in visual acuity and contrast sensitivity.
- These effects, while reversible, pose an immediate safety hazard.

Policy implications
- Manufacturers of DMIPA and DMAE, or of compounds containing them, should consider listing visual disturbances as an adverse health effect.

is occasional use of fluorescent inks, but no use of UV inks. The prime division has seven printing presses which operate at lower speeds (150–175 feet per minute) and also use mainly water based inks. UV and fluorescent inks are used in the prime division, but less commonly than water based inks. Each press has several five-gallon pails for holding inks before the inks are pumped to ink troughs where plate rolls and cylinders are mounted.

The water based inks contain 1% dimethylaminoethanol (DMEA) (synonym is dimethylethanolamine) and, depending on the specific ink, varying concentrations of ammonia.

Abbreviations: CFM, cubic feet per minute; CI, confidence interval; DMAE, dimethylaminoethanol; DMEA, dimethylethylamine; DMIPA, dimethylisopropanolamine; NIOSH, National Institute for Occupational Safety and Health; NMAM, NIOSH Manual of Analytical Methods; OR, odds ratio; PBZ, personal breathing zone; SF6, sulphur hexafluoride; TEA, triethylamine; TWA, time weighted average; UV, ultraviolet
isopropyl alcohol, and glycol ether. A compound called clean print additive (containing 45% DMAE and 55% water) is used, primarily on the prime side, to increase drying time on the inks. A pH adjuster containing dimethylisopropanolamine (DMIPA) (synonyms dimepranol and 1-dimethylamino-2-propanol) is used daily, primarily in the line division. Print additives, such as the pH adjuster and clean print additive, are manually added to inks stored in the five-gallon pails as needed.

Each press was equipped with blowers to cool UV lamps, and exhaust ventilation to control ozone generated by UV lamps. Conditioned make-up air is supplied to the production areas by fan coil units. The exhaust ducts on the outside of the building had previously terminated on the north wall below the roof line. Concerned that the re-entry of air contaminants from printing presses exhaust back into the building may be causing or contributing to the eye problems, the company had the duct work extended above the roofline. The extensions were configured to curve downward at the end, aiming the discharge towards the surface of the slightly sloped roof.

Amines

Aliphatic amines are ammonia derivatives in which an alkyl or alkanol group replaces one or more hydrogen atoms. They are classified as primary, secondary, or tertiary amines based on the number of substitutions. They are used as solvents, chemical intermediates, catalysts, preservatives, drugs, and herbicides.

The tertiary amines are irritants to both the skin and mucous membranes. Systemic symptoms related to inhalational exposure to tertiary amines include headache, nausea, and faintness. A number of reports describe blurred vision, halo vision, or blue-grey vision (glauropsia) among persons exposed to DMEA. Animal experiments did not cause similar effects, indicating that exposure to brief peak concentrations may account for at least some of the effects reported by workers.

A study of industrial exposure to TEA in foundry cold box workers measured airborne concentrations ranging from less than 0.3 to 20.3 mg/m³. Symptoms of blurred vision, halo vision, and blue hazy vision were more common in workers with exposure to TEA greater than 10 mg/m³, but this finding was not statistically significant. Corneal thickness did not increase significantly by the end of the shift, either in exposed workers or in symptomatic workers. In another study, Jarvinen and Hyvärinen measured contrast sensitivity of foundry cold box core makers with exposure to TEA. Contrast sensitivity decreased significantly over the shift, but this did not correlate with concentrations of TEA in the urine. Airborne concentrations of TEA ranged from 0.3 to 60 mg/m³, with very high peak concentrations, suggesting that exposure to high peak concentrations may be responsible for symptoms, or that it may be an “on-off” as opposed to a dose-response phenomenon. The Occupational Safety and Health Administration permissible exposure limit for TEA is 100 mg/m³, and the American Conference of Governmental Industrial Hygienists threshold limit value is 4.14 mg/m³.

Blurred, hazy vision has also been reported with exposure to DMAE. Symptoms were reported at DMAE concentrations of 6–10 mg/m³ of air as an eight hour TWA, and 25–29 mg/m³ over 15 minutes in three workers at an aluminium casting foundry. Workers without symptoms had exposure to concentrations of DMAE below 5 mg/m³. Therefore investigators concluded that the visual disturbances were caused by short term exposures to high peak concentrations of DMAE. Corneal oedema and increased corneal thickness, along with visual disturbances, were noted at airborne concentrations of DMAE of 40–50 mg/m³ over eight hours in human experiments. The same paper reports that in an occupational setting with median eight hour TWA exposures of 3.3 mg/m³, two of 12 workers experienced visual symptoms and one had corneal oedema in one eye. These two workers’ exposures were about 25 mg/m³ as an eight hour TWA with peak exposures above 100 mg/m³. The authors concluded that the differences between their findings and reports of visual disturbances at lower concentrations in workplace settings may be caused by high peak concentrations in the workplace. There are no occupational exposure limits for DMAE.

DMAE, which is present in the inks used in the study plant, is another tertiary amine. No reports were found in the literature of humans experiencing visual disturbances after exposure to DMEA. However, animal experiments did document corneal opacification, corneal oedema, and ulcerative keratitis at exposures greater than 288 ppm (861
limits for either DMAE or DMIPA.

disturbances in humans. There are no occupational exposure
used in the study plant, has not been reported to cause visual

corneal opacity that regressed during non-exposure periods.

of the building.

opening of one of the curved exhaust discharges on the roof,

that were tested included silica gel, Carbosieve S III, carbon
molecular sieve (CMS), XAD-2 resin, and XAD-7 resin. In the
desorption study, using methanol as a solvent, DMAIPA and
DMIPA were recovered at the highest rate from XAD-7 tubes,
and at the lowest rate from silica gel. Therefore, an air
sampling strategy using the XAD-7 tubes was devised for fur-
ther industrial hygiene monitoring.

For eight workdays comprehensive industrial hygiene
monitoring was performed to assess workers’ full shift and
short term exposures to DMIPA and DMAE. A total of 108 full
shift personal breathing zone (PBZ) air samples for the amines
were collected, 93 in the line division and 15 in the prime divi-
sion. Twelve area air samples were collected in the office area
of the plant and outdoors. Each air sample was collected on an
XAD-7 tube connected to air sampling pumps pre- and
post-calibrated at 100 cc/min of air per min. In accordance
with NMAM No. 2007, each sample collected was analysed for
both DMIPA and DMAE by gas chromatography equipped
with a flame ionisation detector.

Ventilation

A qualitative assessment of the ventilation system was
performed by releasing a glycol based aerosol “fog” from the
new exhaust discharge location on top of the roof on the north
side of the building and from below the roof line, high on the
north outside wall of the building, simulating the previous
exhaust discharge location. The fog was observed and
videotaped.

A tracer gas study was conducted to quantitatively
determine if exhaust re-entered the plant through air intake
grilles located close to the exhaust discharges on the north
side of the building. Ten MIRAN-203 infrared specific vapour
analysers, three B&K-1302 photoacoustic infrared multi-gas
monitors, and an INOVA-1312 photoacoustic multi-gas moni-
tor were positioned inside the plant. Six instruments (four
MIRANs, a B&K, and the INOVA) were placed at widely sepa-
rated locations in the line division, one MIRAN was located in
the office area, two MIRANs were placed near the shredder/
compactors in the warehouse area, one MIRAN was placed in
the ink area, and two MIRANs and a B&K were set up in the
prime division. One B&K multi-gas monitor was used for
mobile monitoring wherever needed. A low toxicity gas,

sulphur hexafluoride (SF₆) was then released first from the
opening of one of the curved exhaust discharges on the roof,
then from the previous exhaust discharge location on the side
of the building.

Tracer gas was also used inside the building to assess the
transport and dispersion contaminants in the line division.

The concentrations recorded by the instruments were
stored in a digital format to be analysed later, both tabulated
on computer spreadsheets and visualised on concentration
versus time charts. Starting with the known time of SF₆
release, the visualised concentration charts were inspected for
any increases that could be identified as coming from the
released SF₆. If peaks were identified, the time between the
release of SF₆ and the appearance of the peak was noted, as
was the duration and magnitude of the peak.

Medical

All employees in the line division of the plant were recruited
to take part in the evaluation. All participants gave written
informed consent. Those who were wearing contact lenses at
the time of the evaluation were not eligible to participate
because of the possibility of absorption of the chemicals into
the contacts and because contact lenses can cause changes
in the corneal epithelium. Workers were informed of this
in advance so they could discontinue contact lens use in order
to participate, if desired. The medical evaluation consisted of a
baseline questionnaire to determine whether the worker had
blurred or foggy vision, halo vision, or blue-grey vision in the
past year, if these symptoms were accompanied by eye irrita-
tion, and if they caused difficulty working or driving home. A
history of eye disease or injury was obtained as well.

The same baseline questionnaire was administered to
workers in the prime division. Workers in the prime division
who reported having experienced blurred, halo, or blue-grey
vision in the past were asked to participate in the study.

Eye examinations were performed each day from Monday
to Thursday at the beginning and end of both shifts. The
examination consisted of visual acuity, contrast sensitivity at
2.5% and 1.2% contrast, ultrasonic pachymetry to determine
corneal thickness, and a slit lamp examination to determine
the presence of corneal opacity. Visual acuity and contrast
sensitivity were performed at a distance of 10 feet with a
luminance level of 125 candelas per square metre (Precision
Vision, LaSalle, Illinois). A loss of at least one line or row on
the chart was considered a reduction in visual acuity or
contrast sensitivity. Corneal thickness was performed using an
ultrasonic pachymeter (Sonomed, Inc., Micropach model
200P) reported in mm. Corneal opacity was graded on a scale
of 0 (normal or clear), 1 (minimal/mild opacity), 2 (moderate
opacity), and 3 (marked opacity). The slit lamp examinations
and pachymetry were conducted by a board certified ophthal-
mologist. Employees were administered a brief questionnaire
each examination documenting current symptoms. The visual
test examiners were unaware of current visual
symptoms of employees.

Statistical analysis

SAS version 8.1 software (SAS Institute, Cary, North Carolina)
was used for the statistical analyses. SAS Proc Mixed, which
can take into account the multiple measures for some
subjects, was used to compare amine exposure means for
those in the line and prime divisions, and for those with
and without visual symptoms/signs. A p value of <0.05 was
considered statistically significant. SAS Proc Genmod, which
also handles repeated measures for subjects, was used to per-
form logistic regression analyses. Logistic regression was used
to examine (SF₆) relations between visual symptoms/signs
and the amine exposure levels. The OR reflects a per unit
increase of 1 mg/m³ in amine concentration. The logistic
regression analyses generated an odds ratio (OR) as a measure
of association. Odds ratios greater than one indicate a positive relation between a symptom/sign and an amine exposure level. Together with the OR, a 95% confidence interval (CI) for the OR was calculated. The OR is considered statistically significant if the 95% CI does not include the number one.

RESULTS

Industrial hygiene

Table 1 summarises the full shift PBZ air sampling results. The mean TWA concentration of DMIPA was significantly higher in the line division than in the prime division (7.70 v 2.08 mg/m³, p < 0.01), as was the mean TWA concentration for total amines (9.96 v 5.56 mg/m³, p < 0.01). The mean TWA concentration of DMAE was higher in the prime division than the line division (3.47 v 2.27 mg/m³, p < 0.01). Total amine TWA concentrations in the office areas ranged from 0.2 to 1.9 mg/m³ and were non-detectable outdoors.

Ventilation

From the outside, the smoke-like fog revealed that air flowed into the plant through all doorways. Inside the plant, air flowed into the line division from all surrounding areas. Within the line division, air moved from the southeast corner to the north and east where the label printing equipment local exhaust removed it from the plant.

A small amount of tracer gas (SF₆) was detected inside the building following both outside releases. However, because of the inability to determine a concentration of tracer gas in the outdoor air in the unbounded vicinity of the air intakes, in the presence of variable, wind-driven air currents, a numerically accurate quantification of the amount of contaminant re-entering the building could not be calculated.

A much greater response of the instruments resulted when tracer gas was released inside the building. An air exchange rate of 1.2 air changes per hour was calculated from the tracer gas decay curve. Based on a floor area of over 14 000 ft² and an average ceiling height of 20 ft, the ventilation rate for the line side is estimated at approximately 6000 cubic feet per minute (CFM).

Medical

One hundred per cent of line and prime workers present at the time of the study filled out the baseline questionnaire, 24 from the prime division and 36 from the line division of the plant. Eighty nine per cent of line workers reported having experienced blurry vision while at work in the past 12 months, compared to 12.5% of prime workers (p < 0.01). Findings were similar for halo and blue-grey vision, with 72% of line workers reporting halo vision compared to 8% of prime workers (p < 0.01), and 14% of line workers reporting blue-grey vision compared to 0% of prime workers (p = 0.08). None of the workers reported medical conditions that would affect their vision. Forty seven per cent of those reporting blurry, halo, or blue-grey vision experienced eye irritation along with the visual changes, 44% reported difficulty performing their job as a result of the visual changes, and 39% reported difficulty driving home.

Three of the 24 prime workers reported blurry vision while at work and therefore participated in the remainder of the study for at least one day. Twenty seven of the 36 line workers participated in the remainder of the study for at least one full day. Therefore, 30 workers participated from one to four days each, for a total of 96 observations. Each observation includes both pre- and post-shift eye examinations and environmental sampling. No workers declined to participate because of contact lens use.

None of the participants had any corneal opacity at the beginning of the shift on any day. Baseline, or beginning of shift, bilateral visual acuity was 10/10 or better, bilateral contrast sensitivity at 2.5% contrast was 10/32 or better, and bilateral contrast sensitivity at 1.25% contrast was 10/50 or better for all participants. During the course of the study, there were 43 episodes of blurred vision reported, 20 episodes of halo vision, and 15 episodes of blue-grey vision. All reports of halo or blue-grey vision occurred in workers who also reported blurry vision; however, the converse is not true. Symptoms developed an average of 4.3 hours after the beginning of the shift. There were 16 episodes of decreased (defined as loss of

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Full shift personal breathing zone concentrations for amines by location (in mg/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Line (n=93)</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
</tr>
<tr>
<td>Dimethylaminoethanol (DMAE)*</td>
<td>2.27</td>
</tr>
<tr>
<td>Dimethylisopropanolamine (DMIPA)*</td>
<td>7.70</td>
</tr>
<tr>
<td>Total amines*</td>
<td>9.96</td>
</tr>
</tbody>
</table>

*Mean amine concentrations differ by location (p<0.01).
There was a positive association between reported visual symptoms and PBZ concentrations of total amines. Exposures to higher levels of total amines were associated with increased risk of reporting blurry vision (OR 1.78, 95% CI 1.41 to 2.26), halo vision (OR 1.38, 95% CI 1.20 to 1.58), and blue-grey vision (OR 1.77, 95% CI 1.31 to 2.39) at the end of a shift. All OR reported in this paper reflect a per unit increase of 1 mg/m$^3$ in amine concentration. Symptom reporting increased with exposure to increasing concentrations of amines (table 2). Results were similar when evaluating the relation between symptom reporting and exposure to the individual amines (DMIPA and DMAE).

The risk of developing corneal opacity over a shift rose with increasing exposure to total amines (OR 1.15, 95% CI 1.02 to 1.30). The prevalence of corneal opacity also increased with exposure to increasing concentrations of total amines (table 3). Similar results were found when evaluating exposure to DMIPA and DMAE separately.

The prevalence of increased corneal thickness in either eye over a shift increased with higher levels of exposure to total amines, as did both the mean and median changes in thickness (table 3). There was a positive association between increases in across-shift corneal thickness and concentrations of total amines; however, it was not statistically significant (OR 1.08, 95% CI 0.95 to 1.23). Results were similar when evaluating exposure to DMIPA and DMAE separately, and when looking at each eye individually. Median corneal thickness increased with increasing grades of corneal opacity (table 4).

The prevalence of across-shift decrements in vision by total amine concentration increased with increasing exposure to total amines (OR 1.2, 95% CI 1.001 to 1.43; OR 1.28, 95% CI 1.14 to 1.43, respectively). Similar results were found for DMIPA and DMAE separately, but were not statistically significant for DMAE. There was not a significant association between bilateral visual acuity, 22 episodes of decreased bilateral contrast sensitivity at 2.5% contrast, and 35 episodes of decreased bilateral contrast sensitivity at 1.25% contrast. Decrements in bilateral visual acuity ranged from one to two rows, decrements in bilateral contrast sensitivity at 2.5% contrast ranged from one to eight rows, and at 1.25% contrast ranged from one to six rows. There were 23 observations of corneal opacity in the left eye (16 were grade 1, five were grade 2, and two were grade 3) and 24 in the right eye (13 were grade 1, nine were grade 2, and two were grade 3) at the end of the shift. In all instances of corneal opacity, there was complete clearing by the beginning of the worker’s next shift (see fig 2).

Table 2  Prevalence of reported visual symptoms by total amine concentrations

<table>
<thead>
<tr>
<th>Full shift total amine concentrations (mg/m$^3$)*</th>
<th>n</th>
<th>Blurry vision</th>
<th>Halo vision</th>
<th>Blue-grey vision</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.84–7.30</td>
<td>26</td>
<td>3 (12%)</td>
<td>1 (4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>7.31–13.80</td>
<td>57</td>
<td>26 (46%)</td>
<td>11 (19%)</td>
<td>7 (12%)</td>
</tr>
<tr>
<td>13.81–20.33</td>
<td>13</td>
<td>12 (92%)</td>
<td>7 (54%)</td>
<td>8 (62%)</td>
</tr>
</tbody>
</table>

*Range was divided into three groups of equal width.

Table 3  Corneal changes across shift by total amine concentration

<table>
<thead>
<tr>
<th>Full shift total amine concentrations (mg/m$^3$)</th>
<th>n</th>
<th>Presence of corneal opacity in either eye*</th>
<th>Prevalence of increased corneal thickness either eye</th>
<th>Mean change in corneal thickness (mm) (SD)</th>
<th>Median change in corneal thickness (mm)</th>
<th>Range of change in corneal thickness (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.84–7.30</td>
<td>26</td>
<td>3 (12%)</td>
<td>17 (65%)</td>
<td>-0.0155 (0.0073)</td>
<td>0.0003</td>
<td>-0.0250 to 0.0055</td>
</tr>
<tr>
<td>7.31–13.80</td>
<td>57</td>
<td>13 (23%)</td>
<td>39 (68%)</td>
<td>0.0004 (0.0060)</td>
<td>0.0010</td>
<td>-0.0155 to 0.0200</td>
</tr>
<tr>
<td>13.81–20.33</td>
<td>13</td>
<td>8 (62%)</td>
<td>12 (92%)</td>
<td>0.0065 (0.0087)</td>
<td>0.0050</td>
<td>-0.0055 to 0.0285</td>
</tr>
</tbody>
</table>

*Either grade 1, 2, or 3.

Table 4  Corneal thickness changes across shift by corneal opacity

<table>
<thead>
<tr>
<th>Corneal opacity grade</th>
<th>Change in corneal thickness, left eye (mm)</th>
<th>Change in corneal thickness, right eye (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean</td>
</tr>
<tr>
<td>0</td>
<td>77</td>
<td>-0.0006</td>
</tr>
<tr>
<td>1</td>
<td>16</td>
<td>0.003</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>0.007</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>0.022</td>
</tr>
</tbody>
</table>

Table 5  Prevalence of across-shift decrements in vision by total amine concentration

<table>
<thead>
<tr>
<th>Full shift total amine concentrations (mg/m$^3$)</th>
<th>n</th>
<th>Decreased bilateral visual acuity</th>
<th>Decreased bilateral contrast sensitivity at 2.5% contrast</th>
<th>Decreased bilateral contrast sensitivity at 1.25% contrast</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.84–7.30</td>
<td>26</td>
<td>2 (8%)</td>
<td>1 (4%)</td>
<td>9 (35%)</td>
</tr>
<tr>
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<tr>
<td>13.81–20.33</td>
<td>13</td>
<td>6 (46%)</td>
<td>8 (62%)</td>
<td>6 (46%)</td>
</tr>
</tbody>
</table>
reduced contrast sensitivity at 1.25% contrast and concentrations of total amines, DMAE, or DMIPA. Table 5 depicts the prevalence of decrements in visual acuity and contrast sensitivity at 2.5% and 1.25% contrast by concentration of total amines.

DISCUSSION

There have been case reports of blurry, halo, and/or blue-grey vision in workers exposed to a variety of amines. Experimental exposure to TEA and DMEA produced visual symptoms, increased corneal thickness, corneal oedema, and decrements in visual acuity and contrast sensitivity in study subjects. In contrast, industrial studies have failed to associate these findings with average exposures to DMEA and TEA. It has been postulated that this is because visual findings may be caused by high peak exposures to amines as opposed to average exposures.

We documented an association between symptoms of blurry, halo, and blue-grey vision, corneal opacity, decrements in visual acuity, and contrast sensitivity at 2.5% contrast and TWA exposure to two tertiary amines, DMAE and DMIPA. Neither DMAE nor DMIPA have previously been reported to cause visual disturbances in humans. Concentrations of DMAE and DMIPA were highly correlated, making it difficult to separate the effects of each amine. In addition, the two compounds are very similar, and it would be expected that they would produce similar health effects. However, DMIPA is the amine most likely to be causing visual changes in this group of workers for several reasons. Visual symptoms were much more common in the line division, where concentrations of DMAE were significantly lower than in the prime division. In contrast, DMIPA concentrations were significantly higher in the line division. Overall, DMIPA was present at levels approximately 3–4 times higher than DMAE. DMIPA is more volatile than DMAE, with a vapour pressure of 14.7 torr compared to 4.0 torr for DMAE. Plant management reports that they have been diluting the pH adjuster with water since discovering it might be the cause of employees’ visual disturbances, but that there have been no complaints since taking this action. NIOSH investigators interviewed 27 of the 36 (75%) line division workers who participated in the study (the other 9 were not at work at the time of the interview) to confirm the cessation of visual disturbances. All 27 employees reported that they had not experienced any visual disturbances since the process of diluting the pH adjuster had been in place, and had not heard any other employees report visual disturbances.

In the previous studies of both human and animal subjects exposed to tertiary amines other than DMIPA and DMAE, investigators have used terms such as toxicity and corneal oedema. This implies that the amines directly injure the corneal epithelium, resulting in cellular dysfunction and swelling. Some of the studies have shown increased corneal thickness, while others have not. However, our study’s observations also support another mechanism, that of direct deposition of tertiary amines into the corneal epithelium without significant cellular dysfunction or toxicity. The opacity caused by direct deposition might be the result of incomplete solubility of tertiary amines into the corneal epithelium. The corneal epithelium is a highly lipophilic tissue, and tertiary amines are typically largely hydrophilic and water soluble. Several observations in this study may support the hypothesis of direct deposition as the mechanism of producing opacity. First, there was a minimal increase in corneal thickness in those subjects with corneal opacity. This implies a lack of endothelial dysfunction, and a lack of stromal oedema. Other studies have similarly noted a lack of endothelial cell dysfunction. The corneal opacity was more prominent inferiorly, in the interpalpebral fissure, where classically environmental exposure is greatest (as opposed to superiorly, where the upper lid imparts partial protection to the epithelium). Other studies have noted this localised effect with exposure to different amines, and that clinical and variance of the opacity was also different from true epithelial oedema. Typical oedema causes an increase in the intercellular fluid content of the epithelium, resulting in cyst-like spaces, called microcystic oedema. None of the subjects in this evaluation showed microcystic changes, but rather a diffuse and uniform opacity. With toxic effects, rapid cell death and epithelial shedding often occur, resulting in punctate corneal erosions or frank epithelial defects. However, none of the subjects in this study showed any increase in loss of epithelial cells. In fact, all subjects, once removed from the workplace, showed rapid re-epithelialization with complete clearing by the next day and complete recovery to baseline vision, corneal thickness, and corneal clarity. There were no apparent cumulative effects or long term corneal injury. However, there may have been insufficient person-time to fully exclude long term toxicity to the cornea. Finally, the subjects in this study reported a fairly mild degree of irritation and did not show any conjunctival inflammation, which would be expected with epithelial toxicity given the typically painful presentation of microcystic oedema because of the rich supply of corneal pain receptors. This does not mean that DMIPA and DMAE are completely non-toxic to the cornea, but means that at the concentrations seen in this study, toxicity in the classic sense did not seem to occur. Further studies involving the behaviour of the cornea at various concentrations of representative tertiary amines would be of great value. Additionally, histological examination of animal corneas after exposure would be of use in assessing the various levels of tertiary amine penetration, the presence or absence of true oedema, and the degree, if any, of tissue damage on a cellular level.

Re-entry of air exhausted from the printing machines was not determined to be a problem on the day of the tracer gas testing as the amount of SF entering the building was so small as to be barely detectable. However, on that day, the wind blowing from the north would have carried exhausted SF away from the outdoor air intakes and entry points to the building. On the day the aerosol “fog” was used to visualise the movement of air around the exhaust discharges and building air intakes, the wind was out of the south; and, although most of the smoke was carried away from the building, some “fog” was observed circulating into the area of the outdoor air intakes. For this reason, it is expected that re-entry would be more of a problem with prevailing winds from the south, which is typical for this area of the country.

Inside the building, the tracer gas spread quickly throughout the line division when released from a central point in that area. It also dispersed quickly from the sampling locations. For 25–30 workers per shift on the line side, the ventilation rate was approximately 200 CFM per person, suggesting an adequate amount of outside air. There are no specific standards for general ventilation in a manufacturing plant such as this other than a guideline minimum of 15 CFM per person of outdoor air. It is, however, essential that the incoming outdoor air does not contain high concentrations of environmental contaminants, including those previously exhausted from the building. Recommendations were made to improve local exhaust ventilation, and to reposition the exhaust discharges and air intakes to prevent/reduce entry of exhausted contaminants back into the building. It was recommended that local exhaust ventilation be ducted to discharges on the outside of the building as close to the northeast corner of the building as practicable. If more that one discharge duct exits the building, the exhaust discharges should be grouped tightly together to take advantage of the larger effective diameter of the combined jet to achieve greater plume height. The discharge ductwork should extend at least 6 feet above the edge of the roof on the north side of the building and have a diameter such that the exhaust exits the
end of each duct at a velocity not less than 2000 ft/min and not greater than 3000 ft/min. The outdoor air intakes should be located as far to the west of the exhaust discharge point as practicable.

CONCLUSIONS
Exposure to tertiary amines in this plant was associated with blurry, halo, and blue-grey vision, corneal opacity, and decrements in visual acuity and contrast sensitivity at 2.5% contrast. While this appears to be a reversible phenomenon, the visual changes pose a safety hazard, both on the job and when driving home. Dilution of the pH adjuster, which decreases the concentration of DMIPA and thus employee exposure, has eliminated employee reports of visual disturbances.

The re-entry of exhausted air is a potential problem, and the ventilation in the line division is not adequate under current work practices. Although increasing the general ventilation may provide some reduction in exposure, a more cost effective solution would be to improve the local exhaust ventilation controlling the sources of tertiary amines associated with the printing machines, and then to also reposition the outdoor air intakes and exhaust discharge locations.

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