Effectiveness of the European Chromium VI Directive for cement implementation on occupational allergic contact dermatitis occurrence

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Dear Editor,

Hexavalent chromium is the main sensitizer in wet cement and a common cause of occupational allergic contact dermatitis (OACD), especially among workers in the construction industry.[1,2] The European Chromium VI directive[3] transposed into national regulations in France and UK respectively on May and January 2005, prohibits selling or using of hydrated cement with more than 0.0002% of chromium. This was achieved through the addition of ferrous sulphate to the dry product, allowing to reduce chromium VI to chromium III which is less sensitizing. Previous studies from national surveillance systems on contact allergy have described a temporal decrease in the prevalence of chromate sensitization in the general population.[4,5] However their analysis did not provide information on the actual sources of chromium and their occupational relevance. Conversely, chromium OACD still remains a problem in some countries, as Australia.[6]

In the UK, is a surveillance collects incident reports of work-related skin diseases as reported by who also specify the suspected causal agent(s), occupation and industry. EPIDERM belongs to a family of work-related disease surveillance schemes known as The Health and Occupation reporting network (THOR). Since 2001 in France, the National Network for Vigilance and Prevention of Occupational Diseases (RNV3P, Réseau National de Vigilance et de Prévention des Pathologies Professionnelles) has continuously monitored new medically certified Occupational Diseases, including OACD, assessed by experienced occupational medical experts, most of the time dermatologists or allergists, their diagnosis being based on positive patch test results and their occupational relevance.[7] The aim of this paper is to assess the impact of the implementation of the European directive on OACD occurrence attributed to chromium in cement notified in the RNV3P, and THOR network.[8]

The study was designed as a controlled 'before and after' study. It compares the change in the number of incident notified cases per month in each network in target groups (expected to be

impacted by the regulation) and in a comparison group (not expected to be impacted by the regulation), before and after the regulation (respectively time 1 [2002-2004] and time 3 [2006-2010]); the 2005 year (time 2) corresponds to intervention year). The post-intervention change in incidence of reported OACD is described by the ratio of incidence in time 2 and time 3 respectively relative to that in time 1. This ratio can be regarded as an Incidence Rate Ratio (IRR) considering rate denominators constant over time.[9] We identified two classes of exposure which could be impacted by the intervention: (i) cement, i.e. most likely chromate in cement; (ii) chromate in construction occupations. The resulting cases groups 1, 2 and 3 were considered to be probably or certainly associated with occupational exposure and expected to be affected by the intervention, while group 4 was chosen as a control group (Table 1). In order to compare the change in incidence in the target groups (cases 1-3 and in comparison group, we estimated the ratio of two Incidence Rate ratios (RIRRs). Year 2001 was excluded to avoid including prevalent cases during the first year of the network. Statistical analyses were performed on R software (V.3.0.1) and Stata 13. Statistical significance was defined as $p<0.05$.

In the French network, during the post-directive period (2006-2010) compared to the pre-directive period (2002-2004), there was a significant increase in occurrence of all OACD (IRR=1.09) (Table 2). However the increase was confined to the comparison group (IRR=1.14), whereas occurrence of OACD related to cement, chromate or both in exposed occupations decreased. These declines were significant relative to the comparison (unexposed) group (RIRR=0.49, 0.62, 0.58 for groups 1 to 3). In the UK there was a similar decline in OACD related to cement or to chromate in exposed occupations (IRR=0.62, 0.35 and 0.40 for groups 1 to 3); there was also a decline in the comparison group (IRR=0.76) but the changes in target groups 2 and 3 were significantly greater. No significant changes were shown during 2005 compared to the pre-directive period.

For the first time in France, through a network based on occupational health experts, we have provided evidence for the effectiveness of an occupational health intervention aimed to reduce exposure to chromium VI in cement. Both the French and UK reporting schemes observed a reduction by almost half of notified OACD due to chromate in cement compared to non-exposed workers suggesting a beneficial effect of the European cement directive in more than one European country.

Regarding the exposure of interest, few reporting physicians identified this causal agent precisely. To limit this measurement bias, we selected different groups of OACD to better capture the exposure to chromium VI in cement. Thus, group 1 reflects OACD due to cement and very likely to chromium VI in cement. Group 2 included cases attributed to chromate (without any mention of cement) in construction sector which comprises occupations likely to be exposed to cement.

A limiting factor in our OACD study is that it is not based on the entire French occupational population, but on a specific subpopulation captured by the centres.[7] However we have no reason to expect that the trends are impacted by this bias. The inclusion of a comparison group that did not undergo the intervention (group 4) is a way to control for other factors that could impact on OACD trends in the RNV3P network: for example, changes in OACD diagnosis procedures over the study period, change in one centre's activity, organisation or in the medical team, and others threats to internal validity.[9]

Post-intervention period was long to take into account the time period latency between modification of exposure and clinical effect. It is well known that contact allergy is usually acquired after a long standing irritant cement dermatitis.[1]

In summary, the significant reduction by almost half in the occurrence of OACD attributed to chromium VI in cement observed in two distinct occupational surveillance schemes in France and UK, following regulatory actions demonstrated effectiveness of European cement directive in both countries. As of 1 May 2015, the content of chromium VI in leather articles has similarly be restricted

in Europe.[10] As recommended, RNV3P, EPIDERM and analogous surveillance schemes could be used in the future to evaluate the impact of 2014 Chromium VI regulation on the health of workers.

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Ethics approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The RNV3P network received the approval of the National Board enforcing data protection legislation (CNIL); the EPIDERM network which is one of the Health and Occupation reporting network (THOR) received the Multicentre Research Ethics Committee approval (02/8/72).

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Table 1: Definition of occupational allergic contact dermatitis (OACD) cases group according to their exposures and their occupations in France and UK.

Target group	**Cases definition**
- Group 1	all OACD attributed to cement exposure
- Group 2	all OACD attributed to chromate in construction occupations [a]
- Group 3	all OACD attributed to cement or to chromate in construction occupations [a]
Comparison group (control group) : Group 4	all OACD occurring in occupations other than construction and **excluding** OACD attributed to cement or chromate

[a]**: French construction workers included:** builders, bricklayers and stonemasons, concrete placers, concrete finishers and related workers, carpenters and joiners, building frame and related trades workers not elsewhere classified, roofers, floor layers and tile setters, plasterers, construction labourers. **UK construction workers included:** bricklayers and masons, roofers, roof tilers and slaters, carpenters and joiners, construction trades not elsewhere classified, plasterers, floorers and wall tilers, road and rail construction operatives, construction operatives not elsewhere classified, labourers building and woodworking trades, labourers other construction trades not elsewhere classified.

Table 2: Estimated changes in the incidence of occupational allergic contact dermatitis (OACD) after the cement European directive (January 2005) in France (n=3357) and UK (n=3818).

		2005/2002-2004								2006-2010/2002-2004							
	N	IRR[a]				RIRR (relative to control)[b]				IRR[c]				RIRR (relative to control)[b]			
Group		IRR	95% CI		p-value	RIRR	95% IC		p-value	IRR	95% CI		p-value	RIRR	95% IC		p-value
France	**RNV3P data in France**																
1. OACD to cement	108	0.74	0.38	1.43	0.37	0.73	0.38	1.41	0.89	0.55	0.36	0.84	0.0006	0.49	0.32	0.74	0.01
2. OACD to chromate in construction workers	110	0.95	0.51	1.74	0.86	0.95	0.51	1.79	0.9	0.71	0.47	1.06	0.1	0.62	0.41	0.94	0.01
3. OACD to cement and/or (chromate in construction workers)	192	0.82	0.5	1.34	0.42	0.82	0.49	1.36	0.91	0.66	0.48	0.91	0.001	0.58	0.42	0.8	0.01
4. Control*	2824	0.99	0.86	1.18	0.89	.	.	.	.	1.14	1.02	1.24	0.01	.	.	.	.
UK	**EPIDERM data in the UK**																
1. OACD to cement	46	0.31	0.07	1.31	0.11	0.35	0.08	1.48	0.15	0.62	0.33	1.15	0.13	0.88	0.48	1.62	0.69
2. OACD to chromate in construction workers	125	0.64	0.35	1.14	0.13	0.73	0.40	1.33	0.31	0.35	0.23	0.53	<0.001	0.50	0.33	0.74	0.0001
3. OACD to cement or (chromate in construction workers)	148	0.56	0.31	1.00	0.05	0.64	0.35	1.17	0.15	0.40	0.28	0.58	<0.001	0.58	0.41	0.84	0.004
4. Control	3366	0.88	0.78	1.00	0.06	.	.	.	.	0.76	0.69	0.83	<0.001	.	.	.	.

[a]: Incidence rate ratio (IRR) in time 2 (2005) compared to time 1 (2002-2004). For each group (1- 4) monthly case counts were analysed using a 2 level negative binomial regression model with random effects as previously described.[8,9] The 2 level model assumed a hierarchical structure with time nested within centre. The main predictor of interest, time period, was treated as a categorical variable as defined above. A further covariate was month of year to allow for seasonal changes in reporting. For the UK data other covariates specific to the network features were included as described previously.[8]

[b]: For Ratio of incidence rate ratio comparing IRR between each groups (1-3) and all other OACD, interaction terms representing the product of the dummy time variable and the group (comparison/target) variables were included in the model. The comparison of change between groups is expressed as the Ratio of two Incidence Rate Ratios (RIRRs) for the time periods specified:[9] RIRR =(incidence during time 2 or 3/incidence during time 1) for target group / (incidence during time 2 or 3/incidence during time 1) for comparison group.

[c]: Incidence rate ratio (IRR) in time 3 (2006-10) compared to time 1 (2002-2004).