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Hazardous Chemical Agents Regulations, 2021

Biological Monitoring

07 June 2021

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Member of Technical Committee 7

DEPARTMENT OF EMPLOYMENT AND LABOUR

NO. R. 280

29 March 2021

OCCUPATIONAL HEALTH AND SAFETY ACT, 1993

REGULATIONS FOR HAZARDOUS CHEMICAL AGENTS, 2021



- ▲ Introduction to Biological Monitoring (including clarification of terms)
- ▲ Biological Monitoring in Annexure 3 of the RHCA
- ▲ Introduction to the new Biological Exposure Indices (BEI's)
- ▲ The link between the new OELs & the new BEIs
- ▲ Discussion



What is Biological Monitoring?



“The measurement and assessment of **agents** or their **metabolites** either in **tissues**, **secreta**, **excreta**, **expired breath** or any combination of these to **evaluate exposure** and **health risk** compared to an **appropriate reference**”

note

styrene, toluene, benzene

Mandelic acid, o-Cresol, s-Phenylmercapturic Acid

Biological Exposure Indices (BEIs)

blood, hair, nails

sweat, saliva, milk

urine, faeces

solvents

Absorption, Distribution, Metabolism, Excretion (ADME)



Source
(chemical)



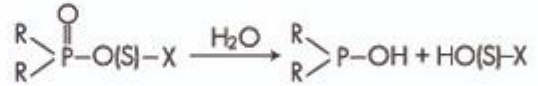
Exposed
medium
(people)



Internal
dose
(uptake)



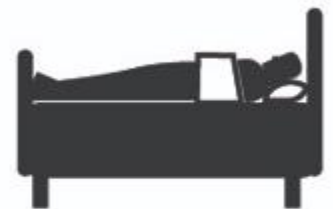
Target dose
(organs)



Biochemical
or cellular effect
(eg enzyme changes)



Adverse (reversible)
health effect
(early impairment eg
reduced haemoglobin)



Disease
(eg asthma, kidney
failure)

**AMBIENT
MONITORING (AIR)**

BIOLOGICAL MONITORING

**BIOLOGICAL EXPOSURE
MONITORING**

**BIOLOGICAL
EFFECT
MONITORING**

Individual variability,
interfering factors

**MEDICAL (HEALTH)
SURVEILLANCE**



- ▲ Includes absorption (uptake) of a chemical via **all routes**, including the lung, skin & GIT.
- ▲ Addresses the issue of uptake in circumstances that affect **the degree of exposure**, such as the **physical effort required by the job** (high breathing rates), or **extended work hours**
- ▲ Provides a means to **test the efficacy of PPE and work practices** (eg job rotation)
- ▲ To assess the **effectiveness of medical removal** procedures (eg lead, mercury, arsenic, others)
- ▲ Includes exposure as a result of **worker mobility** in the working environment (eg roving jobs)
- ▲ Assesses exposure over an **extended time period** (eg the full work week, or longer)
- ▲ Addresses the problem of **individual variability** (where individual factors influence the toxicokinetics of the chemical; for example, **age, sex, genetic factors**, or the health of the organs where the chemical undergoes metabolism and excretion).



Time of sampling

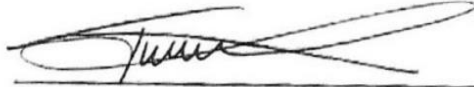
- ▲ Influenced by the rates of metabolism & excretion of the agents to be measured.
- ▲ To guide this, Table 4 in the HCA regs provides a recommendation (“end of shift”, “end of workweek”, etc.)

Interfering factors that affect the interpretation of the levels

- ▲ Physiological factors - *state of hydration* can make urine more / less dilute – corrected by using a ratio of urinary creatinine (ie xxx µg/g creatinine)
- ▲ Physiological factors – *diet* (eg fish & arsenic/mercury), *sex* and *age*
- ▲ Personal habits - *smoking and alcohol consumption*
- ▲ *Contamination* during collection / processing (dust from clothing lands in the sample)
- ▲ *Impaired organ function* (eg impaired kidney function and cadmium levels)
- ▲ *Multiple exposures* to toxic substances at work (they can interfere with each other's biotransformation or excretion)
- ▲ *Medications?*



- ▲ To update the Biological Exposure Index (“BEI”) definition & values in alignment with the updated OELs (Table 4)
- ▲ To update the Guidance Note in Annexure 3 with expanded content on Biological Monitoring
- ▲ NO CHANGES to the “Medical Surveillance” regulation (Reg 7)

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DEPARTMENT OF EMPLOYMENT AND LABOUR		
NO. R. 280	29 March 2021	
OCCUPATIONAL HEALTH AND SAFETY ACT, 1993		
REGULATIONS FOR HAZARDOUS CHEMICAL AGENTS, 2021		
The Minister of Employment and Labour has, under section 43 of the Occupational Health and Safety Act, 1993 (Act No. 85 of 1993), after consultation with the Advisory Council for Occupational Health and Safety, made the regulations in the Schedule.		
		
MR TW NXESI, MP		
MINISTER OF EMPLOYMENT AND LABOUR		
DATE: 03/03/2021		

New definition for Biological Exposure Indices



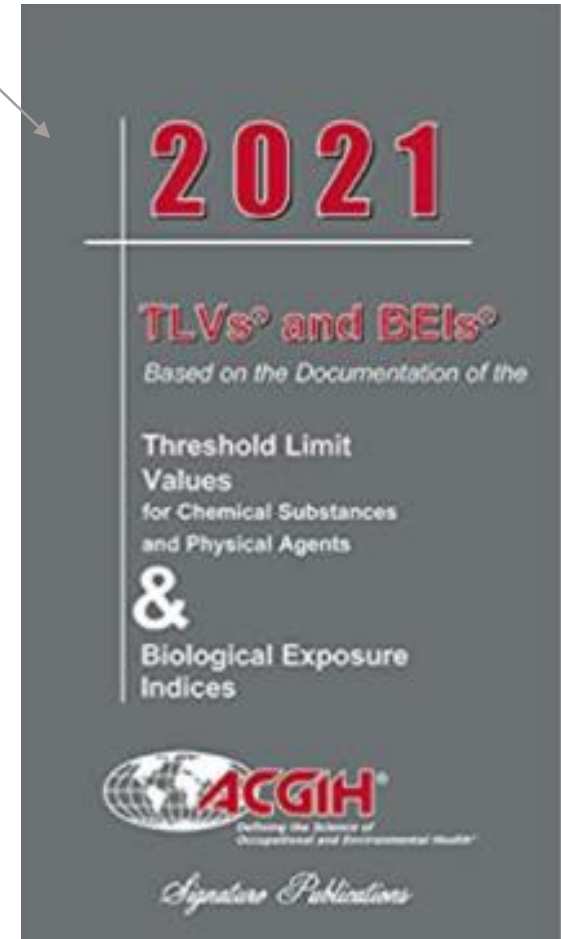
Note – “health-based”

Note – non-enforceable guideline values

Influenced by the ACGIH description of the term “BEI”

“BEI” or “Biological Exposure Index” is a **value for assessing biological monitoring results**, intended as a **reference guideline** for the **likelihood of adverse health effects**, and generally represents the level of determinants that are most likely to be observed in specimens collected from healthy employees who have been exposed to HCAs with inhalation exposure at the occupational exposure limit, as listed in Table 4 of Annexure 2 hereby, as revised from time to time and published in the Gazette;

Old definition for BEI in RHCS: “is a reference value intended as a guideline for the evaluation of potential health hazards as listed in Table 3 of Annexure 1 hereby as revised from time to time and listed in the Government Gazette.”



OH&SA definition for biological monitoring: “means a planned programme of periodic collection and analysis of body fluid, tissues, excreta or exhaled air in order to detect and quantify the exposure to or absorption of any substance or organism by persons.” (very similar to the ILO definition)



ANNEXURE 3

HAZARDOUS CHEMICAL AGENT GUIDELINES

Prevention and control of exposure

1. Exposure of employees to agents hazardous to health should be prevented or, where this is not reasonably practicable, adequately controlled. This is a fundamental requirement of the Regulations for Hazardous Chemical Agents (HCA), 2020. Exposure can occur by inhalation, ingestion or absorption through the skin, but inhalation is usually the main route of entry into the body. Tables 2 and 3 of Annexure 2 list the OELs which should be used in determining the adequacy of control of exposure by inhalation, as required by the HCA Regulations.
2. The advice in this document should be taken in the context of the requirements of the HCA Regulations, especially regulation 5 (Assessment of exposure) regulation 10 (Control of exposure), regulation 12 (Maintenance of control measures) and regulation 6 (Air monitoring). Agents hazardous to health are defined in regulation 1. There is separate legislation for lead and asbestos and these agents are not covered in detail in this document. This document also does not apply to exposure below ground in mines or exposure to hazardous biological agents.
3. Adequate control of exposure (when prevention is not reasonably practicable) should be achieved by one or more of a range of control measures described in regulation 10 of the HCA Regulations. Control by personal protective equipment should be applied only when other means are not reasonably practicable.

ANNEXURE 3

Medical surveillance

Guidance on medical surveillance and biological monitoring

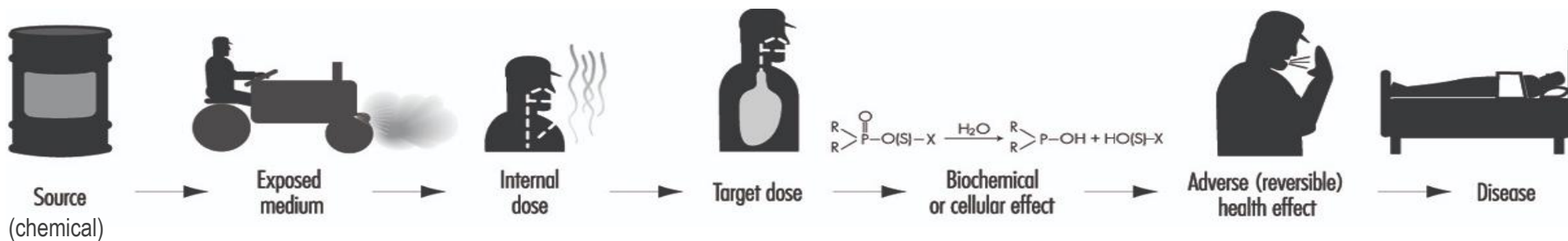
Important concepts

4. Medical surveillance refers to the overall monitoring of employees to identify changes in their health status because of exposure to certain chemical agents. These monitoring activities are not limited to only medical testing. Monitoring activities also include the monitoring and analysis of the individual and group outcome data, including historical data, derived from the medical testing.
5. Medical testing, therefore, is that aspect of medical surveillance that involves the use of interviews, questionnaires and standard clinical assessments to detect the presence of adverse health effects. This can also include tests like spirometry (lung function), radiography (e.g. chest X-rays) and laboratory tests (e.g. full blood counts).

HAZARDOUS CHEMICAL AGENT GUIDELINES



7. Biological monitoring is discussed in detail in paragraph 23. It is often incorrectly categorised as a type of medical surveillance. **Biological monitoring** provides an additional means to assess the exposure to an HCA by measuring metabolites of the HCA, or other similar markers of exposure. Therefore, it does not represent an adverse effect or an occupational disease – it only reflects exposure. A positive finding during biological monitoring does not necessarily mean that there has been a breach of the safety standard, but is a positive indication of employee exposure.
8. The distinction between early **biological effects** and **established disease** is not always clear, there tends to be a severity gradient in which one blends into the other. An occupational disease may be said to be present when the adverse biological effect progresses to clinically detectable organ damage requiring treatment or permanent impaired function. The categorisation of the condition is, therefore, sometimes at the discretion of the responsible medical practitioner. The distinction becomes important when considering a case for statutory reporting, as described in paragraphs 20, 21 and 22, where reporting of cases of established occupational disease is legally prescribed.



Annexure 3: Distinction between biological monitoring, biological exposure monitoring and biological effect monitoring



23. In these regulations, biological exposure monitoring and biological effect monitoring are subsets of the overarching term, biological monitoring.
24. **Biological exposure monitoring** is the measurement and assessment of chemicals or their metabolites (substances the body converts the chemical into, for purposes of elimination) in exposed workers. These measurements are made on samples of exhaled air, urine, blood or other biological materials, or any combination of these. Biological monitoring **measurements reflect the total uptake of a chemical by an individual by all routes (inhalation, ingestion, through the skin or by a combination of these routes)**. Biological exposure monitoring, therefore, does not represent an adverse effect or an occupational disease – it only reflects exposure, but it is often incorrectly listed as a type of medical surveillance.
25. **Biological effect monitoring** is the measurement and assessment of **early non-adverse reversible subclinical physiological effects caused by absorption of chemicals** (i.e. prior to established clinical disease). It typically involves measuring biochemical responses. For example, measuring plasma and erythrocyte cholinesterase activity in workers exposed to organophosphate pesticides; or measuring increases in urinary protein following exposure to cadmium; or changes in functioning of enzymes.
26. **Biological effect monitoring should be distinguished from medical testing** for *established clinical disease*, which is also known as **effect monitoring**. For example, changes in blood cell counts following exposure to bone marrow toxins do not constitute biological effect monitoring.



28. The main objective of biological monitoring is to provide a **complementary technique to air monitoring** when air sampling techniques alone may not give a reliable indication of exposure. Hence, it may be particularly useful in the following ways:
- a) to detect and determine absorption via the skin or gastrointestinal system, in addition to that by inhalation; **[total uptake]**
 - b) to test the **efficacy of personal protective equipment** and monitor work practices;
 - c) to compliment air monitoring in circumstances when **work practices are not normal**, such as abnormally long or variable working hours or very strenuous work (high breathing rates = increased chemical intake);
 - d) to detect **non-occupational exposures**;
 - e) to assess **total body burden**;
 - f) to **reconstruct past exposure** in the absence of other exposure measurements for chemicals with long half-lives; and
 - g) to assess the **effectiveness of medical removal procedures** when indicated for certain chemicals (e.g. arsenic)



31. Biological exposure indices (BEIs) are reference values **intended as guidelines** for the evaluation of potential health hazards in the practice of industrial hygiene. **BEIs must not be used as statutory reference values.**
31. A BEI represents in theory the level of an HCA or metabolite most likely to be observed in a specimen collected from a healthy worker who has been exposed to an HCA to the same extent as a worker with inhalation exposure to an OEL-TWA. **BEIs do not represent a sharp distinction between hazardous and non-hazardous exposures.** For example, owing to biological variability, it is possible that an individual's measurements can exceed the BEI without incurring an increased health risk. Conversely, there may be some susceptible individuals who may be harmed at levels below the BEI.
31. If measurements in specimens obtained from a worker on different occasions persistently exceed the BEI, or if the majority of measurements in specimens obtained from a group of workers at the same workplace exceed the BEI, **the cause of the excessive values must be investigated** and proper action be taken to reduce the exposure.

Table 4: the Biological Exposure Indices (“BEI”s)



Table 4: BIOLOGICAL EXPOSURE INDICES (BEIs) FOR HAZARDOUS CHEMICAL AGENTS

AGENT/DETERMINANT	CAS NUMBER	SAMPLE MATRIX	SAMPLING TIME	VALUE	UNIT	NOTATION
A						
Acetone	67-64-1					
Acetone		urine	End of shift	25	mg/L	Ns
Acetylcholinesterase inhibitors						
Cholinesterase activity in red cells		blood	Discretionary	70	% of baseline	Ns
Aniline	62-53-3					
p-Aminophenol		urine	End of shift	50	mg/L	B, Ns, Sq
Arsenic, elemental and soluble inorganic compounds (excluding gallium arsenide and arsine)	7440-38-2					
Inorganic arsenic plus methylated metabolites		urine	End of workweek	35	µg/L	B
B						
Benzene	71-43-2					
S-phenylmercapturic acid (SPMA)		urine	End of shift	25	µg/g creatinine	B
t,t-Muconic acid (ttMA)		urine	End of shift	500	µg/g creatinine	B
1,3-Butadiene	106-99-0					
1,2-Dihydroxy-4-(N-acetylcysteinyl)-butane		urine	End of shift	2,5	mg/L	B, Sq
Mixture of N-1-and N-2-(hydroxybutenyl)valine haemoglobin adducts		blood	Not critical	2,5	mg/g	B, Sq
2-Butoxyethanol	111-76-2					
Butoxyacetic acid (BAA)		urine	End of shift	200	mg/g	B
C						
Cadmium and inorganic compounds	7440-43-9					
Cadmium		urine	Not critical	5	µg/g creatinine	B

B: "Background"

The determinant collected from subjects exposed, at a concentration that allows for interpretation of the background concentrations and

B: “Background”

The determinant may be present in biological specimens collected from subjects who have not been occupationally exposed, at a concentration which could affect interpretation of the results. Such background concentrations are incorporated in the BEI value.

Table 4: the Biological Exposure Indices (“BEI”s)



Table 4: BIOLOGICAL EXPOSURE INDICES (BEIs) FOR HAZARDOUS CHEMICAL AGENTS

AGENT/DETERMINANT	CAS NUMBER	SAMPLE MATRIX	SAMPLING TIME	VALUE	UNIT	NOTATION
A						
Acetone	67-64-1					
Acetone		urine	End of shift	25	mg/L	Ns
Acetylcholinesterase inhibitors						
Cholinesterase activity in red cells		blood	Discretionary	70	% of baseline	Ns
Aniline	62-53-3					
p-Aminophenol		urine	End of shift	50	mg/L	B, Ns, Sq
Arsenic, elemental and soluble inorganic compounds (excluding gallium arsenide and arsine)	7440-38-2					
Inorganic arsenic plus methylated metabolites		urine	End of workweek	35	µg/L	B
B						
Benzene	71-43-2					
S-phenylmercapturic acid (SPMA)		urine	End of shift	25	µg/g creatinine	B
t,t-Muconic acid (ttMA)		urine	End of shift	500	µg/g creatinine	B
1,3-Butadiene	106-99-0					
1,2-Dihydroxy-4-(N-acetylcysteinyl)-butane		urine	End of shift	2,5	mg/L	B, Sq
Mixture of N-1-and N-2-(hydroxybutenyl)valine haemoglobin adducts		blood	Not critical	2,5	pmol/g Hb	Sq
2-Butoxyethanol	111-76-2					
Butoxyacetic acid (BAA)		urine	End of shift	200	mg/g creatinine	-
C						
Cadmium and inorganic compounds	7440-43-9					
Cadmium		urine	Not critical	5	µg/g creatinine	B

Ns: “Non-specific”

The determinant is non-specific, since it is also observed after exposure to other chemicals.

Table 4: the Biological Exposure Indices (“BEI”s)



Table 4: BIOLOGICAL EXPOSURE INDICES (BEIs) FOR HAZARDOUS CHEMICAL AGENTS

AGENT/DETERMINANT	CAS NUMBER	SAMPLE MATRIX	SAMPLING TIME	VALUE	UNIT	NOTATION
A						
Acetone	67-64-1					
Acetone		urine	End of shift	25	mg/L	Ns
Acetylcholinesterase inhibitors						
Cholinesterase activity in red cells		blood	Discretionary	70	% of baseline	Ns
Aniline	62-53-3					
p-Aminophenol		urine	End of shift	50	mg/L	B, Ns, Sq
Arsenic, elemental and soluble inorganic compounds (excluding gallium arsenide and arsine)	7440-38-2					
Inorganic arsenic plus methylated metabolites		urine	End of workweek	35	µg/L	B
B						
Benzene	71-43-2					
S-phenylmercapturic acid (SPMA)		urine	End of shift	25	µg/g creatinine	B
t,t-Muconic acid (ttMA)		urine	End of shift	500	µg/g creatinine	B
1,3-Butadiene	106-99-0					
1,2-Dihydroxy-4-(N-acetylcysteinyl)-butane		urine	End of shift	2,5	mg/L	B, Sq
Mixture of N-1-and N-2-(hydroxybutenyl)valine haemoglobin adducts		blood	Not critical	2,5	mg/L	B, Sq
2-Butoxyethanol	111-76-2					
Butoxyacetic acid (BAA)		urine	End of shift	200	mg/g creatinine	-
C						
Cadmium and inorganic compounds	7440-43-9					
Cadmium		urine	Not critical	5	µg/g creatinine	B

Sq: “Semi-quantitative”

The biological determinant is an indicator of exposure to the chemical, but the quantitative interpretation of the measurement is not clear.

Table 4: the Biological Exposure Indices (“BEI”s)



ADOPTED BIOLOGICAL EXPOSURE DETERMINANTS				
Chemical [CAS No.] (Documentation date)	Determinant	Sampling Time	BEI®	Notation
METHYL ETHYL KETONE [78-93-3] (2012)	Methyl ethyl ketone in urine	End of shift	2 mg/L	Ns
METHYL ISOBUTYL KETONE [108-10-1] (2009)	Methyl isobutyl ketone in urine	End of shift	1 mg/L	—
N-METHYL-2-PYRROLIDONE [872-50-4] (2006)	5-Hydroxy-N-methyl-2-pyrrolidone in urine	End of shift	100 mg/L	—
NAPHTHALENE [91-20-3] (2012)	1-Naphthol★ + 2-Naphthol★	End of shift	—	Nq, Ns
NITROBENZENE [98-95-3] (2013)	Methemoglobin in blood	See Methemoglobin Inducers BEI®	—	—
‡ PARATHION [56-38-2] (1992)	Total p-Nitrophenol in urine (Cholinesterase activity in red cells)	End of shift (Discretionary)	0.5 mg/g creatinine (70% of individual's baseline)	Ns (B, Ns, Sq)
PENTACHLOROPHENOL [87-86-5] (2013)	Pentachlorophenol in urine★	Prior to last shift of workweek	—	Nq
PHENOL [108-95-2] (2005)	Phenol in urine★	End of shift	250 mg/g creatinine	B, Ns

Nq: “Non-quantitative”

Biological monitoring should be considered for this compound based on the ACGIH review; however, a specific BEI could not be determined due to insufficient data.



Bear in mind that:

- ▲ A BEI usually represents a level of an agent that is most likely to be observed in a specimen collected from a healthy worker who has been exposed to the chemical to the same extent as a worker with an inhalation exposure at the ACGIH TLV (threshold limit value) time-weighted average (TWA). (There are some exceptions to this rule, such the BEI for lead)
- ▲ This means that when an employee's biomonitoring level reaches the BEI value, that employee's exposure has reached the level of the health-based (ACGIH) TLV, above which adverse effects are increasingly likely to emerge, and mitigation measures should start to be implemented.
- ▲ BEIs and ACGIH TLVs are both health based non-enforceable guideline values

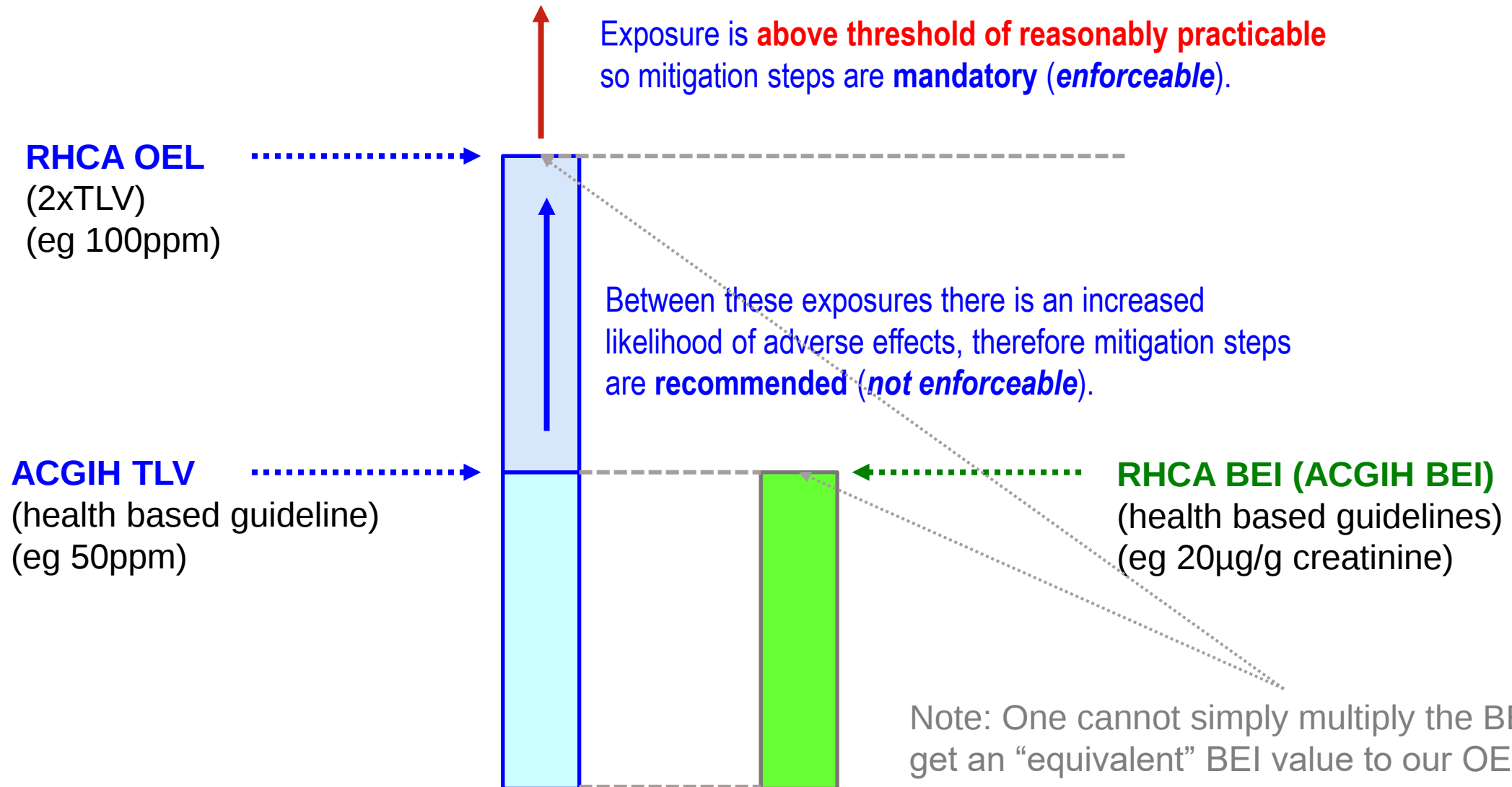
Given the 2x relationship between the ACGIH TLV and the RHCA OEL:

- ▲ the RHCA can simply adopt the ACGIH BEIs, with all the documented research that has gone into their development, and
- ▲ an employee who is exposed at the level of the (non-enforceable) BEI can be considered to be at approximately 50% of the RHCA'S (enforceable) OEL.

Relationship between RHCA OEL, ACGIH TLV and RHCA BEI (2)

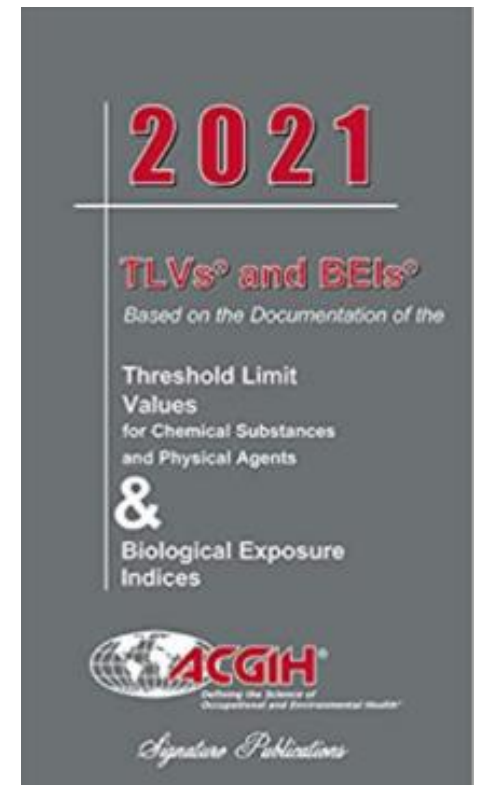
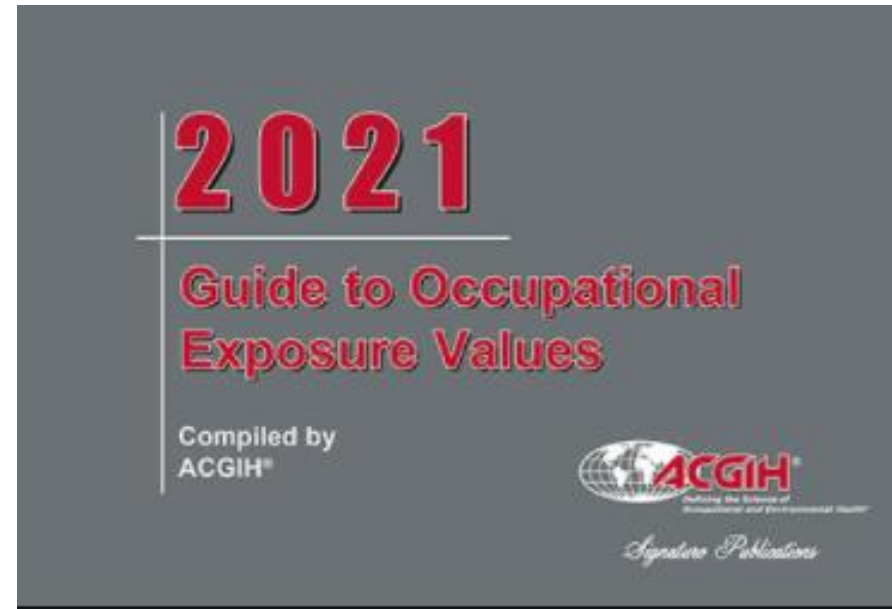
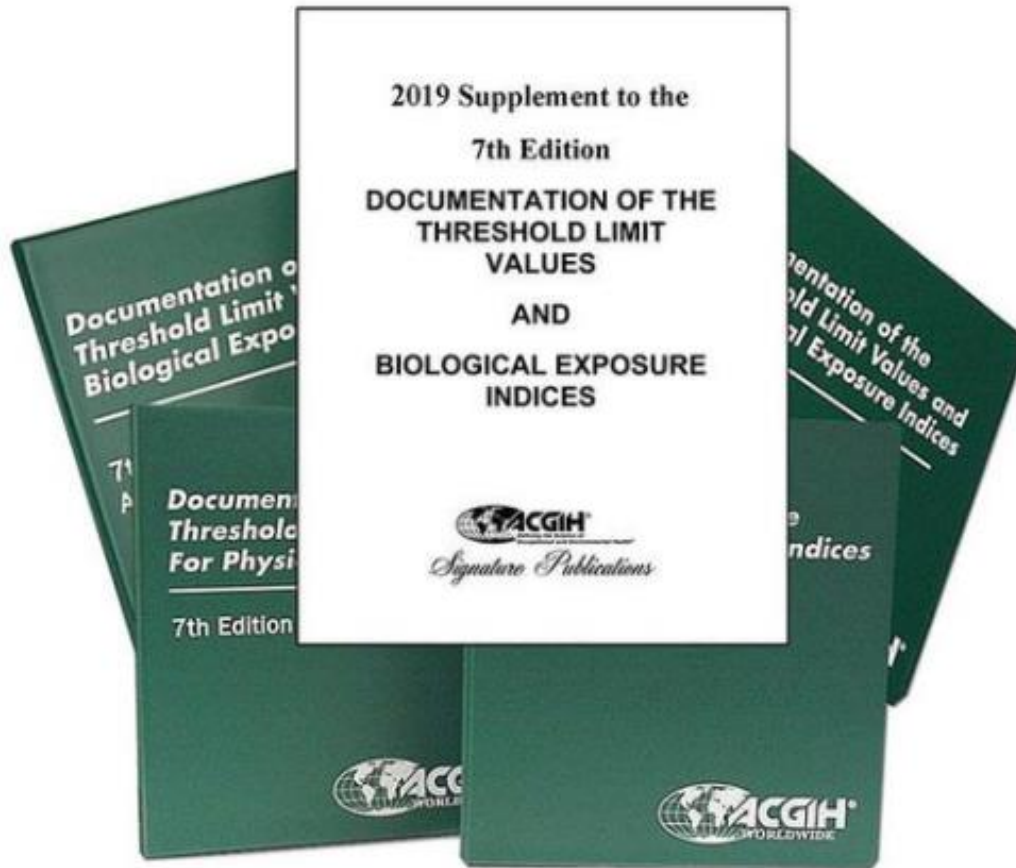


Using a fictitious chemical with a new RHCA OEL of 100ppm and a new BEI of 20µg/g creatinine





- ▲ **Biological Monitoring has an important part to play in protecting the health of workers**
- ▲ The Biological Exposure Indices are health-based guidance values
- ▲ Test selection and timing requires careful thought
- ▲ Interpreting test outcomes requires an understanding of the limitations of Biological Monitoring
- ▲ Where levels exceed the BEI, the exposure should be investigated and steps should be taken for mitigating the exposure.





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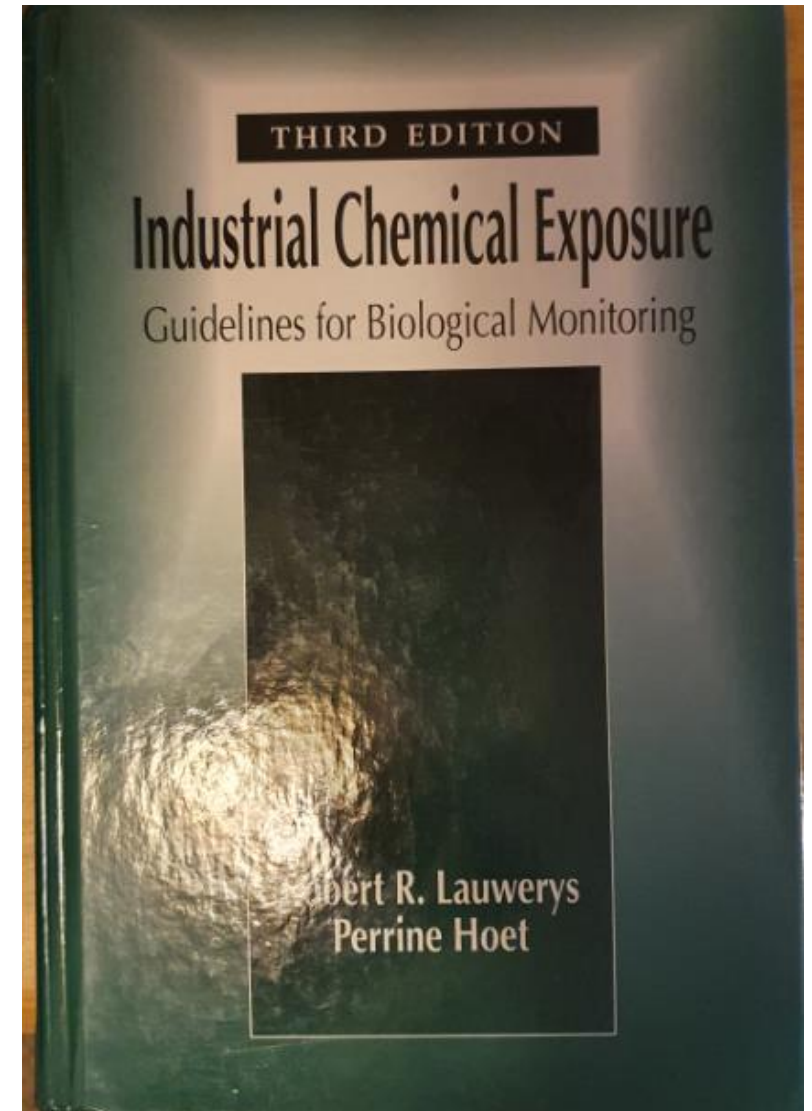
Jan / Feb 2013

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Health Surveillance Report (Biological Monitoring and Biological Effect Monitoring)

Dr Murray Coombs – Occupational Medicine Specialist, Chairman SASOM Biological Monitoring Scientific Committee. e-mail: mcoombs@iafrica.com

<http://www.occhealth.co.za/?/viewArticle/1406>





Thank you for your attention