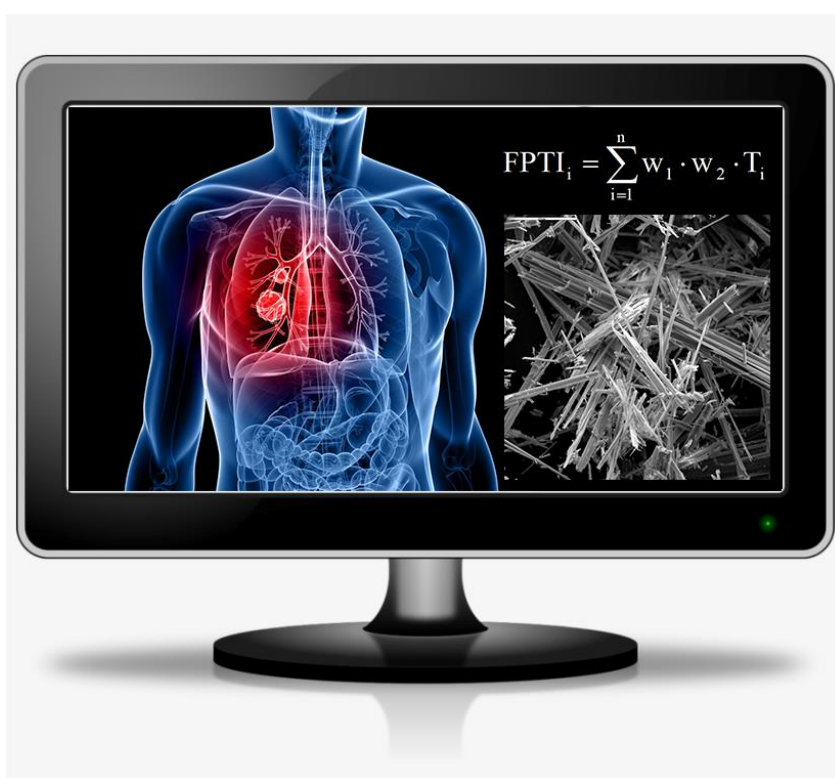# WebFPTI

A software tool to predict the toxicity/pathogenicity of mineral fibres including asbestos.

Manual

v.4c - February 5th, 2025

Alessandro F. Gualtieri[a], Mauro Leoncini[b]

[a]Department of Chemical and Geological Sciences, University of Modena and Reggio Emilia, Via Campi 103, Modena, I-41125, Italy.

[b]Department of Physical, Computer Science and Mathematics. University of Modena and Reggio Emilia, Via Campi 213/b, Modena, I- 41125, Italy

Table of contents

1. The WebFPTI application.

WebFPTI is a web-based application developed by the research group leaded by Prof. Alessandro F. Gualtieri (Department of Chemical and Geological Sciences - University of Modena and Reggio Emilia) with the support of Prof. Mauro Leoncini (Department of Physical, Computer Science and Mathematics - University of Modena and Reggio Emilia).

For further details visit the website: fibers.unimore.it. This web-based application allows the user to assess the potential toxicity/pathogenicity index (FPTI) of a mineral fiber. FPTI is a quantitative predictive model of toxicity/pathogenicity of minerals fibers based on their physical/chemical and morphological parameters. Before performing operations with the WebFPTI application the user is encouraged to consult the following reference:

Gualtieri, A. F. (2021). Bridging the gap between toxicity and carcinogenicity of mineral fibres by connecting the fibre crystal-chemical and physical parameters to the key characteristics of cancer. Current Research in Toxicology, 2, 42-52.

Gualtieri A.F. Towards a quantitative model to predict the toxicity/pathogenicity potential of mineral fibers. Toxicol. Appl. Pharmacol. 2018, 361, 89-98.

Gualtieri, A.F. Mineral Fibres: Crystal Chemistry, Chemical-Physical Properties, Biological Interaction and Toxicity. European Mineralogical Union: London, UK, 2017, pp. 533.

To calculate the FPTI of a mineral fiber and predict the toxic/pathogenic potential, the following parameters are considered: Morphometric parameters (mean fiber length, mean fiber diameter, crystal curvature, crystal habit, density, hydrophobic character, specific surface area; Chemical parameters (iron content, content of ferrous iron, surface iron and its nuclearity, content of metals other than iron); Parameters related to biodurability (dissolution rate, rate of iron dissolution/release, rate of silica dissolution/release, rate of release of metals from the fiber); Parameters related to surface reactivity (ξ potential, aggregation state of the fibers in suspension, cation exchange capacity for fibrous zeolite species). For each parameter, a score is assigned depending on the measured value and the susceptibility in inducing adverse effects. Because the parameters of the model can be correlated with each other, a hierarchical scheme taking cross-correlations into account is applied [1]. A weighing scheme is associated with each parameter of the model according to the step/hierarchy H where $w_1 = 1/H$ with H=1, 2 or 3. A weight defined as $w_2 = 1/U$

is also applied to each parameter of the model. It accounts for the uncertainty in the determination of a specific parameter (n, m) and it is defined by the penalty parameter U (1 = low to null uncertainty, 2 = some degree of uncertainty, 3 = high uncertainty). Having defined the weighing scheme of the parameters, the $FPTI_i$ is calculated according to the equation:

$$FPTI_i = \sum_{i=1}^{n} w_1 \cdot w_2 \cdot T_i$$

with T_i= class value of the parameter i of the model; w_1=1/H weight of the parameter according to the hierarchy H; w_2=1/U weight of the parameter according to the uncertainty U of the determination. The parameters of the model used for the calculation of the FPTI, the classification and the relative normalized scores $FPTI_i$ are reported in the section "**Parameters**" of the WebFPTI application. Moreover, WebFPTI allow the user to consult and compare the FPTI index of different materials already listed in the FPTI database.

The calculation of the errors on the specific parameters is described in **Appendix 1** of this manual.

2. Explore the home page.

The manual starts with a brief overview of the home page. Several options (**Home**, **Parameters**, **Materials**, **Chart** and **Login**) are present on the top bar and the functions will be illustrated shortly. On the left of the screen the user will find the number of parameters used to compute the FPTI index (**Parameters**: 18), the number of materials already stored into the database (**Materials**) and a link to the paper Gualtieri, 2018 [1] that will introduce the reader to the FPTI model (For more details visit this page) (see Fig.1).

| Home | Parameters | Materials | Chart | Login |

WebFPTI Home
Welcome to WebFPTI, a website developed as part of the *FPTI* project!

Dynamic content
WebFPTI allows you to compute the toxicity index of mineral fibers (FPTI) by specifing the value of a number of relevant parameters.

Also, WebFPTI let you consult the FPTI index of a number of material already in the FPTI database.
For more details visit this page
The FPTI database has the following parameters and materials record counts:
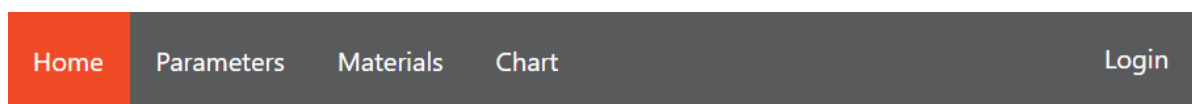
- **Parameters:** 18
- **Materials:** 11

Fig. 1. The home page of the WebFPTI.

2.1) The description of the parameters of the model.

From the home page, the user discovers the characteristics of each parameter used by the system to compute the toxicity index. The option "**Parameters**" opens the "List of relevant parameters stored in database" (see Fig. 2). For simplicity, Fig. 2 illustrates only the first seven ones but the list continues up to the last parameter (nr. 18), the cation exchange capacity. By selecting a parameter permits the access to a page that describes the type of parameter (relation to the morphometry, to the chemistry or the surface properties of the fiber), the uncertainty, the measure unit and possibly

a note concerning the instrumentation or the method used for the determination (see Fig. 3). As an example, the mean length is measured by electron microscopy. Depending on the experimental value, the contribution of the parameters to the toxicity index is different and the table on the bottom of the screen illustrates the scores relationship.

See **Appendix 2** for important operative indications and comments on the model parameters.

Fig. 2. The parameters list of the WebFPTI.

Fig. 3. Detailed information about the parameter (definitions, extension and scores).

2.2) A detailed report about a selected material.

The WebFPTI page is a database useful to the scientists working with mineral fibers. It is possible to insert own data about a new investigated material making them available to the scientific community. It is possible to see the list of the materials already stored into the WebFPTI simply selecting the "**Materials**" option. The button opens the "List of materials with corresponding FPTI index" (see Fig. 4). For simplicity, Fig. 4 illustrates only six materials but the list includes many others like the fibrous glaucophane from San Anselmo (Marin Co., California – US), the most recent material tested by our group [2]. Here the user selects a specific material or searches it typing the name on the bar and then clicking "**Submit**". If the desired material is absent, the following message appear over the materials list: "*this material does not exist*".

Fig. 4. List of the materials.

If a specific material is selected, the WebFPTI returns a detailed section about it. Here, information about the source and a brief description are given along with the FPTI index value, the associated error and if available, an image of the material (see Fig. 5).

Fig. 5. Detailed report about the selected material. Example with the fibrous glaucophane.

On the same page illustrated in Fig. 5, the user can have access to the detailed values of each parameter for the selected material. To speed up the selection it is possible to click directly on the desired parameter (light-blue writings) or simply scrolling down the page to see the entire list. Fig. 5 illustrates an example for the fibrous glaucophane from San Anselmo. This material has a computed FPTI index of 2.88 with an error of 0.22. The mean length of the glaucophane fibres is 4.0 µm.

2.3) Compare different materials.

The main goal of the WebFPTI is to return a direct comparison of the indices of different materials. However, it is important to underline that a complete characterization of the material must proceed side by side with other tests, using *in vitro* cells or *in vivo* animals with the aim to evaluate other specific parameters. The "**Chart**" option from the home page allows to select the stored materials and create a histogram by clicking "**Submit**" where the FPTI indices are compared (see Fig. 6). The chart in Fig. 6 compares as example the indices of 6 materials: UICC amosite, chrysotile from Balangero (Italy), tremolite from Val d'Ala (Italy), the fibrous glaucophane from San Anselmo (USA) and two fibers responsible of epidemic malignant mesothelioma, the Turkish fibrous erionite [3] and the Sicilian fluoro-edenite [4].
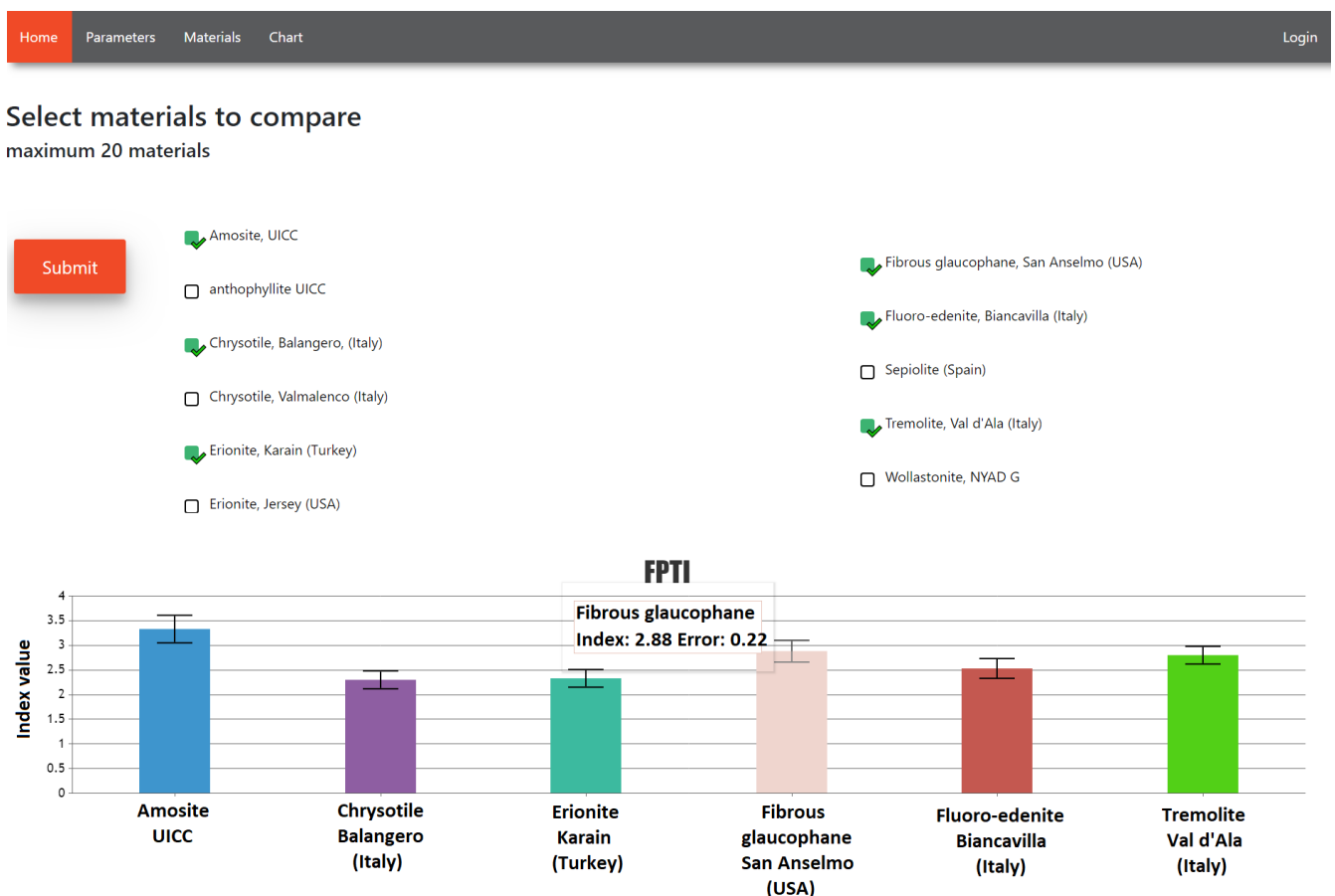

Fig. 6. Different FPTI indices compared each other.

To generate the histogram, the user selects from a minimum of 2 to a maximum of 20 materials. Moving the cursor over one of the bars, a blank label appears showing the index value and the associated error.

3. Explore the editing section.

As described in the previous pages, it is possible to insert data about a new studied material. To perform some of the specific functions (including the insertion of a new material) being logged-in is mandatory. The user home page is similar to the one described at the beginning of the manual with few differences like the writing "**Welcome**", the user name (example: **lorenzo**), the function "**Insert new material**", the "**Log out**" button and the option "**Register a new user**" available only for the superuser (see Fig. 7)

3.1) Access to the personal account.

On the top right of the screen the "**Login**" button serves for the access to the user account (see Fig. 8). There are several types of users that can create a personal account:

Generic user takes advantage of the following functionalities: lists all the materials; inspects the features of a given material (i.e., the values of the chemical/physical parameters assigned to the material); consults possible human annotations and the suggested bibliography; computes and compares the FPTI index of various materials.

Contributing user (in addition to the privileges allowed to generic users), inserts a new material (inserting parameter data, annotation and bibliography); edits and possibly deletes materials previously inserted by the same user.

Coordinator use supervises the scientific content available in WebFPTI. The coordinator edits/deletes consolidated materials; performs all the basic actions granted to generic and contributing users, reviews and validates the materials inserted by the contributing users. Materials approved by the coordinator cannot be further edited (nor deleted) by the contributing users.

Super user supervises management and security activities. Super user performs: user-related administering activities such as adding user and resetting passwords, data

management activities such as backup and restores the WebFPTI database, inserts, edits and deletes parameters.

WebFPTI Home

Welcome to WebFPTI, a website developed as part of the *FPTI* project!

Dynamic content

WebFPTI allows you to compute the toxicity index of mineral fibers (FPTI) by specifing the value of a number of relevant parameters.

Also, WebFPTI let you consult the FPTI index of a number of material already in the FPTI database.
For more details visit this page
The FPTI database has the following parameters and materials record counts:

- **Parameters:** 18
- **Materials:** 11

Fig. 7. WebFPTI user home page

Fig. 8. The login page of the WebFPTI.

The following part of the manual illustrates how to insert a new material and how to modify/delete an existing one.

3.2) Insert a new material.

Once a complete set of parameters about a new material has been determined, it is possible to insert the data into the database. To do so, the inserting screen (see Fig. 9) can be reached directly by clicking "**Insert new material**" on the upper part of the user home page. Here preliminary information are entered: the name of the material, the source, a short description and an image (optional) of the material (no .tiff format otherwise the image cannot be seen while .jpeg or .png formats are accepted). Finally, the remaining blanks with the numerical values of the parameters and the corresponding errors have to be filled. If the inserted value is out of the specified range (consult the parameters list), an error message is returned.

Fig. 9. The inserting page.

Fig. 9 shows an example of inserting page and for simplicity only the mean length and mean diameter lines are illustrated. The reader should not get confused: the two ellipses are not real and

the list continues with the other parameters. Once the insertion is finished it is possible to register the new material into the database by clicking "**Submit**".

3.3) Edit an existing material.

It may happen that the entered values are incorrect even if the given extensions are respected. Therefore, editing of an existing material is needed. The editing option can be reached in 2 steps. From the user home page, the username between "**Welcome**" and "**Insert new material**" must be selected. Next, a personal page with several options appears (see Fig. 10). The "**Edit material**" button opens the "List of materials you can edit" where the user searches the material that needs to be updated (see Fig. 11). After the desired material is selected the editing page is opened: it is similar to the inserting one but with all the blanks filled. Here it is possible to update the material from the general information to the numerical values. Clicking on "**Submit**" all the changes will be saved.
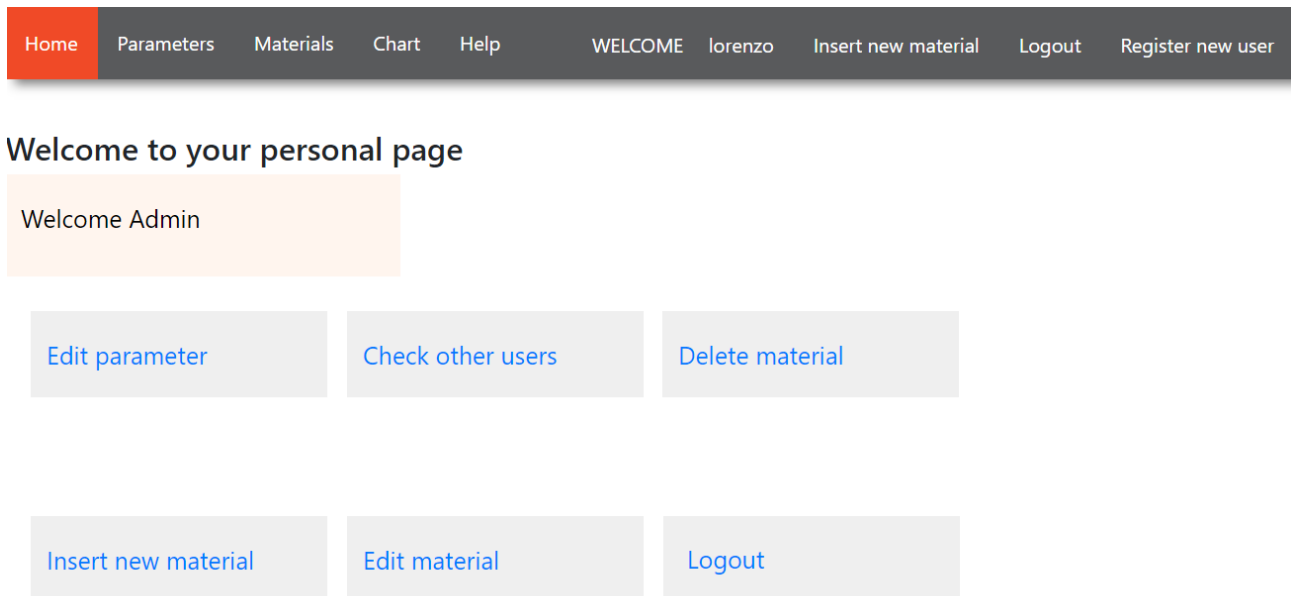
Fig. 10. The user personal page.

Fig. 11. The list of materials available for editing.

3.4) Delete an existing material.

An existing material can be eventually updated or deleted. The deleting option like the editing ones can be reached in 2 steps. From the personal page it is possible to select the "**Delete material**" option which opens the "List of materials you can delete" where the user searches the material that needs to be deleted (see Fig. 12). Once the desired material is selected, it can be deleted by clicking on the "**Delete**" option (see Fig. 13). If the process is successful a message appears on the screen.

Home | Parameters | Materials | Chart | Help | WELCOME | lorenzo | Insert new material | Logout | Register new user

List of materials you can delete

- Amosite, UICC
- anthophyllite UICC
- Chrysotile, Balangero, (Italy)
- Chrysotile, Valmalenco (Italy)
- Erionite, Karain (Turkey)
- Erionite, Jersey (USA)
- Fibrous glaucophane, San Anselmo (USA)
- Fluoro-edenite, Biancavilla (Italy)
- Sepiolite (Spain)
- Tremolite, Val d'Ala (Italy)
- Wollastonite, NYAD G

Search material name.. | Submit

Fig. 12. The list of materials available for deleting.

Home | Parameters | Materials | Chart | Help | WELCOME | lorenzo | Insert new material | Logout | Register new user

Delete

Material: Tremolite, Val d'Ala (Italy)
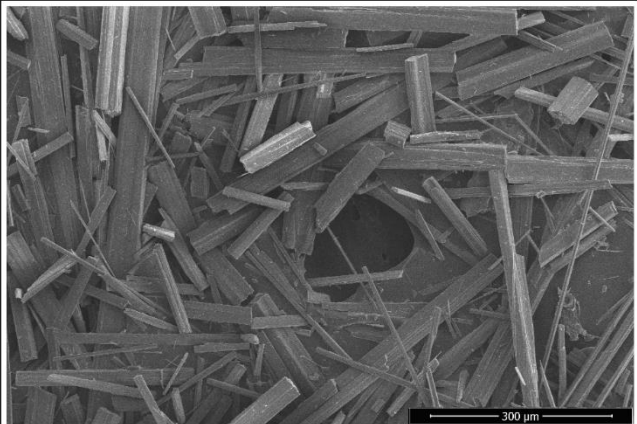
GENERAL INFO	IMAGE
Provenance: Lanzo Valley, Piedmont (Italy) **Description:** Tremolite asbestos occur in the serpentinites of the Ultrabasic Lanzo Massif in the Occidental Alps (Lanzo Valley, Piedmont) was selected for the study. **FPTI index:** 2.80 **FPTI error:** 0.18	300 µm

Fig. 13. The screen before deleting is confirmed.

3.5) Check the other users.

Also, it is possible to verify which user is registered and his/her list of materials. The checking process is very simple and it can be done by selecting the "**Check other users**" option from the personal page. A page which illustrates the user list will be returned (see Fig. 14). In the given example, only the administrator (e.g the superuser) is registered.
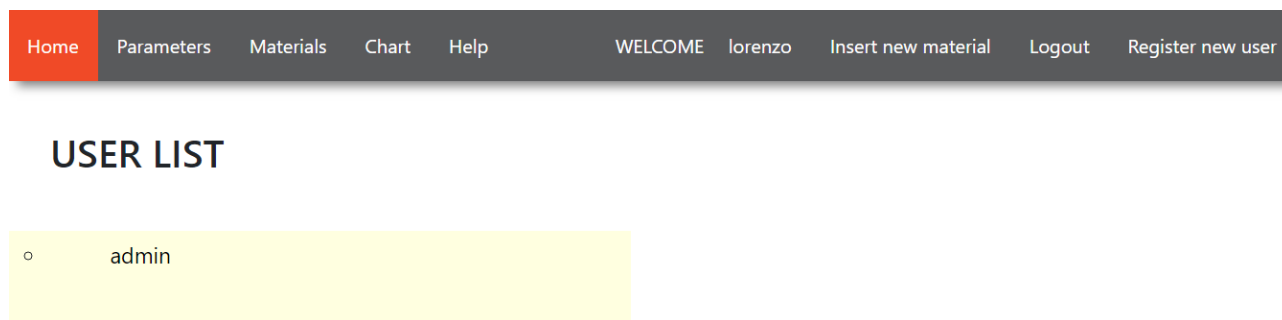
Fig. 14. The users list.

3.6) Register a new user.

As described in the paragraph "Accessing to the personal account" only the superuser creates new accounts. The superuser creates an account for which is impossible to edit the parameters. No one except the administrator can do this operation and reliable parameters are guaranteed. The superuser creates a new account from his personal page by selecting the "**Register new user**" option. A username and a password are needed for the registration of a new account. Both must be chosen respecting different requirements. The setting of a new account is completed filling the remaining blanks with the names (first and last), a valid e-mail contact, the institute membership and finally clicking on the "**Registration**" button (see Fig. 15).

| Home | Parameters | Materials | Chart | Help | WELCOME | lorenzo | Insert new material | Logout | Register new user |

Registration page

Username: [   ] Required. 150 characters or fewer. Letters, digits and @/./+/-/_ only.

Password: [   ]

- Your password can't be too similar to your other personal information.
- Your password must contain at least 8 characters.
- Your password can't be a commonly used password.
- Your password can't be entirely numeric.

Password confirmation: [   ] Enter the same password as before, for verification.

First name: [   ]

Last name: [   ]

Email: [   ] Insert valid email

Institute membership: [   ]

[Register]

Fig. 15. The registration page.

4. References.

[1] A.F. Gualtieri. Towards a quantitative model to predict the toxicity/pathogenicity potential of mineral fibers. *Toxicol. Appl. Pharmacol*. **2018**, *361*, 89-98.

[2] D. Di Giuseppe, M. Harper, M. Bailey, B. Erskine, G. Della Ventura, M. Ardit, L. Pasquali, G. Tomaino, R. Ray, H. Mason, M.D. Dyar, M. Hanuskova, C. Giacobbe, A. Zoboli, A.F. Gualtieri. Characterization and assessment of the potential toxicity/pathogenicity of fibrous glaucophane. *Environ. Res.* **2019**, *178*.

[3] M. Carbone, Y.I. Baris, P. Bertino, B. Brass, S. Comertpay, A.U. Dogan, G. Gaudino, S. Jube, S. Kanodia, C.R. Partridge, H.I. Prass, Z.S. Rivera, I. Steele, M. Tuncer, S. Way, H. Yang, A. Miller. Erionite exposure in North Dakota and Turkish villages with mesothelioma. *Proc. Natl. Acad. Sci. USA*. **2011**, 108(33), 13618-13623.

[4] P. Comba, A. Gianfagna, L. Paoletti. The pleural mesothelioma cases in Biancavilla are related to the new fibrous amphibole fluoro-edenite. *Arch. Environ. Health*. **2003**, *58*, 229-232.

Further specific literature:

Gualtieri, A. F. (2021). Bridging the gap between toxicity and carcinogenicity of mineral fibres by connecting the fibre crystal-chemical and physical parameters to the key characteristics of cancer. Current Research in Toxicology, 2, 42-52.

Mossman, B. T., & Gualtieri, A. F. (2020). Lung cancer: Mechanisms of carcinogenesis by asbestos. In Occupational cancers (pp. 239-256). Springer, Cham.

Gualtieri, A. F. (2022). Journey to the Centre of the Lung. The Perspective of a Mineralogist on the Carcinogenic Effects of Mineral Fibres in the Lungs. Journal of Hazardous Materials, 130077.

Appendix 1 - Calculation of the errors for each FPTI value

An error is associated to each normalized score of the model. The error takes into account how close the value of the fibre parameter is to the neighbour class. For the threshold values, the error is the half of the variation (Δ) between adjacent FPTI scores. The error varies with the distance from the threshold values following an exponential decay:

$$(\Delta/2)/e^s$$

with Δ=half of the variation between adjacent FPTI scores; s=step between the values of the parameters. The following **tables** calculate the errors associated to the FTPI score for each fibre parameter in the fibre parameter interval of values. <u>The user must read these errors and insert them in the input of the application.</u>

Let us consider an example relative to the fibre length L parameter. If the measured value of the mean fibre length L=10 μm, the error associated to the FPTI score of the fibre length L parameter is 0.05. This number is half of the difference values between the class of FPTI 0.1 and 0.2 (0.2-0.1=0.1; 0.1/2=0.05). Error decreases following the exponential decay above with the distance from the threshold value (10 μm). If the measured value of the mean fibre length L=13 μm, the error associated to the FPTI score of the fibre length L parameter is 0.002489, that is $[(0.05)/2]/e^{(13-10)}$. The qualitative parameters (1,3), (1,4), (1,6), (1,16), and (1,18) has an associated Error=0.

Parameter	classes	Normalized score FPTI$_i$
(1,1) length L (μm)	L≤5.0	0.0
	5.0<L≤10.0	0.1
	10.0<L≤20.0	0.2
	L>20.0	0.4
L (μm)	**Error**	
<5	0	
5	0.05	

6	0.018394	
7	0.006767	
8	0.006767	
9	0.018394	
10	0.05	
11	0.018394	
12	0.006767	
13	0.002489	
14	0.000916	
15	0.00045	
16	0.001832	
17	0.004979	
18	0.013534	
19	0.036788	
20	0.1	
21	0.036788	
22	0.013534	
23	0.004979	
24	0.001832	
25	0.000674	
26	0.000248	
>26	0	
(1,2) diameter D	$D>3.0$ $1.0<D\leq3.0$ $0.25<D\leq1.0$ $D\leq0.25$	0.0 0.1 0.2 0.4
W (μm)	**Error**	
0,01	0.001832	
0,05	0.004979	
0,1	0.013534	

0,2	0.036788	
0,25	0.1	
0,3	0.036788	
0,4	0.013534	
0,5	0.004979	
0,6	0.001832	
0,7	0.004979	
0,8	0.013534	
0,9	0.036788	
1	0.1	
1,1	0.036788	
1,2	0.013534	
1,3	0.004979	
1,4	0.001832	
1,5	0.000674	
1,6	0.000248	
1,7	0	
1,8	0	
1,9	0	
2	0	
2,1	0	
2,2	0	
2,3	0	
2,4	0.000124	
2,5	0.000337	
2,6	0.000916	
2,7	0.002489	
2,8	0.006767	
2,9	0.018394	
3	0.05	
3,1	0.018394	

3,2	0.006767	
3,3	0.002489	
3,4	0.000916	
3,5	0.000337	
3,6	0.000124	
>3,6	0	
(1,3) crystal curvature	flat surface	0.05
	altered surface	0.1
	cylindrical surface	0.2
	Error = 0	
(1,4) crystal habit	Curled	0.1
	mixed Curled/acicular	0.2
	acicular	0.4
	Error = 0	
(1,5) fibre density (g/cm³)	$\rho \leq 2.75$	0.05
	$2.75 < \rho \leq 3.5$	0.1
	$\rho > 3.5$	0.2
d (g/cm³)	**Error**	
<2,3	0	
2,3	0.000168	
2,4	0.000458	
2,5	0.001245	
2,6	0.003383	
2,7	0.009197	
2,75	0.025	
2,8	0.009197	
2,9	0.003383	
3	0.001245	
3,1	0.0007	

3,2	0.002489	
3,3	0.006767	
3,4	0.018394	
3,5	0.05	
3,6	0.018394	
3,7	0.006767	
3,8	0.002489	
3,9	0.000916	
4	0.000337	
4,1	0.000124	
>4,1	0	
(1,6) hydrophobic character of the surface	hydrophobic amphiphilic hydrophilic **Error = 0**	0.05 0.1 0.2
(1,7) specific surface area (m²/g)	SSA>25.0 5.0<SSA≤25.0 SSA≤5.0	0.05 0.1 0.2
SSA (m²/g)	**Error**	
<1	0.000337	
1	0.000916	
2	0.002489	
3	0.006767	
4	0.018394	
5	0.05	
6	0.018394	
7	0.006767	
8	0.002489	
9	0.000916	
10	0.000337	

11	0.000124	
12	0	
13	0	
14	0	
15	0	
16	0	
17	0	
18	0	
19	0	
20	0.000168	
21	0.000458	
22	0.001245	
23	0.003383	
24	0.009197	
25	0.025	
26	0.009197	
27	0.003383	
28	0.001245	
29	0.000458	
30	0.000168	
>30	0	
(1,8) total iron content Fe$_2$O$_3$+FeO (wt%)	$Fe_2O_3+FeO=0.0$ (no iron) $0<Fe_2O_3+FeO\leq1$ $1<Fe_2O_3+FeO\leq10$ $Fe_2O_3+FeO>10$	0.0 0.05 0.1 0.2
total iron content Fe$_2$O$_3$+FeO (wt%)	**Error**	
<0,5	0	
0,5	0.000168	
0,6	0.000458	
0,7	0.001245	

0,8	0.003383	
0,9	0.009197	
1	0.025	
2	0.009197	
3	0.003383	
4	0.001245	
5	0.0004	
6	0.000916	
7	0.002489	
8	0.006767	
9	0.018394	
10	0.05	
11	0.018394	
12	0.006767	
13	0.002489	
14	0.000916	
15	0.000337	
16	0.000124	
>16	0	
(1,9) ferrous iron FeO (wt%)	FeO=0.0 (no ferrous iron) 0.0<FeO≤0.25 0.25<FeO≤1.0 FeO>1.0	0.0 0.05 0.1 0.2
FeO (wt%)	**Error**	
<0,1	0.001245	
0,1	0.003383	
0,2	0.009197	
0,25	0.025	
0,3	0.009197	
0,4	0.003383	

0,5	0.001245	
0,6	0.0007	
0,7	0.002489	
0,8	0.006767	
0,9	0.018394	
1	0.05	
1,1	0.018394	
1,2	0.006767	
1,3	0.002489	
1,4	0.000916	
1,5	0.000337	
1,6	0.000124	
>1,6	0	
(1,10) nuclearity of iron atoms n	n=0 (no iron atoms) n>2 n=2 n=1	0.0 0.02 0.03 0.07
Fe nuclearity n	**Error**	
1	0.0165	
2	0.01	
3	0.01	
>3	0.004	
(1,11) content of metals other than iron* (ppm/ppm)	$\sum_i \dfrac{C_i}{L_i}=0.0$ (no metals) $0.0<\sum_i \dfrac{C_i}{L_i}\leq 1.0$ $1.0<\sum_i \dfrac{C_i}{L_i}\leq 5.0$ $\sum_i \dfrac{C_i}{L_i}>5.0$	0.0 0.1 0.2 0.4
Content of metals*		

	Error	
<0,5	0.015	
0,5	0.030327	
1	0.05	
2	0.018394	
3	0.006767	
4	0.036788	
5	0.1	
6	0.036788	
7	0.013534	
8	0.004979	
9	0.001832	
10	0.000674	
11	0.000248	
>11	0	
(1,12) fibre dissolution time t^{**} (y)	$t \leq 1.0$ $1 < t \leq 40.0$ $t > 40.0$	0.05 0.1 0.2
Fibre dissolution rate[**]	**Error**	
<1	0.009197	
1	0.025	
2	0.009197	
3	0.003383	
4	0.001245	
5	0.000458	
6	0.000168	
7	0	
8	0	
9	0	
10	0	

11	0	
12	0	
13	0	
14	0	
15	0	
16	0	
17	0	
18	0	
19	0	
20	0	
21	0	
22	0	
23	0	
24	0	
25	0	
26	0	
2	0	
27	0	
28	0	
29	0	
30	0	
31	0	
32	0	
33	0	
34	0.000124	
35	0.000337	
36	0.000916	
37	0.002489	
38	0.006767	
39	0.018394	
40	0.05	

41	0.018394	
42	0.006767	
43	0.002489	
44	0.000916	
45	0.000337	
46	0.000124	
>46	0	
(1,13) velocity of iron release v_R[***] **(wt%/y)**	$v_R=0.0$ (no iron) $0.0<v_R\leq0.1$ $0.1<v_R\leq1$ $v_R>1$	0.0 0.03 0.07 0.13
Velocity Fe release[***]	**Error**	
<0,1	0.00607	
0,1	0.0165	
0,2	0.00607	
0,3	0.002233	
0,4	0.000821	
0,5	0.00025	
0,6	0.000604	
0,7	0.001643	
0,8	0.004466	
0,9	0.01214	
1	0.033	
1,1	0.01214	
1,2	0.004466	
1,3	0.001643	
1,4	0.000604	
1,5	0.000222	
>1,5	0	

(1,14) velocity of silica dissolution v_S**** (wt%/y)	v_S=0.0 (no silica)	0.0
	0.0<v_S ≤0.5	0.02
	0.5<v_S≤1.0	0.03
	v_S>1.0	0.07
velocity Si dissolution**	**Error**	
<0,1	0	
0,1	0.000151	
0,2	0.000411	
0,3	0.001117	
0,4	0.003035	
0,5	0.00825	
0,6	0.003035	
0,7	0.001117	
0,8	0.002	
0,9	0.00607	
1	0.0165	
1,1	0.00607	
1,2	0.002233	
1,3	0.000821	
1,4	0.000302	
1,5	0.000111	
>1,5	0	
(1,15) velocity of release of metals v_M***** (ppm/y)	v_M=0.0	0.0
	0.0<v_M≤1.0	0.03
	1.0<v_M≤10.0	0.07
	v_M>10.0	0.13
Velocity release of metals***	**Error**	
<1	0.00607	
1	0.0165	
2	0.00607	

3	0.002233	
4	0.000821	
5	0.00025	
6	0.000604	
7	0.001643	
8	0.004466	
9	0.01214	
10	0.033	
11	0.01214	
12	0.004466	
13	0.001643	
14	0.000604	
15	0.000222	
>15	0	
(1,16) ζ potential (mV)	(-) at pH=4.0-4.5 (-) at both pH=4.0-4.5 and 7.0-7.4 **Error = 0**	0.1 0.2
(1,17) ζ values[ℵ] inducing fibres' aggregation (mV) **ζ potential (mV)**	ζ>20.0 or ς<-20.0 10.0<ζ≤20.0 or -20.0≤ζ<-10.0 0.0≤ζ≤10.0 or -10.0≤ζ≤0.0 **Error**	0.03 0.07 0.13
<5	0	
5	0.000222	
6	0.000604	
7	0.001643	
8	0.004466	
9	0.01214	
10	0.033	
11	0.01214	

12	0.004466	
13	0.001643	
14	0.000604	
15	0.000222	
16	0.00025	
17	0.000821	
18	0.002233	
19	0.00607	
20	0.0165	
21	0.00607	
22	0.002233	
23	0.000821	
24	0.000302	
25	0.000111	
>25	0	
(1,18) Cation exchange (in zeolites)	cation Exchange 0.067 no cation exchange 0 **Error = 0**	

$^{*}\sum_{i}\dfrac{C_i}{L_i}$ =sum of the concentrations of heavy metals (Sb, As, Hg, Cd, Co, Cr, Cu, Pb, Ni, Zn, V, Be) C_i in the

fibre (ppm) divided by the limit L_i for that metal according to the existing regulatory system (Tóth et al., 2016) except for Be with limit = 0.5 ppm;

[**]the total dissolution time of the fibre calculated in years (y) following the standardized acellular *in vitro* dissolution model at pH=4.5 described in Gualtieri et al. (2018);

[***]total content of elemental iron in the fibre (wt%) possibly made available as active iron at the surface of the fibre divided by the total dissolution time (y) of the fibre (y);

[****]total content of Si of the fibre (wt%) divided by the total dissolution time (y) of the fibre;

[*****]total content (ppm) of heavy metals (Sb, As, Hg, Cd, Co, Cr, Cu, Pb, Ni, Zn, V, Be, Mn) divided by the total dissolution time (y) of the fibre;

[א]at the pH=7.4 of the extracellular environment.

Appendix 2 – Important operative remarks

Parameter (1,1) Fibre length

If the mean length of the fibres is <5µm, the FPTI insert value should be 0.

Parameter (1,2) diameter D (W)

The values of W to be inserted must be ≤3 µm (respirable fibres) otherwise the fibre is not respirable and the FPTI calculation is non-sense.

Parameters (1,4) Fibre crystal habit

The term "acicular" here means "**needle-like**" (rigid fibre). For nano-fibres, like nano-chrysotile, with mean length of the fibres is <5µm, distinction between "curled" and "acicular" crystal habit is of little sense. In this case, it is suggested to choose for the "Mixed-curled/acicular" value (0.2).