



National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

New and emerging risks of Chemicals (NERCs) in occupational health

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Risk assessment principles

- Hazard** = the potential of an agent to cause adverse effects
- Exposure** = the concentration/amount of an agent via exposure route
- Risk** = the probability of an adverse effect following exposure

$$\text{Hazard} \times \text{Exposure} = \text{Risk}$$





Definition New and Emerging Risks (WHO)

- (Un)known hazard of a chemical
- New exposure/use (e.g. different route of exposure)
- Increased risk (more workers exposed)



Proactive vs Reactive systems

Proactive ("exposure first")

- Forward looking
- Technological developments
- Societal developments

Reactive ("disease first")

- Signals from the field
- Cases, clusters, trends
- Detection: occupational health specialists



Risk assessment of substances

Policy hazardous substances:

1. Inventory of all substances/ process generated substances and their hazards
2. Exposure assessment and comparison with Occupational Exposure Limits
3. Take measures when indicated (according to Strategy of Control)
4. Re-evaluate in case of changes, teaching/instruction, Medical Surveillance

Despite Risk assessments: New and Emerging risks of Chemicals (NERCs)



Old risks which were once new

Product	Since	Industrial use	First reports on cancer	Important publications/reports	Regulatory steps
Asbestos	1879	Asbestos mining, insulation, building material etc.	1935–49 Lung cancer cases reported in asbestos manufacturing workers; 1959–60 Mesothelioma cancer in workers and public identified in South Africa	1955 Doll establishes high lung cancer risk in Rochdale asbestos workers; 1959–60 Mesothelioma cancer in workers and public identified in South Africa;	First asbestos ban 1989 Iceland and ongoing.
Benzene	1900	Solvent in production of artificial leather, rubber goods, glue, printing, paint, coatings, dry cleaning, automobile manufacturing, etc.	In 1928 first case of benzene-induced leukemia: acute lymphatic leukemia in a pharmaceutical worker with high benzene exposure levels	1977 - Infante et al. publish the first cohort study of workers linking benzene exposure directly to leukemia	1982 -IARC evaluated benzene as having “sufficient evidence that benzene is carcinogenic to man,”
Radium	1898	Among others, painting watches with radium containing paint	1923 - first bone sarcoma recorded in this group of women in; there have been 55 cancers in a population of nearly 3000 women (including leukaemia and breast cancer).	1949 - International Committee on Radiological Protection (ICRP): no dose threshold for radiation-induced cancer	1996 - EU Directive on Ionising Radiations based on ICRP 60 which will be mandatory on member states.
Vinyl chloride	1930	Production of vinyl chloride and derivatives; PVC processing, hairdressers and barbers using hairspray containing vinyl chloride	1967 - 1973, 4 cases of angio sarcoma of the liver among men employed in the polyvinyl chloride polymerization section of tyre plant	Two cohort studies publishing in 1981 (USA) and 1991 (Europe)	Vinyl chloride was considered by previous IARC Working Groups in 1974, 1978, 1987, and 2007 (IARC, 1974, 1979, 1987, 2008).



Examples of NERCs

Butter flavouring (diacetyl):

- Used in popcorn, coffee, cookies, dairy products.....
- Causes a rare and life threatening lung disease (BO)
- Current I-OEL is too high → new SCOEL advise
- REACH-RMOA is prepared



Indium Tin Oxide (ITO):

- Used in LCD, solar cells, found in whole ITO life chain
- Causes alveolar lung fibrosis – rare life threatening
- REACH-RMOA indium trioxide is proposed



Tricresylphosphate (TCP):

- Jet oil constituent; exposure via AIRCO
- Aerotoxic syndrome (neurological effects)?
- REACH-SEv, CEN standard, EASA, dialogue in sector





Methodology

Evidence for causality



- **Signal detection:**
 - Text mining (Literature)
 - Data mining (Databases)
 - Reports (Clinical Watch systems)
 - Active detection (Health Surveillance)
- **Signal strengthening**
- **Confirmation of a Signal**
- **From signal to action:**
 - Risk communication
 - Research
 - Measures



Identification



Evaluation



Measures



Identificatie





Identification NERCs; Early warning systems

Types of early warning systems:



Clinical watch system:

Collection spontaneous reported cases:

- Health effect
- Exposure



Database on exposure and health effect:

- Hypothesis generation
- Epidemiological research



Biological (effect) monitoring:

Higher incidence of Health effects among Exposed workers?

- Exposure is leading
- Causal effect easier to prove



Identification; different targets



Food Products



Non-Food products



Household and do-it-yourself products



Cosmetics



Toys



Textiles



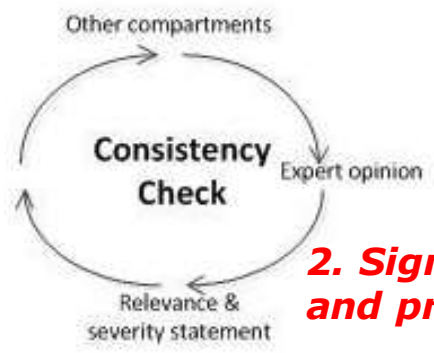
Tattoo ink





Methodology: main steps in identifying NERCs

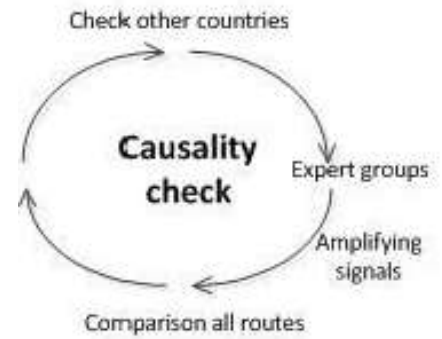
1. Signal identification



2. Signal evaluation and prioritization



3. Follow-up actions





Detecting emerging risks for workers and follow-up actions, RIVM Rapport 601353004
Palmen NGM, Salverda-Nijhof JGW, van Kesteren PCE, ter Burg W (2013)

Substance	Worker population/tasks	Observed health effect	Emerging risk (concern)
Formaldehyde	Hair dressers - use of hair straightening products	Irritation skin, eyes and respiratory tract, allergies	Increased/illegal use of the products
Indium tin oxide	Manufacture of flat-panel displays (LCD, plasma screen)	Pulmonary fibrosis	New technology
Crystalline silica (sand)	Sandblasting of textiles	Silicosis	New use, intensified exposure
Synthetic polymeric fibres	Textile workers from a nylon flocking plant	Interstitial lung disease (Flock worker's lung)	New risk
Tricresyl phosphate	Cockpit and cabin crew	'Aerotoxic syndrome' (neurological symptoms)	New exposure scenario
Diacetyl-containing flavorings	flavoring production and application	Bronchiolitis obliterans	New risk
5-Aminosalicylic acid	Drug manufacturing	Occupational asthma	New risk
Hexamethylene diisocyanate	Paint quality controller	Acute life-threatening extrinsic allergic alveolitis	New risk Dermal exposure is New route of exposure
Methylene diphenyl diisocyanate (MDI)	Orthopedic plaster casts workers	Occupational asthma	exposure levels lower than OEL

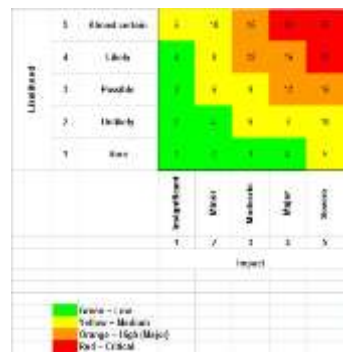


Prioritization

	Urgent	Not urgent
Important	Immediate action	PLAN
Not important	Delegate	DELETE



Operationalization of **Impact analysis**



Impact: severity health effect

1. Insignificant: discomfort or nuisance; e.g. dermal irritation.
2. Minor: discomfort or nuisance; e.g. airway irritation.
3. Moderate: functionality interference
4. Major: probability of disability to work; e.g. sensitization of airways, possible carcinogen
5. Severe: health threatening; e.g. proven carcinogen, lifelong invalidity or death

Likelihood: amount of evidence

1. Rare: occurrence is classified as unlikely
2. Unlikely: unlikely, but possible (eg. (case) study that has to be elaborated further; health effects caused by mixtures)
3. Possible: possible, but there is little information on exposure; category for elaborate case studies.
4. Likely: several studies claim causal relationship, but discussions are still ongoing; epidemiological studies with little exposure information.
5. Almost certain: consensus among scientists on the causal relationship



Prioritization

Risk score human health	Manufacturing/use in the Netherlands	Risk priority
20 – 25: Red	Yes	1: red
20 – 25: Red	Limited In the past for his use, but possibly elsewhere Strongly reduced	2: orange
20 – 25: Red	No	3: green
12 – 16: Orange	Yes	2: orange
12 – 16: Orange	Not likely but possible	2: orange
12 – 16: Orange	No	3: green
5 – 11: Yellow	Yes	3: green
5 – 11: Yellow	No	3: green
1 – 4: Green	Yes	3: green
1 – 4: Green	No	3: green

Priority = risk score x production/use in NL

Priority

- **Red:** Direct action needed
- **Orange:** Action needed
- **Green:** Minimal action



Prioritization; 3 examples

Prioritization of NERCs; *Palmen and Verbist, 2015*)

Substance name	CAS-number	Classification	Observed health effect	Occupation	Risk score	Use in NL	Risk Priority
Diacetyl-containing flavourings	431-03-8	Flam. Liq. 2 Acute tox 3: inhaled Acute tox 4. swallowed, inhaled Skin Irrit 2 Skin Sens 1 Eye Dam. 1 Eye irritation 2 STOT RE 2 (damage organs) STOT RE 3 (resp irr) Aquatic chronic 3	Bronchiolitis obliterans	Workers in flavouring production facility and workers that apply flavours (microwave popcorn production facility, cookie factory, coffee processing facility)	25	Yes	1
Indium tin oxide	50926-11-9	Skin irrit: 2 Eye irrit: 2 STOT SE 3: may cause respiratory irritation	Pulmonary fibrosis, pulmonary alveolar proteinosis	Manufacture of flat-panel displays (LCD, plasma screen). Use at universities and laboratories, possibly also waste treatment (recycling).	25	limited	2
Fibreglass with styrene resins	N.a.	n.a.	Bronchiolitis obliterans	Yacht builders/ Work with glass reinforced plastics	15	Yes	2



Evaluation of causal relationship





Methodology: main steps in identifying NERCs

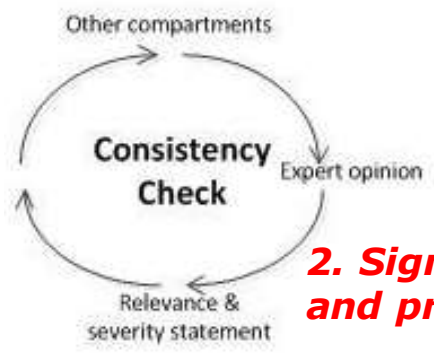
1. Signal identification

Internet
Literature
Databases
Interviews
Networks

Workers

Consumers

Environment

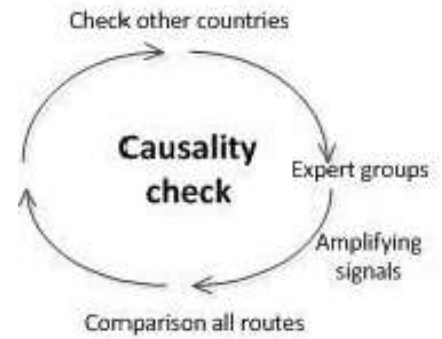


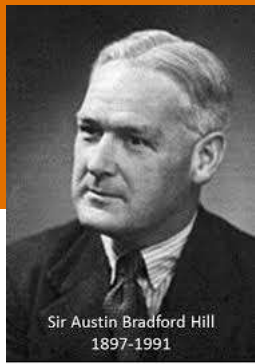
2. Signal evaluation and prioritization



3. Follow-up actions

Risk management options





Bradford Hill criteria

Table 2: Definitions of Hill's Criteria

Criteria	Definition
1 Strength	The size of the risk as measured by appropriate tests.
2 Consistency	The association is consistent when results are replicated in studies in different settings using different methods.
3 Specificity	When a single putative cause produces a specific effect.
4 Temporal sequence	Exposure always precedes the outcome.
5 Dose response	An increasing level of exposure (in amount and/or time) increases the risk.
6 Experimental evidence	The condition can be altered (prevented or ameliorated) by an appropriate experimental regimen
7 Biologic plausibility	The association agrees with currently accepted understanding of pathobiological processes.
8 Coherence	The association should be compatible with existing theory and knowledge.
9 Analogy	A finding of analogous associations between similar factors and similar diseases.

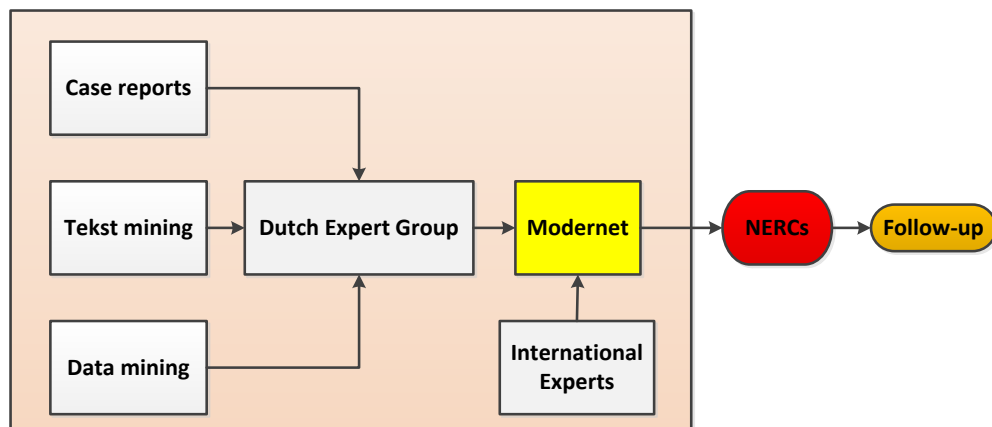


Control





From signal to action:



Follow-up (actions):

- Informing relevant inspection and professional societies of Occ. Health
- Substance already being regulated in REACH/CLP process?, If not RMOA (Risk Management Options Analysis):
 - Derivation OEL (SCOEL)
 - Identification as Substance Very High Concern (SVHC) + authorization REACH
 - Proposal for harmonized classification and labeling
 - Substance evaluation (REACH); asking for more data
 - Other legislation (pharmaceuticals, cosmetics, biocides..)



Elements needed for a successful signaling system



AN ACTIVE AND INTERDISCIPLINARY NETWORK OF PEOPLE



A PODIUM FOR DIALOGUE AND FOR ACTIVE DISCUSSIONS

HARMONIZED METHODOLOGY



AN INFRASTRUCTURE

- A KNOWLEDGE SHARING PLATFORM
- PROCESSES TO REACH RISK MANAGERS TO ENSURE FOLLOW UP ACTIONS ARE TAKEN



Let's start working together and share knowledge!





Thanks for your attention