

CLINICAL TOXICOLOGY

Prof. Dr. Raphaël DENOZ
 Pharmacist Bio/ogist
 Tel: 00-32/4 323 88 16
 Raphael.Denoz@chuliege.be

Marine DEVILLE
 Pharmacist Bio/ogist Tel:
 00-32/4 323 76 79
 M. Deville@chuliege.be

MEDICO-LEGAL TOXICOLOGY
In Liège and Charleroi

Prof. Dr. Raphaël DENOZ
 Pharmacien Biologiste
 Forensic expert
 Tel: 00-32/4 323 88 16
 GSM : 0498175 70 94
 Raphael. Denoz@chuliege.be

Marine DEVILLE
 Pharmacist Bio/ogist Tel :
 00-32/4 323 76 79 GSM :
 0498/31.13.71
 M. Deville@chuliege.be

In Charleroi

Isabelle RENAUX-MUYLKENS
 Pharmacist Forensic
 scientist
 Tel: 00-32171 32 91 25
 GSM : 0472/88 60 93
 Isabelle. Muiykens@chuliege.be

ENVIRONMENTAL TOXICOLOGY

Dr Catherine PIRARD
 Master in Chemical Sciences
 Tel: 00-32/4 323 88 16
 C. Pirard@chuliege.be

Julien CLAESSENS
 Pharmacist
 Tel: 00-32/4 323 80 95
 Julien. Claessens@uliege.be

CORPORATE TOXICOLOGY

Dr Nathalie DUBOIS
 /Industrial sector
 Tel: 00-32/4 323 76 82
 Nathalie. Dubois@chuliege.be

GLP UNIT - AEPT
**GLP Analysis and Evaluation Unit
 Preclinical and Toxicological**

Dr Patrice CHIAP
 Pharmacist
 Tel: 00-32/4 323 28 67
 Patrice. Chiap@chuliege.be

Thomas DUBROWSKI
 Bioing!!nieur
 Tel: 00-32/4 323 28 66
 Thomas. Dubrowski@chuliege.be

Dr Nathalie DUBOIS
 Ing!!nieure Industriale
 Tel : 00-32/4 323 76 82
 Nathalie. Dubois@chuliege.be

Executive Secretary

Shirley PARENT - secretoxico@chuliege.be
 Tel : 00-32/4 323 76 83 - Fax : 00-32/4 323 88 89

Administrative Secretary (Liège)

Audrey GUILLAUME -Audrey. Guillaume@chuliege.be
 Tel : 00-32/4 323 76 83 - Fax : 00-32/4 323 88 89

Administrative secretary (Charleroi)

Cilline DEBAIX - Cellne. Debaix@chuliege.be
 Tel : 00-32171 32 91 25 - Fax : 00-32171 47 07 25

**DETERMINATION OF PERFLUORINATED SUBSTANCES IN
 THE BLOOD OF PEOPLE LIVING NEAR AN
 INDUSTRIAL SITE**

Perfluorinated substances (PFAS) represent a family of molecules with a carbon chain in which all carbon atoms are substituted by fluorine atoms. They have been synthesized since the 1950s for their water-repellent properties, and are used in non-stick surfaces for utensils and cookware, food packaging, anti-stain treatment for carpets and fabrics, waterproof clothing and excipients for certain creams, with the role of surfactant, wetting agent, emulsifier or dispersant. In addition to their high hydrophobicity and lipophobicity, their carbon-fluorine bond is one of the strongest in organic chemistry, giving them high stability. When found in the environment, PFAS are extremely persistent, capable of long-range transport and bioaccumulation in living organisms. Since 2009, when PFOA and PFOS were classified as Persistent Organic Pollutants (POPs) under the Stockholm Convention, their uses have been greatly reduced. Nevertheless, the former massive production and use of these products contaminated the environment, and numerous studies have shown their presence in the different links of the food chain, whether in the animal or plant kingdom, in surface and drinking water, but also in indoor air and house dust. Once they enter the body, through ingestion, inhalation or dermal contact, PFASs bind to blood proteins. Since they are not metabolized very much, they will

accumulate in the body. Their blood levels reflect long-term exposure.

The Investigation program (RTBF) has entrusted the Toxicology laboratory of the University Hospital of Liege with the determination of several PFAS, including PFOA and PFOS, in blood samples taken from

people living in Spinetta Marengo on the one hand, and in the vicinity of Solvay industrial site (fluoropolymer production site), and a few kilometers further on, in Alessandria (Piemont), Italie). The aim was to objectify a suspicion of particularly high exposure to PFAS of the people living near Solvay, linked to the activities and emissions of the company, and therefore a higher PFAS contamination of this population.

TOXICOLOGY DEPARTMENT**Professor Dr Corinne CHARLIER - C.Charlier@chuliege.be***Head of Department, Ordinary Professor - Judicial Expert*

In addition to the blood samples, participants in both locations also **completed** a short questionnaire about their age, occupation, some of their personal interests, and their family background.

their dietary habits, and other factors known to potentially influence their PFAS contamination rate such as smoking status. The determination of the following 7 PFAS was performed on the collected serum: perfluorohexanoic acid (PFHxA), perfluoroheptanoic acid (PFHpA), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluorohexane sulfonate (PFHxS) and perfluorooctane sulfonate (PFOS). Analytical procedure used which consists of a solid phase extraction followed by an injection on a liquid chromatograph coupled to a tandem mass spectrometer (LC-MS/MS) operating in Multiple Reaction Monitoring (MRM), and has been described in detail in Dufour et al., 2018 (Environ. Pollut. 238, 389-396). Quantification was performed by isotope dilution using its own carbon-labeled isotope for each of the measured PFAS.

13 (¹³C₄). Each set of samples consisted of a calibration line made up of standards composed of beef serum spiked at 8 different concentrations (0.5 to 50 µg/l for PFOA and PFOS, and 0.1 to 10 µg/l for all other PFAS) and extracted as

real samples, 1 reagent blank, 1 bovine serum blank, and 2 reference materials from external quality assurance programs (AMAP, Centre de Toxicologie du Quebec, Institut National de Sante Publique du Quebec). This method was previously validated according to the total error approach using Enoval V4.0 software (Arlenda, Liege, Belgium). In addition, the laboratory has successfully passed the ICI/EQUAS exercises organized in the framework of the HBM4EU project and has been certified as a HBM4EU qualified laboratory for

The analysis of these 7 PFAS in human serum. The limits of quantitation (LOQ), defined as the smallest measurable concentrations in spiked beef serum samples with a total error not exceeding 30%, are listed below:

PFHxA, PFHpA, PFHxS, PFNA: 0.1 µg/L each; PFDA:

0.15 µg/L;

PFOA, PFOS: 0.5 µg/L each.

Statistical tests (Mann-Whitney, Spearman, multiple regressions) were performed at

Using Statistica 12 software, taking into account the different factors that can affect the serum concentrations of PFAS (confounding factors), we determined whether the contamination of the participants in Spinetta is significantly different from that of the participants in Alessandria.

Executive Secretary

Shirley PARENT - secretoxico@chuliege.be
Tel: 00-32/4 366 76 83 - Fax: 00-32/4 366 88 89

Administrative secretary (Liege/

Audrey GUILLAUME -Audrey. Guillaume@chuliege.be
Tel : 00-32/4 366 76 83 - Fax : 00-32/4 366 88 89

Administrative secretary (Charleroi/

C6llne DEBAIX - Celine. Debaix@chuliege.be
Tel: 00-32/71 32 91 25 - Fax: 00-32/71 47 07 25

RESULTS

The table below (Table 1) shows the characteristics of the two groups of participants.

Table 1: Characteristics of the two populations

	Spinetta	Alessandria
N	31	21
Women	14 (45%)	12 (57%)
Hemmes	17 (55%)	9 (43%)
Age	65 years old	46 years old
N<50 years	1 (3%)	12 (57%)
N>50 years	30 (97%)	9 (43%)
Employee (former) Solvay	6 (19%)	1 (5%)
Fish consumption	12 (39%)	9 (43%)
Consumption of fruits/vegetables from the garden	15 (48%)	1 (5%)
Consumption of eggs premises	7 (23%)	1 (5%)
Smokers	7 (23%)	14 (67%)

One person from the Alessandria group currently resides about 50 km away, but has lived there until 2019. The population recruited in Spinetta is much older than in Alessandria (average age 65 vs. 46), includes slightly more men (55% vs. 43%), more former workers of the Solvay plant (who have been professionally exposed to PFAS), more people consuming or having consumed before (during the PFOA activity) products (fruits and/or vegetables) from their garden or from very local production (48% vs. 5%), more consumers (or former consumers) of eggs from local farms, and fewer smokers (23% vs. 67%). The two populations are therefore very different in terms of characteristics potentially related to PFAS impregnation rates, which may induce a bias in the results obtained, which is why we have chosen to focus on the two populations.

led to comparisons between subgroups (see below) and the use of multivariate statistical tests.

TOXICOLOGY DEPARTMENT
Professor Dr Corinne CHARLIER - C.Charlier@chuliege.be
Head of Department, Full Professor - Forensic Expert

Tables 2 and 3 present the concentrations of the 7 PFAS measured in the serum of each participant

Table 2: PFAS concentrations measured in the serum of each Spinetta participant, expressed in µg/L.

Spinetta	PFHxA	PFHpA	PFHxS	PFOA	PFNA	PFOS	PFDA
Participant number	µg/L	µg/L	µg/L	µg/L	µg/L	µg/L	µg/L
A1	<0.10	<0.10	0.56	2.95	0.56	2.68	0.23
A2	<0.10	<0.10	0.70	10.20	0.81	2.91	0.32
A3	<0.10	<0.10	0.83	7.33	0.58	3.78	0.27
A4	<0.10	<0.10	0.27	2.58	0.58	2.48	0.36
AS	<0.10	<0.10	0.34	5.49	0.43	2.16	0.15
AG	<0.10	0.10	0.94	17.50	0.87	4.14	0.40
A7	<0.10	<0.10	0.73	22.37	0.48	1.18	<0.15
A8	<0.10	<0.10	0.52	13.29	0.32	1.53	<0.15
A9	<0.10	<0.10	0.83	14.92	0.86	2.66	0.15
A10	<0.10	<0.10	1.25	13.91	2.23	6.79	0.71
A11	<0.10	<0.10	0.68	10.10	0.48	4.02	0.26
A12	<0.10	<0.10	0.69	11.23	0.82	3.35	0.37
A13	<0.10	<0.10	0.29	4.65	0.36	1.44	<0.15
A14	<0.10	<0.10	0.59	3.57	0.72	3.18	0.31
A15	<0.10	<0.10	0.45	8.99	0.25	0.76	<0.15
A16	<0.10	<0.10	0.82	3.63	0.20	0.55	<0.15
A17	<0.10	<0.10	1.13	26.78	1.03	5.83	0.37
A18	<0.10	<0.10	0.86	44.58	0.75	3.75	0.26
A19	<0.10	<0.10	0.43	21.22	0.44	1.69	<0.15
A20	<0.10	<0.10	1.36	3.58	0.70	3.05	0.21
A21	<0.10	<0.10	0.79	9.23	0.51	2.29	<0.15
A22	<0.10	<0.10	0.90	24.21	0.95	3.57	0.41
A23	<0.10	<0.10	0.67	2.88	0.31	1.88	<0.15
A24	<0.10	<0.10	0.55	13.51	0.88	3.08	0.34
A25	<0.10	<0.10	0.27	3.15	0.64	2.01	0.24
A26	<0.10	<0.10	0.85	16.36	1.49	6.30	0.56
A27	<0.10	<0.10	1.37	5.41	0.64	3.15	0.31
A28	<0.10	<0.10	0.82	33.79	0.60	2.30	0.25
A29	<0.10	<0.10	0.91	78.08	1.25	7.07	0.47
A30	<0.10	<0.10	0.57	10.72	0.45	2.55	<0.15
A31	<0.10	<0.10	0.40	6.79	0.72	2.98	0.48

Executive Secretary

 Shirley PARENT - secretoxico@chuliege.be
 Tel : 00-32/4 366 76 83 - Fax : 00-32/4 366 88 89

Administrative secretary fl/ilae/l

 Audrey GUILLAUME - Audrey.Guillaume@chuliege.be
 Tel : 00-32/4 366 76 83 - Fax : 00-32/4 366 88 89

Secr(aire administrative fCharleroi

 Celine DEBAIX - Celine.Debaix@chuliege.be
 Tel : 00-32/71 32 91 25 - Fax : 00-32/71 47 07 25

TOXICOLOGY DEPARTMENT

Professor Dr Corinne CHARLIER - C.Charlier@chuliege.be

Head of Department, Full Professor - Judicial Expert

Table 3: PFAS concentrations measured in the serum of each participant from Alessandria, expressed in µg/L.

Alessandria	PFHxA	PFHpA	PFHxS	PFOA	PFNA	PFOS	PFDA
Participant number	µg/L	µg/L	µg/L	µg/L	µg/L	µg/L	µg/L
All	<0.10	0.28	1.86	11.48	2.28	9.65	0.89
AL2	<0.10	<0.10	0.39	1.11	0.25	1.03	<0.15
AL3	<0.10	<0.10	0.76	3.74	0.69	3.54	0.31
AL4	<0.10	<0.10	1.62	6.41	0.57	2.63	0.16
AL5	<0.10	<0.10	0.22	1.23	0.59	2.87	0.19
AL6	<0.10	<0.10	0.42	1.89	0.48	1.63	0.19
AL7	<0.10	<0.10	0.16	0.68	0.18	0.54	<0.15
AL8	<0.10	<0.10	0.58	2.50	0.42	1.90	0.15
AL9	<0.10	<0.10	0.34	0.90	0.23	1.02	<0.15
AL10	<0.10	<0.10	0.87	2.08	0.33	1.96	<0.15
AL11	<0.10	<0.10	0.34	1.61	0.32	1.74	0.18
AL12	<0.10	<0.10	0.50	2.55	0.45	1.56	<0.15
AL13	<0.10	<0.10	0.69	2.41	0.34	1.70	<0.15
AL14	<0.10	<0.10	1.09	3.30	0.37	1.57	<0.15
AL15	<0.10	<0.10	1.03	3.96	0.28	1.81	<0.15
AL16	<0.10	<0.10	0.59	2.80	0.68	4.03	0.28
AL17	<0.10	<0.10	0.27	0.97	0.17	0.59	<0.15
AL18	<0.10	<0.10	0.17	1.40	0.32	1.82	0.15
AL19	<0.10	<0.10	0.27	1.46	0.31	0.60	<0.15
AL20	<0.10	<0.10	0.62	2.03	0.50	2.53	<0.15
AL21	<0.10	<0.10	0.19	1.26	0.22	1.31	0.17

Executive Secretary

 Shirley PARENT - secretoxico@chuliege.be
 Tel : 00-32/4 323 76 83 - Fax : 00-32/4 323 88 89

Administrative secretary (Liege)

 Audrey GUILLAUME -Audrey.
 Guillaume@chuliege.be Tel : 00-32/4 323 76 83 - Fax :
 00-32/4 323 88 89

Administrative secretary (Charleroi)

 Celine DEBAIX - Celine. Debaix@chuliege.be Tel:
 00-32/71 32 91 25 - Fax: 00-32/71 47 07 25

TOXICOLOGY DEPARTMENT
Professor Dr Corinne CHARLIER - C.Charlier@chuliege.be
Head of Department, Full Professor - Forensic Expert

Table 4 shows for 7 PFAS the 50 (PS0) and 95 (P95) percentiles of the concentrations measured for all participants residing in Spinetta, Alessandria, and a Walloon population (Liege) of 242 non-occupationally exposed adults recruited in 2015 for comparison. The PS0 value represents the value below which 50% of the participants' results are found (median value). The P95 value indicates the value below which 95% of the participants' results are found (above which the 5% of the most contaminated persons are found).

Table 4: Results of the assays expressed in µg/L

		Alessandria (2022)	Spinetta (2022)	Liege, Wallonia (2015)
Age	Average	46	65	45
PFHxA	PS0 (µg/L)	<0.10	<0.10	<0.10
	P95 (µg/L)	<0.10	<0.10	<0.10
PFHpA	PS0 (µg/L)	<0.10	<0.10	<0.10
	P95 (µg/L)	<0.10	<0.10	0.11
PFHxS	PS0 (µg/L)	0.46	0.70	1.07
	P95 (µg/L)	1.12	1.31	2.73
PFOA	PS0 (µg/L)	1.96	10.20	1.91
	P95 (µg/L)	4.08	39.19	4.72
PFNA	PS0 (µg/L)	0.34	0.64	0.54
	P95 (µg/L)	0.68	1.37	1.41
PFOS	PS0 (µg/L)	1.72	2.91	4.3
	P95 (µg/L)	3.56	6.55	11.8
PFDA	PS0 (µg/L)	0.18	0.32	0.29
	P95 (µg/L)	0.30	0.56	0.82

PFHxA and PFHpA were not detected in any of the serum samples analyzed (except in All for PFHpA).

DISCUSSION

In Table 4, it appears that overall higher concentrations of all PFAS detected (PFHxS, PFOA, PFNA, PFOS and PFDA) were measured in serum samples of the Spinetta participants compared to the Alessandria samples (about 2 times more for most PFAS, 5 to 10 times more for PFOA PS0 and P95). When comparing these results to values reported in a study of PFAS impregnation rates in Wallonia carried out by our laboratory on a population of 242 adults from the general population recruited in 2015 (to our knowledge currently one of the most important studies of the Walloon region).

The most recent available data show that PFOA concentrations are also 5 to 10 times higher, while the other PFAS show values close to or even lower than

TOXICOLOGY DEPARTMENT**Professor Dr Corinne CHARLIER - C.Charlier@chuliege.be***Head of Department, Full Professor - Forensic Expert*

those measured in Wallonia. The concentrations measured in the samples of the participants of Alessandria are close or lower than the beige values of 2015 whatever or the PFAS considered. It is not surprising to see lower impregnation levels on samples collected in 2022 compared to older samples (2015 in this case) because for the last decade, there has been a worldwide decrease in impregnation.

concentrations of PFAS in the blood of the general population, reflecting the restrictions imposed on the use and production of PFOS and PFOA since their inclusion in the list of POPs of the Stockholm Convention.

However, one must be very careful when comparing these results. In fact, the two groups recruited in Spinetta and Alessandria are very different, especially in terms of age.

PFAS are persistent compounds that accumulate in organisms. From numerous studies have shown a relationship between serum PFAS concentrations and age, with older individuals showing higher concentrations as a result of a longer period of exposure and accumulation. It was expected that

In addition, the Alessandria group includes more females, who have mostly lower serum PFAS levels than males, probably related to the elimination pathways of these compounds. In addition, the Alessandria group includes more women, who generally have lower serum PFAS levels than men, probably due to their own pathways of elimination of these compounds (breastfeeding, menstruation) and/or to the fact that they have different lifestyles, dietary habits or food intake.

different from men, resulting in lower contamination. In addition, almost one person in five recruited at Spinetta has worked for many years at the Solvay-Spinetta site and has therefore been potentially subject to occupational exposure. Finally,

A greater number of smokers were present in the Alessandria group, although it has been suggested that smoking may accelerate the metabolism of some xenobiotics, although no study has been able to demonstrate a significant difference in serum PFAS concentration as a function of smoking status. Overall, the difference in the characteristics of the two populations that may have an impact on contamination rates is in the direction of a higher PFAS serum concentration in participants residing in Spinetta.

Therefore, in order to investigate objectively whether one of the two groups has suffered a particular environmental exposure related to the place of residence near the Solvay site, it is necessary to apply multivariate statistical tests (multiple regression) that take into account these different parameters (such as age, sex, smoking status, occupational exposure, consumption of potentially more contaminated foods, etc.).

Table 5 shows the results of multiple regressions for all detected PFAS. To perform these regressions, Spearman correlations were performed (for PFAS concentrations as a function of age as a continuous variable) as well as tests

Executive Secretary

Shirley PARENT- secretoxlco@chullege.be
Tel : 00-32/4 323 76 83 - Fax : 00-32/4 323 88 89

Administrative secretary fl illege/

Audrey GUILLAUME -Audrey. Guillaume@chuliege.
be
Tel : 00-32/4 323 76 83 - Fax : 00-32/4 323 88 89

Administrative secretary (Charleroi/

Citllne DEBAIX - Celine. Debalx@chullege.be
Tel : 00-32/71 32 91 25 - Fax : 00-32/71 47 07 25

TOXICOLOGY DEPARTMENT

Professor Dr Corinne CHARLIER - C.Charlier@chuliege.be
 Head of Department, Ordinary Professor - Forensic Expert

Mann-Whitney test (comparison of 2 independent groups) for the following categorized variables: place of residence (Spinetta vs. Alessandria), gender (female vs. male), occupational exposure (former Solvay worker vs. other job), fish consumption (<1x/week vs. >1x/week), consumption of garden fruits and/or vegetables (yes even if former vs. no), consumption of locally produced eggs (yes vs. no), smoking status (smoker vs. non-smoker). If PFAS concentration was significantly related (p -value < 0.05), this variable was added in the multivariate model. Responses to questions about blood donation and breastfeeding were not used in the statistical tests because there were few positive responses. Alcohol consumption was also not considered because of the highly subjective nature of the responses. The logarithm of the PFAS concentrations was used in the multiple regressions to approximate a normal distribution.

Table 5: Multiple regression results obtained (b = coefficient beta= relative contribution in the model; SE = standard error obtained on b; p-value, considered significant if <0.05)

	PFOA $R^2 = 0,69784671$			PFOS $R^2 = 0,26297714$			PFDA $R^2 = 0,30052592$		
	B	SE	p-value	b	SE	p-value	b	SE	p-value
Intercept	-0.375	0.376	0.3901	0.406	0.336	0.234	-1.628	0.392	0.0001
Place of residence	0.779	0.235	0.0002	0.006	0.210	0.976	0.396	0.245	0.1132
Age	0.023	0.006	0.0009	0.005	0.006	0.427	-0.009	0.007	0.1719
Occupational exposure (Solvay)	1.022	0.247	0.0022	0.623	0.221	0.007	0.872	0.258	0.0015
Fish consumption	0.013	0.180	0.1088	0.256	0.162	0.120	0.422	0.188	0.0299
Consumption of vegetables/fruits from the garden	0.290	0.211	0.9468	0.161	0.189	0.400	-0.075	0.221	0.7341
Smoking status	0.009	0.205	0.9321	-0.254	0.184	0.175	-0.340	0.214	0.1196
	PFHxS $R^2 = 0.32259769$			PFNA $R^2 = 0.34958338$					
	b	SE	p-value	b	SE	p-value			
Intercept	-1.063	0.324	0.0021	-0.959	0.311	0.0036			
Place of residence	0.045	0.189	0.8128	0.209	0.180	0.2517			
Age	0.012	0.005	0.0275	0.000	0.005	0.9410			
Occupational exposure (Solvay)	0.020	0.2287	0.9307	0.736	0.197	0.0006			
Fish consumption	0.199	0.146	0.1804	0.235	0.140	0.1017			
Consumption of garden vegetables/fruits	-0.102	0.173	0.5590	0.013	0.162	0.9353			
Smoking status	-0.084	0.166	0.6136	-0.226	0.159	0.1609			
Gender (women vs. men)	-0.379	0.148	0.0138	0.069	0.138	0.6203			

Executive Secretary

Shirley PARENT - secretoxico@chuliege.be
 Tel : 00-32/4 323 76 83 - Fax : 00-32/4 323 88 89

Administrative secretary (Liljoe)

Audrey GUILLAUME -Audrey. Guillaume@chuliege.be
 Tel : 00-32/4 323 76 83 - Fax : 00-32/4 323 88 89

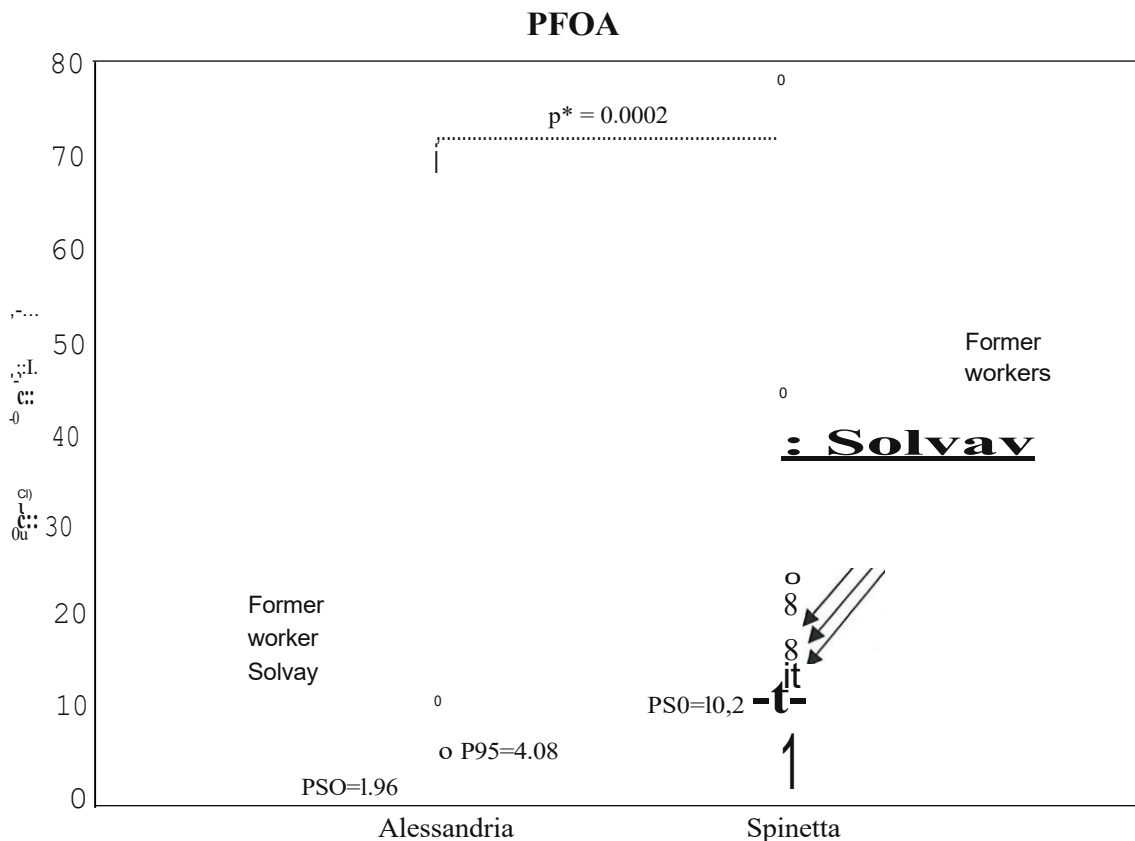
Administrative secretary (Charloir)

Celine DEBAIX - Celine. Debaix@chuliege.be
 Tel : 00-32/71 32 91 25 - Fax : 00-32/71 47 07 25

This table 5 shows that for PFOA, taking into account all the variables that influence the serum concentration (confounding factors), participants living in Spinetta, older people and former employees of the Solvay site in Spinetta are significantly more contaminated than participants from Alessandria, younger people and people who have never worked at the Solvay site. For the other PFAS, the concentrations are significantly higher for former Solvay workers (PFOS, PFDA, PFNA), those who consume fish more than once a week (PFDA), older people (PFHxS) and men (PFHxS).

Figure 1 shows the PFOA concentrations measured in the individual samples of the participants living in Spinetta and Alessandria, highlighting the values obtained in the former Solvay workers. Figure 2 also shows these concentrations observed in the inhabitants of Spinetta and Alessandria, but this time as a function of the age of the participants.

Figure 1: PFOA concentration ($\mu\text{g/L}$) measured for each participant from Spinetta and Alessandria. The p-value was evaluated taking into account the age and the occupational exposure.



p^* : adjusted for age and former Solvay workers

Executive Secretary

Shirley PARENT - secretoxico@chuliege.be
Tel : 00-32/4 323 76 83 - Fax : 00-32/4 323 88 89

Administrative secretary (Liege/

Audrey GUILLAUME -Audrey. Guillaume@chuliege.be
Tel : 00-32/4 323 76 83 - Fax : 00-32/4 323 88 89

Administrative secretary (Charleroi/

Celine DEBAIX - Celine. Debaix@chuliege.be
Tel: 00-32171 32 91 25 - Fax: 00-32/71 47 07 25

Figure 2: PFOA concentration ($\mu\text{g/L}$) measured for each participant from Spinetta (blue) and Alessandria (orange), as well as P95 values obtained in a Liege population recruited in 2015 according to age.

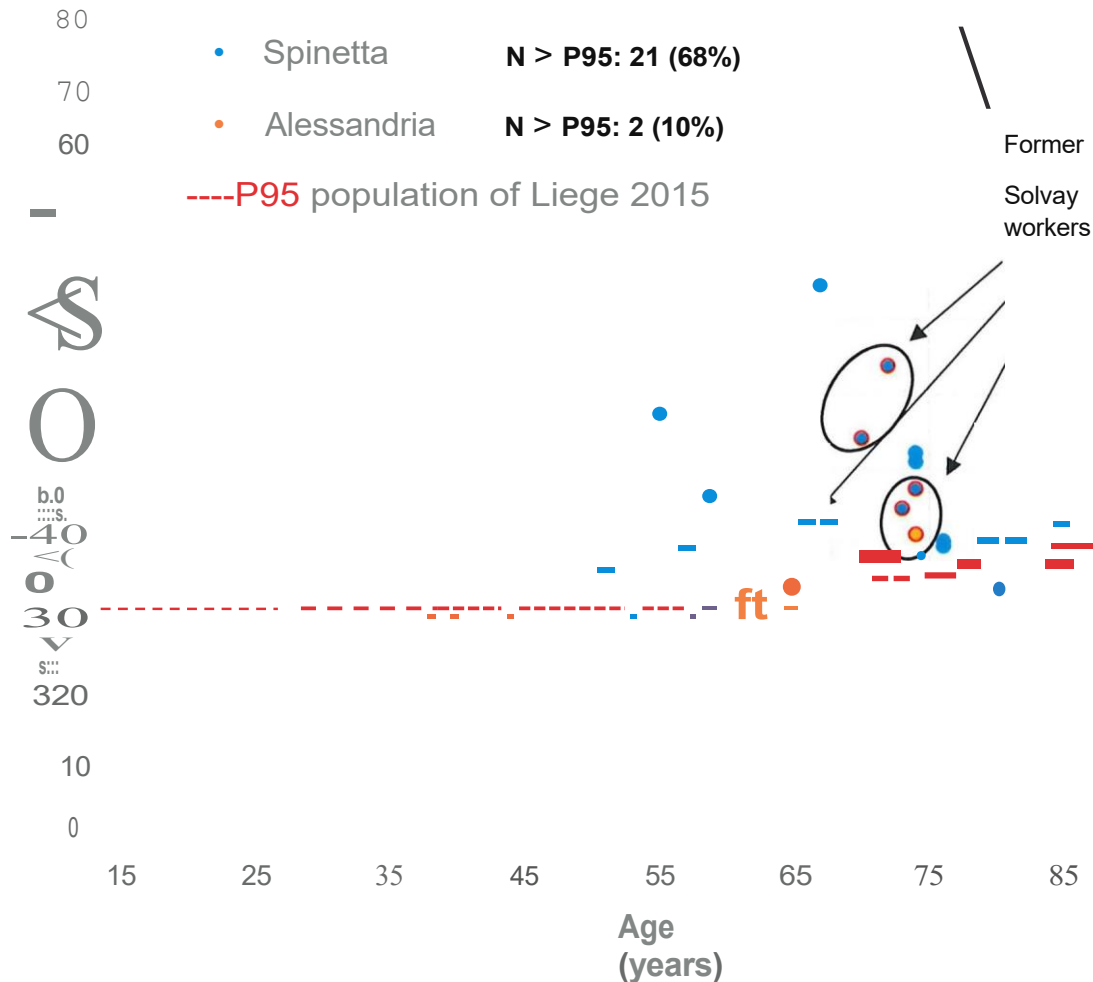


Figure 1 shows a difference in serum PFOA concentration between the inhabitants of Spinetta and Alessandria (P50, P95 and overall distribution), as well as a higher concentration for the former Solvay workers. This representation of the results does not allow to visualize the impact of age and the higher proportion of older people in the Spinetta group. Nevertheless, statistical tests reveal that this difference remains significant ($p = 0.0002$) when adjusting the model for different covariates including age. In figure 2, we observe the influence of age on the measured PFOA concentrations, as well as the fact of having worked at Solvay. It can also be seen in Figure 2 that although few participants from Alessandria exceeded the P95 value obtained for a population of Liege (adjusted for age), more than 2 out of 3 people in Spinetta's group This is especially true for people over 60 years of age. This value of P95 of a This figure also shows the heterogeneity of the two populations. This figure also highlights the heterogeneity of the two populations in terms of age, with the majority of participants recruited in Alessandria having hands 50 years for only 1 participant from Spinetta. Figure 3 shows the number of participants in each 5-year age range for the two recruited populations (excluding former Solvay workers),

as well as the serum PFOA concentration for
All participants over 50 years of age (again excluding former Solvay workers).

Executive Secretary

Shirley PARENT - secretoxico@chuliege.be
Tel : 00-32/4 323 76 83 - Fax : 00-32/4 323 88 89

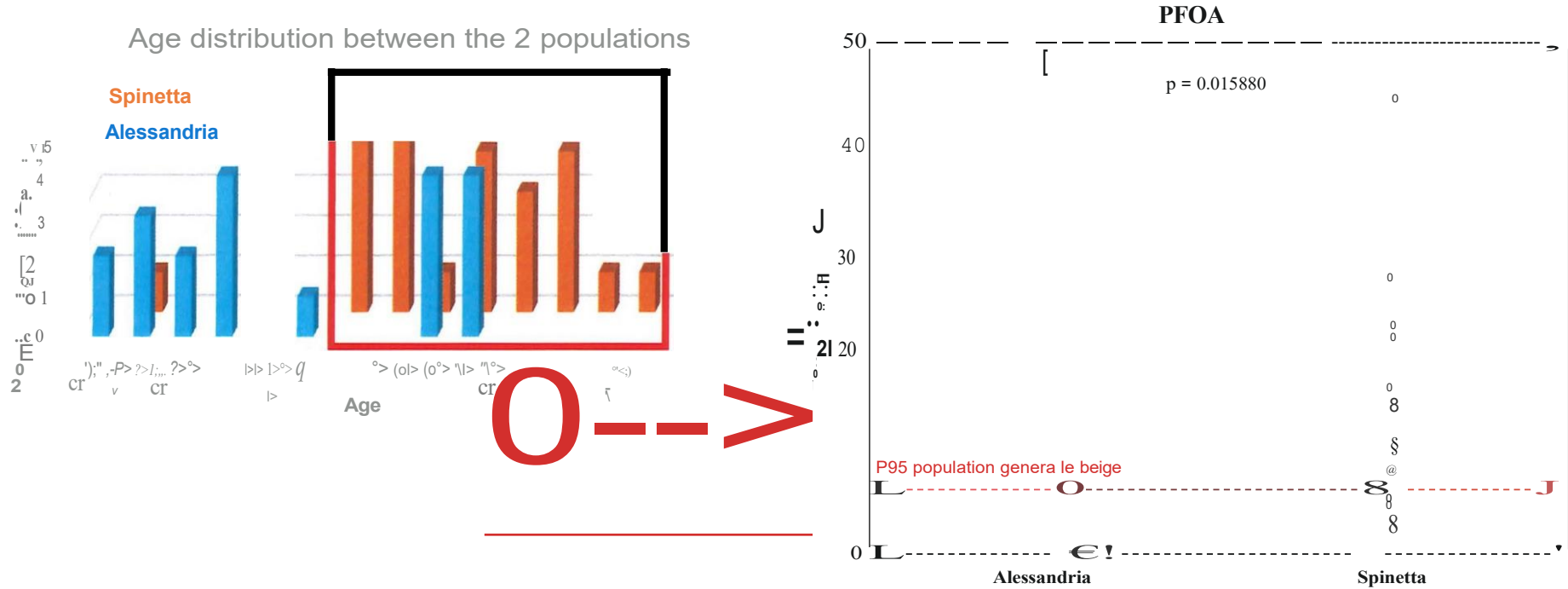
Administrative secretary (Liljæ)

Audrey GUILLAUME - Audrey.Guillaume@chuliege.be
Tel : 00-32/4 323 76 83 - Fax : 00-32/4 323 88 89

Administrative secretary (Charleroi)

Cilline DEBAIX - Celine.Debaix@chuliege.be
Tel: 00-32/71 32 91 25 - Fax: 00-32/71 47 07 25

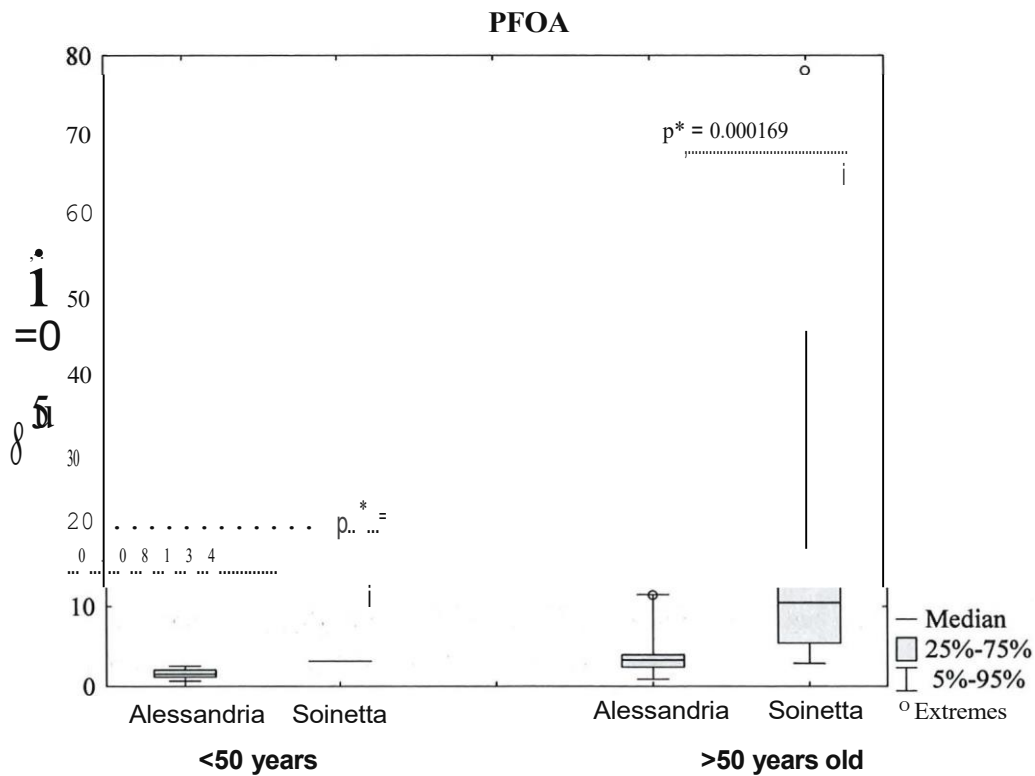
Figure 3: Distribution of participants according to age (left) and serum PFOA concentration (right) for the over 50s (excluding former Solvay workers)



By selecting only people over 50 years of age and excluding former Solvay workers, the number of participants from Alessandria is greatly reduced (N = 8), but this makes it possible to visually compare two rather similar populations in terms of exposure to PFAS. The difference remains significant (p=0.015880) despite the lower statistical weight related to the number of participants taken into account.

Figure 4 shows the P25 and P75 (grey boxes), PS and P95 (whiskers), PS0 (line), maximum ("extreme") of PFOA for all participants in Alessandria and Spinetta (including former Solvay workers) distributed between hands and over 50 years old. The difference of contamination between participants in Spinetta and Alessandria is significant for the over 50s, and at the limit of significance for the under 50s (but only one participant in Spinetta is significant). Spinetta was 50 years old).

Figure 4: Percentiles 5, 25, 50, 75, 95 and maximum PFOA concentration of participants in Spinetta and Alessandria for hands and over 50 years.



A study conducted in the United States, between 2004 and 2005, revealed a significant exposure of the population (N = 161) living around a fluoropolymer production site using PFOA (Washington, West Virginia) with median serum concentrations ranging from 250 to 400 µg/L, 20 to 40 times higher than the (Emmett et al., Journal of Occupational and Environmental Medicine, 2006, 48: 759-770). Contamination of the water supply has been suggested as a primary source of exposure for these residents.

TOXICOLOGY DEPARTMENT

Professor Dr Corinne CHARLIER - C.Charlier@chuliege.be
Head of Department, Full Professor - Forensic Expert

This study is the only one published in a scientific journal **ON** biomonitoring of people living near a PFAS production or use site. It is probably the worst case of contamination reported and quantified. It is therefore difficult to compare the two situations. Moreover, it is difficult to compare the two situations.

the comparison of the figures would only be relevant if the delay between the blood test and the ! was identical, which is impossible **to** determine (past exposure probably more important than current exposure **in** Spinetta).

The German Human Biomonitoring Commission (German HBM Commission), consisting of scientists, experts from the German federal authorities, and representatives of different ministries (Environment, Health, etc.), has defined a series of concentration values for different environmental pollutants in blood or urine to enable interpretation of the results obtained in biomonitoring studies (HBM-1 and II). These values are based on health effects and are derived from epidemiological and toxicological studies on humans. They are recognized by the international scientific community and are widely used. The HBM-1 values represent the concentration of a substance in a biological sample (urine, blood, hair, ...) in

Below which there would be no health risk according to current knowledge and therefore no action **to be** taken. These are rather ideal values **to be** achieved. The HBM-11 values describe concentrations in biological samples from

which may pose a health risk and which necessitate the reduction of

! exposure (Appel et al., 2017, Int. J. Hyg. Environ. Health 220: 152-166; Ewers et al. 1999, Int Arch Occup Environ Health 72:255-260; Schulz et al. 2007, Int. J. Hyg. Environ. Health 210: 373-382). For PFOA these values were established on the basis of fertility studies, on It has also been shown to increase cholesterol levels and to cause type II diabetes. The HBM-1 value for PFOA has been set **at** 2 µg/L, while the HBM-11 value has recently been evaluated **at** 10 µg/L, but with certain reservations. Indeed, given the small number of studies

Due to the availability of data, the uncertainty of the results and the specificity of the groups included in these studies, **these HBM-11 values are not intended to quantify the health risk of an individual** due to his or her level of exposure, but rather **to highlight those individuals for whom measures should be taken to reduce their exposure by applying the precautionary principle**. In this context, only one person out of the 21 individuals residing **at** Alessandria exceeds this value, for 17 out of 31 inhabitants of Spinetta. These results show that if the measurements carried out do not allow to draw any conclusions about **the**

of possible adverse health effects, Spinetta participants experienced significant exposure, which was rated as of concern in relation to HBM-11.

Executive Secretary

Shirley PARENT- secretoxico@chuliege.be
Tel : 00-32/4 323 76 83 - Fax : 00-32/4 323 **BB 89**

administrative secretary fl l6geJ

Audrey GUILLAUME -Audrey. Guillaume@chuliege.be
Tel : 00-32/4 323 76 83 - Fax : 00-32/4 323 88 89

Administrative secretary fCharlerol

C4llne DEBAIX - Cellne. Oealx@chuliege.be
Tel: 00-32/71 32 91 25 - Fax: 00-32/71 47 07 25

TOXICOLOGY DEPARTMENT

Professor Dr Corinne CHARLIER - C.Charlier@chuliege.be
 Head of Department, Full Professor - Forensic Expert

CONCLUSION

The objective of this study was to determine the PFAS concentrations in the blood of people living in the vicinity of an industrial site producing fluoropolymer (in Spinetta-Maringo, Italy) suspected of having, at least in the past, contaminated the environment with PFOA, and compare with the concentrations measured in the blood of a population living a few kilometers away (Alessandria). Seven PFAS (PFOA, PFOS, PFHxA, PFHpA, PFHxS, PFNA and PFDA) were measured in blood samples (serum) of 31 people living in Spinetta, aged between 28 and 87 years (average age: 65 years) and 21 people living in Alessandria, aged between 18 and 74 years (mean age: 46 years). The PFAS concentrations measured in the serum of the Alessandria participants are close to the concentrations currently observed in the general population without any particular exposure. Only two of the 21 Alessandria participants showed higher than expected exposure (above the P95 of a general Walloon population in a recent study), and only one person had a higher than expected exposure.

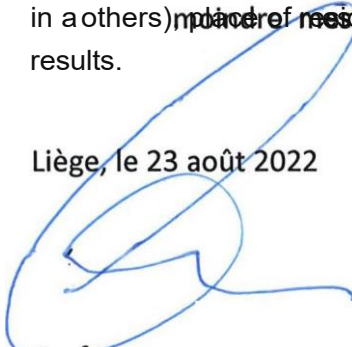
exceeds the HBM-11 value. PFOA concentrations in the serum of Spinetta participants are 5 to 10 times higher (P50 and P95) than those usually measured in the general population, with a large majority (68%) exceeding the values corresponding to a higher than normal exposure (P95 of a general Walloon population during a recent study). The HBM-11 value is exceeded for 17 Spinetta residents. The concentrations of the other PFAS are similar to those observed in the general population.

Despite the great heterogeneity between the two groups, mainly in terms of age, but also in terms of (former) occupational exposure to PFAS, the statistical tests used taking into account the different confounding factors show **significantly higher concentrations in blood samples from people living in**

Spinetta compared to the inhabitants of Alessandria. These results do not allow us to determine the period in which these people were particularly exposed (exposure

The factors that influence the serum PFOA concentrations most significantly are the former work activity (former Solvay workers vs. others). The factors that most significantly influence the serum PFOA concentrations are former professional activity (former Solvay workers vs. in others), place of residence (Spinetta vs. Alessandria), and age, these 3 factors explaining almost 70% of the variability of the PFOA concentrations.

Liège, le 23 août 2022




I: A' PSseure Corinne Charlier
 Head of Department

Catherine Pirard Scientific
 Manager

Executive Secretary

Shirley PARENT - secretoxico@chuliege.be
 Tel : 00-32/4 323 76 83. Fax : 00-32/4 323 88 89

Administrative secretary (Liege/

Audrey GUILLAUME -Audrey. Guillaume@chuliege.be
 Tel : 00-32/4 323 76 83 - Fax : 00-32/4 323 88 89

Administrative secretary (Charleroi)

Celine DEBAIX - Celine. Debaix@chuliege.be Tel:
 00-32171 32 91 25. Fax: 00-32/71 47 07 25

