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QUESTIONNAIRE ON THE CAPABILITIES OF MEMBER STATES REGARDING THE ANALYSIS OF BIOMEDICAL SAMPLES

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Annex

QUESTIONNAIRE ON THE CAPABILITIES OF MEMBER STATES REGARDING THE ANALYSIS OF BIOMEDICAL SAMPLES

1.	State Party	USA	
2.	Laboratory name	Lawrence Livermore National Laboratory	
3.	Contact person	Family name: Alcaraz	First name: Armando
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		Work: 001.925.423.9014	
8.	Is your laboratory currently conducting research into techniques for analysing biomedical samples for the presence of scheduled chemicals, their free metabolites, or other conjugated biomarkers of exposure, such as DNA or protein adducts?	Yes X	No ☐
		If so, please provide a separate list of references to any publications by your laboratory in this area and, if possible, copies of any of these publications that have appeared within the last five years.	
9.	If your laboratory is active in biomedical sampling and analysis, please describe the quality-control systems it has in place, such as external accreditation, and recognition for Good Laboratory Practice.	We are currently participating in "unofficial" Round Robins with other US labs to establish quality-control systems, analytical methods and reporting criteria.	
10.	Is your laboratory interested in participating in an effort to establish an OPCW capability to analyse biomedical samples?	Yes X	No ☐
		Please provide any comments in the space below.	
		LLNL would be interested in participating with OPCW and Member States to establish new capabilities in the analysis of biomedical samples.	

11.	Is your laboratory willing to be designated by the Director-General of the Secretariat to analyse biomedical samples in the context of OPCW activities and proficiency testing?	Yes: X	No ☐
		Please provide any comments in the space below.	
		LLNL is currently an OPCW Designated laboratory and has participated in OPCW proficiency testing since 2001.	
12.	Is your laboratory willing to participate in inter-laboratory confidence-building exercises?	Yes X	No ☐
		Please provide any comments in the space below.	
		Our participation in inter-laboratory exercises would depend on funding allocations and may vary.	
13.	Is your laboratory willing to participate in proficiency testing with a view to being selected as an OPCW Designated Laboratory?	Yes:X	No ☐
		Please provide any comments in the space below.	
		LLNL is currently an OPCW Designated laboratory and would like to extend its scope to the analysis biomedical samples.	
14.	Is your laboratory willing to share its knowledge and skills regarding the analysis of biomedical samples-for example, by providing training to technicians from other Member States?	Yes: X	No ☐
		Please provide any comments in the space below.	
		Yes, if funding were made available.	
15.	Would your laboratory be willing to analyse samples obtained by the OPCW in connection with an investigation into the alleged use of chemical weapons?	Yes: X	No ☐
		Please provide any comments in the space below.	
		Yes, if funding were made available.	

Appendix 1

SAMPLING AND ANALYSIS OF BIOMEDICAL SAMPLES FOR THE PRESENCE OF CHEMICAL AGENTS: KEY METHODS[1]

The following tables list analytical methods that the temporary working group on biomedical samples considers to be particularly useful. Please indicate, in the fourth column, what capability, if any, your laboratory has for each method listed. Please make any additional comments in the last column.

TABLE 1: ANALYTICAL METHODS TO CHECK FOR THE PRESENCE OF SULFUR MUSTARD

Sample Type	Key Biomarkers	Analytical Methods Currently Available	Is the Method Available in Your Laboratory?		Comments
			Yes	No	
Urine	Thiodiglycol (TDG)	GC-MS-MS	X	☐	Currently not ISO-17025 validated and detection limits have not been optimized
	TDGO β-lyase metabolites	LC-MS-MS	X	☐	Currently not ISO-17025 validated and detection limits have not been optimized
Blood	Protein adducts:	Chemical or enzymatic digestion, followed by:	☐	No	If provided with a literature reference or OPCW protocol we could conduct the analysis
	N-terminal valine on Hb	GC-MS or GC-MS-MS	☐	No	If provided with a literature reference or OPCW protocol we could conduct the analysis
Blood, continued	Protein adducts:	Chemical or enzymatic digestion, followed by:			

[1] Adapted from Appendix 6 to the report of the Seventh Session of the SAB (SAB-7/1).

Legend for abbreviations used in this Annex:

BA: Benzilic acid	**DNA:** Deoxyribose nucleic acid	**Hb:** Haemoglobin	**Q:** 3-quinuclidinol
BuChE: Butyryl-cholinesterase	**EI:** Electron impact	**HETE:** Hydroxyethylthioethyl	**TDGO:** Thiodiglycol oxide
BZ: 3-quinuclidinyl benzilate	**ELISA:** Enzyme-linked immunosorbent assay	**HR:** High resolution	
CVAA: 2-chlorovinyl-arsenous acid	**GC-MS-MS:** gas chromatography–mass spectrometry–mass spectrometry	**LC-MS-MS:** Liquid chromatography-mass spectrometry-mass spectrometry	

Sample Type	Key Biomarkers	Analytical Methods Currently Available	Is the Method Available in Your Laboratory?		Comments
			Yes	No	
	Histidine residues on Hb	LC-tandem MS	Y	☐	If provided with a literature reference or OPCW protocol we could conduct the analysis
	Cysteine residue on albumin	LC-tandem MS	Y	☐	If provided with a literature reference or OPCW protocol we could conduct the analysis
	Aspartic acid/glutamic acid residues on blood proteins and keratin	GC-MS	Y	☐	If provided with a literature reference or OPCW protocol we could conduct the analysis
Urine	DNA adducts: Alkylation of deoxyguanosine (N7)	LC-MS-MS for N7-HETE-guanine	Y	☐	If provided with a literature reference or OPCW protocol we could conduct the analysis
Blood	Alkylation of deoxyguanosine (N7)	ELISA for N7-HETE-guanosine-5'-phosphate	☐	N	
	Other biomarkers		☐	☐	

TABLE 2: ANALYTICAL METHODS TO CHECK FOR THE PRESENCE OF NERVE AGENTS

Sample Type	Key Biomarkers	Analytical Methods Recommended	Is the Method Available in Your Laboratory?		Comments
			Yes	No	
Blood	Cholinesterase activity		☐	N	
Blood	Fluoride reactivation method: Phosphylated BuChE (and other proteins)	GC-MS	Y	☐	If provided with a literature reference or OPCW protocol we could conduct the analysis
Blood	Analysis of phosphylated peptides: Phosphylated BuChE	LC-MS-MS (after enzymatic digestion of modified cholinesterase)	Y	☐	If provided with a literature reference or OPCW protocol we could conduct the analysis
Urine/serum	Hydrolysis products: Alkyl methyl-phosphonic acids (does not include tabun)	GC-MS-MS	Y	☐	If provided with a literature reference or OPCW protocol we could conduct the analysis
		LC-MS-MS	Y	☐	If provided with a literature reference or OPCW protocol we could conduct the analysis

Sample Type	Key Biomarkers	Analytical Methods Recommended	Is the Method Available in Your Laboratory?		Comments
			Yes	No	
	Other biomarkers		Y	☐	If provided with a literature reference or OPCW protocol we could conduct the analysis

TABLE 3: ANALYTICAL METHODS TO CHECK FOR THE PRESENCE OF LEWISITE

Sample Type	Key Biomarkers	Analytical Methods Recommended	Is the Method Available in Your Laboratory?		Comments
			Yes	No	
Urine	CVAA	Solid-phase micro-extraction headspace sampling, followed by GC-MS with EI ionisation	Y	☐	Currently not ISO-17025 validated and detection limits have not been optimized
Blood	CVAA (globin bound and free)	GC-MS	Y	☐	Currently not ISO-17025 validated and detection limits have not been optimized
	Other biomarkers		☐	☐	

TABLE 4: ANALYTICAL METHODS TO CHECK FOR THE PRESENCE OF PHOSGENE

Sample Type	Key Biomarkers	Analytical Methods Recommended	Is the Method Available in Your Laboratory?		Comments
			Yes	No	
Blood	Protein adduct: Albumin peptide	LC-MS-MS	Y	☐	If provided with a literature reference or OPCW protocol we could conduct the analysis
	Other biomarkers		☐	☐	

TABLE 5: ANALYTICAL METHODS TO CHECK FOR THE PRESENCE OF CYANIDE

Sample Type	Key Biomarkers	Analytical Methods Recommended	Is the Method Available in Your Laboratory?		Comments
			Yes	No	
Blood	Cyanide itself	GC	Y	☐	If provided with a literature reference or OPCW protocol we could conduct the analysis
Urine	Cystine adduct	HPLC	Y	☐	If provided with a literature reference or OPCW protocol we could conduct the analysis
	SCN	GC–LC	Y	☐	If provided with a literature reference or OPCW protocol we could conduct the analysis
	2-amino-thiazoline, 4-carboxylic acid	GC–LC	Y	☐	If provided with a literature reference or OPCW protocol we could conduct the analysis
	Other biomarkers		☐	☐	

TABLE 6: ANALYTICAL METHODS TO CHECK FOR THE PRESENCE OF BZ

Sample Type	Key Biomarkers	Analytical Methods Recommended	Is the Method Available in Your Laboratory?		Comments
			Yes	No	
Urine	BZ, BA Q	LC-MS-MS	Y	☐	Currently not ISO-17025 validated and detection limits have not been optimized
	Other biomarkers		☐	☐	

Appendix 2

ANALYTICAL METHODS IN USE IN YOUR LABORATORY[2]

Sample Type[3]	Biomarker[4]	Analytical Technique and Instrumentation[5]	Comments[6]

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2 Please include additional copies of this page if necessary.
3 Blood, urine, and so on
4 Phosphylated BuChE, CVAA, and so on
5 GC-MS, LC-MS-MS, and so on
6 Please mention any relevant quality-control procedures, any accreditation the laboratory has earned in respect of this method, and so on.