

## Work-relatedness Assessment of Hexavalent Chromium-induced Occupational Lung Cancer: A Review and Case Investigation

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### ABSTRACT

Stainless steel has long been ubiquitously used in cookware manufacturing. In the production process, workers are potentially subject to exposure to many metal fumes, including chromium. Lung cancer is not uncommon in Thailand; however, lung cancer caused by hexavalent chromium [Cr (VI)] exposure had never previously been reported. A worker presented with respiratory symptoms and weight loss for 3 months. After rigorous investigation, the diagnosis was a non-small cell cancer (adenocarcinoma). He had worked at stainless steel polishing for 25 years without any history of smoking or other health risk factors. Polishing chromium-containing metal and lubricating it with trivalent chromium [Cr (III)] wax can create heat high enough to produce the known human lung carcinogen Cr (VI). Instead of wearing an appropriate respirator, he usually wore an activated charcoal mask. During his health treatment, an occupational medicine physician was consulted regarding the work-relatedness of his cancer. This article reviews the process of work-relatedness assessment of non-small cell lung cancer in Cr (VI) exposure by workers in the stainless steel industry and provides details of the first case of what from an occupational medicine point of view the authors consider an occupational disease.

**KEYWORDS** lung cancer, hexavalent chromium, Cr (VI), occupational disease, occupational medicine, work-relatedness assessment

### INTRODUCTION

Lung cancer is well known as one of the most important causes of morbidity and mortality. In 2011, globally lung cancer was the largest newly diagnosed cancer (1,350,000 cases annually) and had the highest mortality rate (12.4%) of all new cancer cases and resulted in 1,180,000 deaths or 17.6% of all cancer deaths (1). The Thailand Cancer Registry reported 190,636 new cases in 2020. Lung cancer represented 12.4% of those new cancer cases (23,713 cases), the second most common type both in terms of incidence and mortality (2). In Thailand as well as in industrialized countries, lung cancer

has had a rising incidence rate, primarily due to smoking. There are many occupational hazards associated with lung cancer, one of which is hexavalent chromium; however, from 2011 to 2018, the Thailand Workmen's Compensation Fund of the Social Security Office reported only one case of occupational lung cancer which occurred in a sailor (3).

Chromium is a hard, brittle, gray metal which is presently widely used in chrome plating of automotive parts, household appliances, and machinery where the coating enhances corrosion resistance. Chromium-iron alloys are also used in the production of a variety of high-

strength stainless steels and their products. Chromium compounds provide heat resistance properties to refractory materials. Additionally, chromate pigments and preservatives are added to paints, dyes, textiles, rubber, plastics, and inks. Chromium-based orthopedic devices are used in arthroplasty (4). The valence state of the chromium is a critical factor in its toxicity. Hexavalent chromium, also known as Cr<sup>6+</sup> or Cr (VI), chromium with a valence of positive six in any form, is the most toxic and is also carcinogenic. In contrast, trivalent chromium, known as Cr<sup>3+</sup> or Cr (III), is an essential element for human glucose metabolism (5). Workplace monitoring and medical surveillance programs are needed wherever individuals are at risk for Cr (VI) exposure. Exposure to Cr (VI) can be measured by the total chromium in urine. Measurement of chromium in urine (end of shift at end of workweek), i.e., the Biological Exposure Index (BEI), is recommended (6).

Cr (VI) is classified as group A1 (confirmed human carcinogen) by The American Conference of Governmental Industrial Hygienists (ACGIH), as a group A (human carcinogen) by the United States Environmental Protection Agency (EPA), and as a group 1 (known human carcinogen) by the International Agency for Research on Cancer (IARC) (6-8). The International Labor Organization (ILO) as well as the Thailand Workman's Compensation Fund and Thailand's Social Security Office have designated cancer caused by Cr (VI) compounds as an occupational cancer. However, in Thailand since that designation until the present, there have been no reported cases of lung cancer caused by Cr (VI) in the country.

The authors encountered a cookware manufacturing worker who had been chronically exposed to Cr (VI) and experienced lung cancer. The authors reviewed and reported this case and also reviewed the relevant literature to determine the work-relatedness of the cancer to aid in the evaluation of other occupational diseases and case diagnoses in the future.

## METHOD

The patient's occupational history, working environment and industrial hygiene data, social history, past and present history of illness, physical examination results and other inves-

tigations were reviewed and recorded in detail for work-relatedness evaluation. Because the patient had already passed away prior to accessing the relevant data, the authors obtained an informed consent for data release from patient's legal proxy, i.e., his wife. The study protocol was reviewed and approved by the Institutional Review Board (IRB no. 031/2564). Domestic and foreign publications were reviewed with emphasis on the epidemiology and pathophysiology of lung cancer as well as risk factors together with the patient's information to determine the causal relationship between occupational exposure and the disease.

## CASE PRESENTATION

A previous healthy, 51-year-old Thai man experienced chronic non-productive cough and a 5 kg weight-loss over a period of 3 months. Initially, he visited a primary health care unit with symptoms of pain around the left upper chest for 3 days. Because the physical examination was normal with the exception of a mild tenderness at the left chest wall, he was treated for muscle strain and asked to self-monitor.

In the following weeks, his symptoms became worse. He felt an intense sharp pain in his chest exacerbated by deep breathing (pleuritic) chest pain, so he went to the hospital. During the hospital visit, a physical examination revealed his body temperature was 36.9°C, heart rate was 92 beats/minute, respiratory rate was 20 times/minute, blood pressure was 122/22 mmHg and room-air oxygen saturation was 98%. His conjunctiva was not pale and there was no icteric sclera. Nasal septum perforation was not detected. Chest examination revealed decreased breath sound over the left upper lung zone without adventitious sound. Cardiovascular examination was unremarkable. His abdomen was soft, not tender with no distension and normoactive bowel sound. Hepatosplenomegaly and lymphadenopathy were not detected. Extremities did not show peripheral edema. Neurological and other physical examinations were unremarkable.

The laboratory investigation revealed Hb 13.1 g/dL, Hct 39.1%, WBC 9,600 cells/mm<sup>3</sup> (PMN 63.2% and lymphocyte 20.1%), platelets 440,000 cell/mm<sup>3</sup>, PT 13.8 seconds, INR 1.17, PTT 28.8 seconds, BUN 12 mg/dL, creatinine

0.94 mg/dL, GFR(M) 93.5 mL/min/1.7 m<sup>2</sup>. Anti-HIV, sputum gram stain, acid-fast bacilli, and culture were all negative.

A chest radiograph showed a medial left upper lung mass 6 cm. in diameter, left basal pneumonitis, thin pleural effusion, plate-like atelectasis, no pneumothorax, normal heart size and mild scoliosis (Figure 1). A computed tomograph of chest/lungs with contrast media showed an enhanced irregular shaped soft tissue mass with central necrosis at the apico-posterior segment of the left upper lung, size 5.4x4.0x6.8 cm in AP (width and vertical height, respectively) together with left apical pleural nodules, left pleural effusion and multiple enlarged lymph nodes (Figure 2). Lung cancer was suspected, so a pulmonologist was consulted for diagnostic bronchoscopy and tissue diagnosis.

The diagnostic bronchoscopy was normal, so the pulmonologist decided to perform diagnostic thoracentesis. His pleural fluid revealed WBC 1,982 /mm<sup>3</sup>, RBC 21,000 /mm<sup>3</sup>, PMN 29%, mononuclear 71%, LDH 277 U/L (serum LDH 465 U/L), protein 5 U/L (serum protein 7.4 U/L), ADA 24.2 U/L (within normal range). TB profile and culture were negative. Cytology was positive for adenocarcinoma. After obtaining a pathologic diagnosis of cancer, the pulmonologist returned a definite diagnosis of stage IV non-small cell lung cancer with pleural, brain, adrenal, and bone metastasis.

## REVIEW OF PATIENT'S OCCUPATIONAL HISTORY

The patient had worked in the polishing division of a cookware manufacturing factory for 25 years (since 1993) until he was diag-



Figure 1. Chest radiograph 7 June 2018

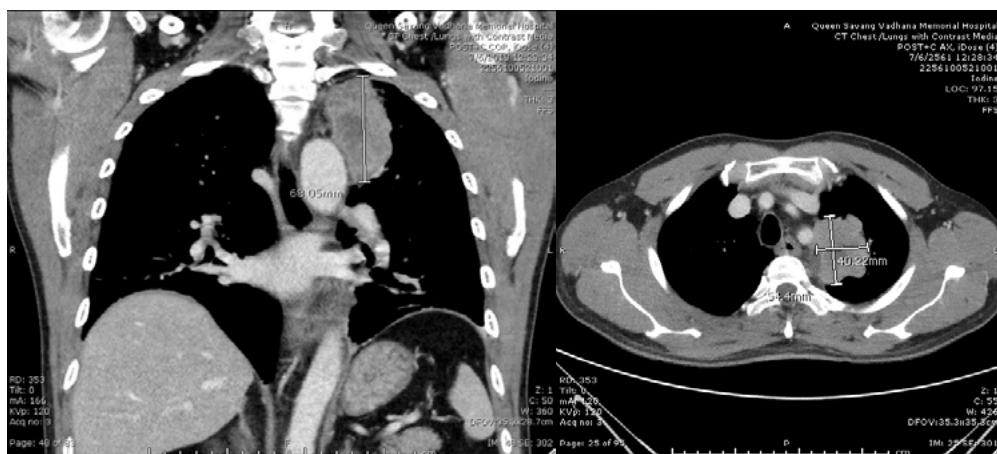


Figure 2. Computer tomography 7 June 2018

nosed with lung cancer and stopped working. His initial job was with the polishing division and consisted of rough grinding, fine grinding and polishing. These jobs were conducted in the same building area with the exception of the polishing which was done in separate room. In the rough and fine grinding processes, the stainless steel cookware was ground first with rough and then with fine sandpaper. These processes could emit splatter and fine silica dust, so local exhaust ventilation devices were installed at all grinders. In the polishing process, pieces of stainless steel cookware were polished with a hemp wheel and a wool wheel. Bar wax containing Cr(III) was used as a lubricant in this process. The patient worked a normal 8-hour day at the polishing process plus several extra working hours. Ten years later, he was promoted to be an assistant foreman. His duties then included assisting in organizing the activities of polishing, inspection, and supervision of work with the polishing machine.

Stainless steel includes a group of iron-based alloys which contain a minimum of approximately 11% chromium. Different types of stainless steel also contain additional elements such as carbon, nitrogen, aluminum, silicon, sulfur, titanium, nickel, and copper. The food-grade stainless steel for cookware manufacturing is 304-type and contains 18–20% chromium by weight. Polishing chromium-containing metal and lubrication with Cr (III) wax can create heat that is high enough to produce Cr (VI). The main route of exposure in this case was inhalation of dusts and fumes.

The annual workplace monitoring data was reviewed, and the most recent time-weighted average chemical monitoring data was obtained. Total chromium level from air sampling in polishing room was 0.0066 mg/m<sup>3</sup>. Silica dust (SiO<sub>2</sub>) was not detected. Total dust sampling in the polishing room was 0.22 mg/m<sup>3</sup>. Respirable dust in samples from the polishing room was 0.10 mg/m<sup>3</sup>. The collecting and analytical methods had been conducted following certain NIOSH protocols: NIOSH 7601 for SiO<sub>2</sub>, NIOSH 7302 for chromium and OSHA method PV2121 for total and respirable dust. There was no air sampling of Cr (VI) or other metals measurements in the patient's workplace monitoring

data. The previous annual workplace chemical air monitoring levels did not exceed the occupational exposure limit set by the Department of Labor Protection and Welfare (DLPW) or the action level (50% of OELs).

Instead of wearing an industrial grade N95 respirator or an adequate filtering face piece based on the specific chemicals in the workplace and the contaminant levels, he usually wore only a carbon earloop mask. Additionally, the existing factory respiratory protection program didn't include a test to ensure the effectiveness of the personal protective equipment. The patient had been working there for 25 years until he was diagnosed with lung cancer. During the treatment process, the attending physician consulted an occupational medicine physician regarding the work-relatedness of the disease and the basis for a workmen's compensation claim.

From the beginning of his employment until 2017, all previous annual medical examinations performed at his company, including chest x-ray and pulmonary function tests, were normal. Moreover, the authors of this study did not find any evidence in the reported spirometry results documenting the test method used or the reliability of the tests, e.g., reproducible and acceptable flow-volume and volume-time, calibration, etc. Total chromium in urine was not included in the medical surveillance program of this patient.

## REVIEW OF PATIENT'S PERSONAL HISTORY

The patient had no history of smoking (either as a primary or secondary smoker) obtained from either the history taking or medical records and he had no family history of lung cancer.

A living environment investigation via home visit and history taking by the authors found he had never been exposed to other known risks of lung cancer such as radioactive radon or uranium nor had he received any previous radiation therapy to the lungs.

## DISCUSSION

An occupational medicine physician was consulted to determine the work-relatedness of the condition. Medical causation is determined

based on scientific criteria establishing a causal association between an injury, illness, disease, or disorder and known risk factors. Legal causation, however, is determined by criteria established by legal authority. In this case, the authors conducted an epidemiological case investigation to determine medical causation in order to report to the Office of Workmen's Compensation Fund under the Social Security Office to establish legal causation and financial compensation consideration.

The authors used the National Institute for Occupational Safety and Health (NIOSH) methodology for medical causation (9) as published in the American College of Occupational and Environmental Medicine (ACOEM) practice guideline 2018 (10) following the five steps described below.

### Step 1. Evidence of disease

In this case, the pulmonologist provided a final diagnosis of a stage IV non-small cell lung cancer (adenocarcinoma) based on the pleural fluid cytology evidence. This was the primary cancer, with pleural, brain, adrenal, and bone metastasis. Lung cancer in non-smokers is almost exclusively non-small cell lung cancer, with adenocarcinoma being the most common type (11).

### Step 2. Epidemiological Evidence of a Causal Association

An experiment by Rowe et al. (12) demonstrated that metal grinding temperature is between 250 and 375°C. The work surface temperature during polishing is typically less than 200°C, substantially lower than in grinding (13). Polishing chromium-containing metal and lubricating it with Cr (III) wax can create a temperature that is high enough to produce the known human lung carcinogen Cr (VI). Assessment reports of Cr (VI) in individual processes of the electroplating industry revealed that the Cr (VI) concentration in plating work is the highest level of all (geometric mean = 4.15 µg/m<sup>3</sup>), followed by polishing work (geometric mean = 1.86 µg/m<sup>3</sup>) and others (geometric mean = 1.28 µg/m<sup>3</sup>) (14). From the aforementioned data, all levels of Cr (VI) in each step of the work exceed NIOSH's REL and ACGIH's TLV-TWA

(Table 1) indicating the presence of occupational carcinogens in the workplace. The authors utilized the Updated Hill's Criteria to evaluate the epidemiological evidence of a causal association.

### The Updated Hill's Criteria

#### a) Temporal association

Because of the variation among studies, it is difficult to draw a conclusion regarding the latency period. For general solid cancers and lung cancer, the estimated latency period is 10 years, but only 5 years with high exposure concentrations (14). In this case, the patient's symptoms occurred after he had been polishing stainless steel for 25 years, exposure that exceeds the estimated latency period.

#### b) Strength of the association

The strength of the association of epidemiological evidence has been determined by several epidemiologic studies published after the IARC (1990) statement that there is sufficient evidence in humans for the carcinogenicity of Cr (VI) compounds causing lung cancer (15). NIOSH considers all Cr (VI) compounds to be occupational carcinogens associated with lung cancer as well as nasal and sinus cancer (16). The U.S. EPA has classified Cr (VI) as Group A, known human carcinogens with inhalation the route of exposure (17).

A recent meta-analysis based on 47 cohort studies covering the period 1985–2016 evaluated the relationship between Cr (VI) exposure and the incidence and mortality of cancers. For lung cancer, the meta-SMR (standardized mortality ratio) was 1.31 (95% CI: 1.17–1.47) from 44 included studies and the meta-SIR (standardized incidence ratio) was 1.28 (95% CI: 1.20–1.37) using a fixed-effects model ( $I^2 = 35.2\%$ ,  $p = 0.093$ ) from 10 included studies. Based on the SIR studies, the duration of employment was found to be correlated with increased cancer risk, especially duration of more than 15 years. The meta-analysis concluded that the incidence and mortality risk of lung cancer was significantly associated with Cr (VI) concentration in the air and to the exposure time (18).

#### c) Dose–response relationship

Cr (VI) is a genotoxic carcinogen for which the threshold dose for carcinogenic potential

has not yet been established although there is a dose-response relationship demonstrating progressively increases with levels of exposure.

Several studies have provided adequate data on the quantitative relationship between Cr (VI) and lung cancer and have proposed cumulative exposure standards. In 1999, the U.S. EPA (17) calculated an inhalation unit risk estimate of  $1.2 \times 10^{-2}$  ( $\mu\text{g}/\text{m}^3$ )<sup>-1</sup> and estimated that if an individual were continuously exposed to breathing air containing chromium at an average of  $0.00008 \mu\text{g}/\text{m}^3$  ( $8 \times 10^{-8} \text{ mg}/\text{m}^3$ ) over a lifetime, that person would theoretically have no more than a one-in-a-million increased risk of developing cancer. Likewise, the U.S. EPA estimated that continuously breathing air containing  $0.0008 \mu\text{g}/\text{m}^3$  ( $8 \times 10^{-7} \text{ mg}/\text{m}^3$ ) would result in not greater than a one-in-a-hundred thousand increased risk of developing cancer during one's lifetime, and breathing air containing  $0.008 \mu\text{g}/\text{m}^3$  ( $8 \times 10^{-6} \text{ mg}/\text{m}^3$ ) would result in not greater than a one-in-ten-thousand increased risk of developing cancer during one's lifetime.

In 2013, a NIOSH publication (16) based on the 'Baltimore Cohort' and the 'Painesville Cohort' reported that in case of 45-year exposure of  $1 \mu\text{g Cr (VI)}/\text{m}^3$ , which was the previous NIOSH's recommended exposure limit (REL), an excess lifetime risk of lung cancer death of 6 per 1,000 workers was noted and approximately 1 per 1,000 workers at  $0.2 \mu\text{g Cr (VI)}/\text{m}^3$ . NIOSH subsequently recommended a revised REL of airborne exposure to Cr (VI) compounds of  $0.2 \mu\text{g Cr (VI)}/\text{m}^3$  for an 8-hr time-weighted average (TWA) exposure, during a 40-hr work-week, and a cumulative exposure standard of  $0.009 \text{ mg}/\text{m}^3\text{-yr}$ . The REL is intended to reduce workers' risk of lung cancer associated with occupational exposure to Cr (VI) compounds over a 45-year working lifetime.

*d) Consistency of the association among multiple epidemiological studies.*

Among major international institutions, the methods of determination of carcinogenicity of Cr (VI) are consistent.

*e) There is coherence in the association with existing physiologic data, trends in exposure levels over time, and other factors.*

Workers involved in chromate production, chrome plating, and chrome alloy work have

been found to have an increased incidence of lung cancer (3). The Occupational Safety and Health Administration (OSHA) reviewed the carcinogenic effects of chromium compounds (19) and reported that in chromium pigment production, there is an increase of lung cancer incidents in comparison with the general population. Excess lung cancer mortality was also found in stainless steel welding workers, but that finding is limited because welding workers are simultaneously affected by asbestos, nickel, and smoke in addition to chromium.

*f) Specificity of the association*

Exposure to Cr (VI) causes one specific health outcome: lung cancer. There is no evidence of other carcinogens apart from Cr (VI).

*g) Plausibility of the purported exposure-disease relationship*

Cr (VI), which has a strong oxidizing property, is highly carcinogenic and corrosive. Mechanisms of Cr (VI) carcinogenicity are DNA damage, genomic instability, and reactive oxygen species (ROS) generation (20).

*h) Experimental evidence from animal models*

Animal studies have shown Cr (VI) to cause lung tumors via inhalation exposure (21).

In that report, the authors do not consider

*i) Reversibility: Lung cancer is an irreversible pathology of the tissues despite cessation or reduction of exposure.*

*j) Performance of the association in predicting future cases of the disease.*

These epidemiological studies of workers have clearly established that inhaled Cr (VI) is a human carcinogen that results in an increased risk of lung cancer.

### Step 3. Evidence of individual exposure

The authors assessed the degree of exposure by considering the intensity or magnitude of exposure, frequency of exposure, duration of exposure and temporal pattern of exposure associated with work.

The patient had been working with stainless steel for 25 years until he was diagnosed with lung cancer. His first job was putting stainless steel workpieces into a polishing machine and lubricating them with Cr (III) wax. After ten years, he was promoted to be an assistant foreman, assisting in organizing the activities of polishing, inspection, and supervision for the

people working with polishing machines. He worked 8 hours per day plus several overtime shifts. His respiratory protection equipment was inappropriate, and the implemented respiratory protection program didn't include fitness testing of protective equipment to ensure their effectiveness.

The exposure-response relationship based on duration of exposure was reviewed. The European Agency for Safety and Health at Work's publication called Information Notices on Occupational Diseases: A Guide to Diagnosis (22) sets out exposure criteria as follows:

1. Minimum intensity of exposure: occupational exposure confirmed by
  - a. History and a study of working conditions providing evidence of prolonged or repeated exposure to Cr (VI) compounds, and, if available;
  - b. Biological monitoring and
  - c. Workplace air monitoring
2. Minimum duration of exposure: 1 year
3. Minimum induction period: 15 years

From the Guidelines of the Thailand Workers' Compensation Fund of the Social Security Office (23), diagnostic evidence for occupational lung cancer criteria are as follows:

1. An obvious history of continuous exposure to occupational carcinogen 20 years before the beginning of symptoms.
2. A pathological diagnosis of lung cancer.

The objective evidence of this patient's inhalation exposure includes the estimation of personal exposure from ambient or general air

levels for total work duration in the polishing room. The present working conditions and the data obtained from the measurements of dust and chemical levels in the working area are insufficient to determine whether working conditions had changed over the past 20 years or not. Although there is some measurement data, for some years the enterprise might not have exceeded the standards set by the DLPW.

In 2017, the DLPW of the Thai Ministry of Labor (24) specified the occupational exposure limits for chromium compounds (Table 2).

Cr (VI) exposure can be evaluated indirectly by inferring from reports about the ratio of Cr (VI) to total chromium in each type of work (14). For example, Shin et al. (25) reported that the average ratio of Cr (VI) to total chromium was 35.5% in metal inert gas (MIG) mild steel welding, while it was 8.4% (6.3–9.7%) in MIG-stainless steel welding. The average Cr (VI) to total Cr ratios ranged from 1 to 30% based on ambient air monitoring (26,27). Using an average ratio of 15%, the Cr (VI) value from the most recent air monitoring data in this case can be estimated to be 0.99  $\mu\text{g}/\text{m}^3$  (range 0.066 to 1.98  $\mu\text{g}/\text{m}^3$ ) which exceeds the cancer risk threshold proposed by the U.S. EPA and NIOSH's REL for airborne exposure to Cr (VI) compounds over an 8-hr TWA period as discussed in step 2c). Consequently, there is a possibility of emitted Cr (IV) in this case presenting a potential cancer risk. Although the level of total chromium might not have exceeded the standard, it is meaningful because the data

**Table 1.** Occupational Exposure Limits (OELs) established parameters

Parameters	NIOSH (16)	OSHA (19)		ACGIH (6)	
	REL (8-hour TWA)	PEL	STEL	TLV (8-hour TWA)	STEL
Total dust	–	15 $\text{mg}/\text{m}^3$	–	–	–
Inhalable dust	–	–	–	10 $\text{mg}/\text{m}^3$ , dust less than 1% Silica <sup>a</sup>	–
Respirable dust	–	5 $\text{mg}/\text{m}^3$	–	3 $\text{mg}/\text{m}^3$ <sup>b</sup>	–
Total chromium as Cr	0.5 $\text{mg}/\text{m}^3$	1 $\text{mg}/\text{m}^3$	–	0.5 $\text{mg}/\text{m}^3$	–
Trivalent chromium compounds as Cr (III)	0.5 $\text{mg}/\text{m}^3$	0.5 $\text{mg}/\text{m}^3$	–	0.003 $\text{mg}/\text{m}^3$	–
Hexavalent chromium compounds as Cr (IV)	0.0002 $\text{mg}/\text{m}^3$	0.005 $\text{mg}/\text{m}^3$	–	0.0002 $\text{mg}/\text{m}^3$	0.0005 $\text{mg}/\text{m}^3$

REL, recommended exposure limits; PEL, permissible exposure limits; TLVs, threshold limit values; STEL, short term exposure limit; TWA, time-weighted average.

<sup>a</sup>ACGIH guidelines recommend airborne concentrations of inhalable dust below 10  $\text{mg}/\text{m}^3$ . (Inhalable dust is collected using a different method than total dust.)

<sup>b</sup>ACGIH guidelines recommend airborne concentrations of respirable dust be kept below 3  $\text{mg}/\text{m}^3$  (Not TLVs)

**Table 2.** The occupational exposure limit of chromium compounds set by the DLPW of the Ministry of Labor

Hazardous chemicals	CAS number	Occupational exposure limit (8-hour TWA)
Calcium chromate, as Cr	13765-19-0	0.001 mg/m <sup>3</sup>
Lead chromate, as Cr	7758-97-6	0.012 mg/m <sup>3</sup>
Strontium chromate, as Cr	7789-06-2	0.0005 mg/m <sup>3</sup>
Zinc chromate, as Cr	13530-65-9, 11103-86-9, 37300-23-5	0.01 mg/m <sup>3</sup>

shows that Cr (IV) is likely to have been present in the working area of this patient. There is a lack of data on Cr (IV) measurements for the period because there was no laboratory in Thailand that could measure Cr (IV) in the air. There was also no biological monitoring, such as urine chromium testing, performed as part of the medical surveillance of this patient.

Despite the need for additional quantitative exposure data such as studies of cumulative hexavalent exposure, it is now generally accepted that the concentration and long-term exposure to hexavalent chromium could cause lung cancer in this patient.

#### Step 4. Consideration of other relevant factors

From the available clinical information, there are no other potential causal factors apart from Cr (VI) relevant to this patient.

- No history of smoking obtained from history taking and medical records.
- No personal or family history of lung cancer.
- No evidence of exposure to other carcinogens in the workplace such as asbestos, arsenic, beryllium, cadmium, silica, vinyl chloride, nickel compounds, coal products, mustard gas, chloromethyl ethers, and diesel exhaust.
- No exposure to radioactive elements such as radon and uranium.
- No previous radiation therapy.

#### Step 5. Validity of testimony

- The information was obtained from reliable sources using appropriate methods.
- The consideration for work-relatedness was conducted by an occupational medicine physician using international standardized procedures.

- None of the physicians involved had known or had any earlier disputes with the patient.

## CONCLUSIONS

As described above in the five steps, this work-relatedness assessment was conducted using medical causation criteria after reaching a conclusive diagnosis, obtaining considerable information about individual exposures, a detailed medical history, reviews of relevant scientific literature, epidemiological evidence of a causal association, and consideration of other relevant factors.

Consistent with medical causation criteria, the authors consider this case to be one of an occupational disease. A report has been submitted to the Office of Workmen's Compensation Fund under the Social Security Office to establish legal causation and a request for financial compensation, including past and future expenses related to treatments and disability evaluations.

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## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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