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HEALS

Health and Environment-wide Associations based on Large population Surveys

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http://www.heals-eu.eu/

D12.1 Report on Prototype Design of the Geospatial Platform

WP12 Exposure and Health Data Management

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1 Introduction

This document describes the requirements and the current design of the HEALS GeoDatabase platform which will support the collection of and access to HEALS data sets. The data sets include both the data collected in HEALS and data developed for HEALS and other health and environmental wide association studies. The platform will enable users to manage and explore spatial data (when applicable), to process these data and to effectively visualize the results of spatially resolved models. Data sets relevant for the HEALS project may contain for example environmental, exposure, population, molecular biology, biochemistry, or clinical data. Such a system can serve many purposes, e.g.:

- Increase understanding about the links between exposure and diseases (research oriented objective) and provide a means for estimating the probability of an individual to develop a disease.
- Provide means for identifying factors that could have caused the onset of a disease (tracking backwards in time)
- Provide input for the regulatory work: monitoring the compliance with regulations and initiation of new regulations.
- Explore the spatial and non-spatial relationships in data

2 Requirements for the HEALS GeoDatabase

This section describes the requirements set for the HEALS GeoDatabase. The next section describes how they will be fulfilled in the HEALS geodatabase platform. The requirements were collected from the DOW as well as from the HEALS partners.

Requirement 1: General requirements

The HEALS GeoDatabase will have the following general features:

1.1 will systematically support the collection of and access to all datasets collected/developed for HEALS case-studies and population surveys

1.2 is web-based

1.3 is flexible and interactive

Requirement 2: Data contents

The HEALS GeoDatabase will act as a data repository and manage the data with the following content:

2.1 data collected or developed for the HEALS project

2.2 a library containing significant documents and guidelines

2.3 links to a number of external databases to access physico-chemical, physiological, metabolic, molecular biology/biochemistry data and clinical datasets

Requirement 3: Functions – data import

To allow data analysis in exposome studies, the HEALS GeoDatabase will store and allow import of data from different data sources and computational tools:

3.1 from the EXHES study (WP17)

3.2 from the external cohort studies addressed in WP14, WP15 and WP16
3.3 from WP8 portal on environmental data (the Environmental data management system (EDMS))
3.4 from WP9 survey database (OpenDataKit)
3.5 from WP9 NRC portal (the individual exposure part)
3.6 from Agilent GeneSpring system (the omics part)
3.7 from the INTEGRA platform used for computational modelling (the modelling part)
3.8 from other external databases

Requirement 4: Functions – data export
The HEALS GeoDatabase will support data export for different data analysis purposes:
4.1 into a file having a row-column format (rows: individuals, columns: attributes)
4.2 into a one file per individual where rows have time stamp of attribute values and columns have attributes (for time series data)
4.3 to the INTEGRA platform for modelling purposes

Requirement 5: Functions – modelling support
The HEALS GeoDatabase will
5.1 support modelling tools that reside on other platforms (e.g., INTEGRA for PBPK modelling) by communicating data and results with them

Requirement 6: Functions – data queries
The HEALS GeoDatabase will allow users to:
6.1 do data queries.

Requirement 7: Functions – data analysis
The HEALS GeoDatabase will provide functionality to:
7.1 basic data analysis

Requirement 8: Functions – data visualisation
The HEALS GeoDatabase will support
8.1 visualisation of data on the web

Requirement 9: Data formats
The HEALS GeoDatabase will support different data formats like
9.1 geo-referenced data and non-spatial data

Requirement 10: Compatibility with standards
The HEALS GeoDatabase should be compatible with
10.1 the EC INSPIRE initiative (Environment and Health cluster specifications)

10.2 the IPCheM platform (Integrated Platform for Chemical Monitoring)

Requirement 11: User groups

The HEALS GeoDatabase will be accessible to at least the following user-groups

11.1 the public who can only access the public part of the HEALS GeoDatabase

11.2 researchers who can access the public and have a limited access to non-public parts of the HEALS GeoDatabase

11.3 HEALS researchers who may have some additional access rights compared to researchers

11.4 administrators who maintain the GeoDatabase and access rights

Requirement 12: Language

The HEALS GeoDatabase will be available in the English language.

3 Description of the HEALS GeoDatabase Platform

This section will describe how the requirements set for the HEALS GeoDatabase will be fulfilled. The technical details of the implementation are explained in the next section.

The planned HEALS GeoDatabase will fulfil the requirements set in the DoW and defined by the HEALS project by implementing a web site with different contents and functions. The web site is available at http://heals.vtt.fi. The next subsections will go through the requirements one-by-one in the same order and explain how the requirements are fulfilled.

3.1 General requirements

3.1.1 Support collection and access to datasets

The main idea of the HEALS GeoDatabase is to support the collection of and access to all datasets collected/developed for HEALS case-studies and population surveys. Additionally, it will provide information both for the project partners and to the public. Components of the HEALS GeoDatabase are depicted in Figure 1**Errore. L'origine riferimento non è stata trovata.**. The HEALS GeoDatabase platform is depicted in the middle. Its main function is to store data and manage access to the data. Data come from several data sources depicted on the left. Some data are provided as raw data files to the HEALS GeoDatabase platform, some data are accessed via programmatic application programming interfaces (APIs) and some data are just linked to via the GeoDatabase platform. The data provided by the HEALS GeoDatabase platform can be accessed via the HEALS web platform depicted on the right. Some web platform functionality will be publicly available (blue), some is restricted for researchers only (green).

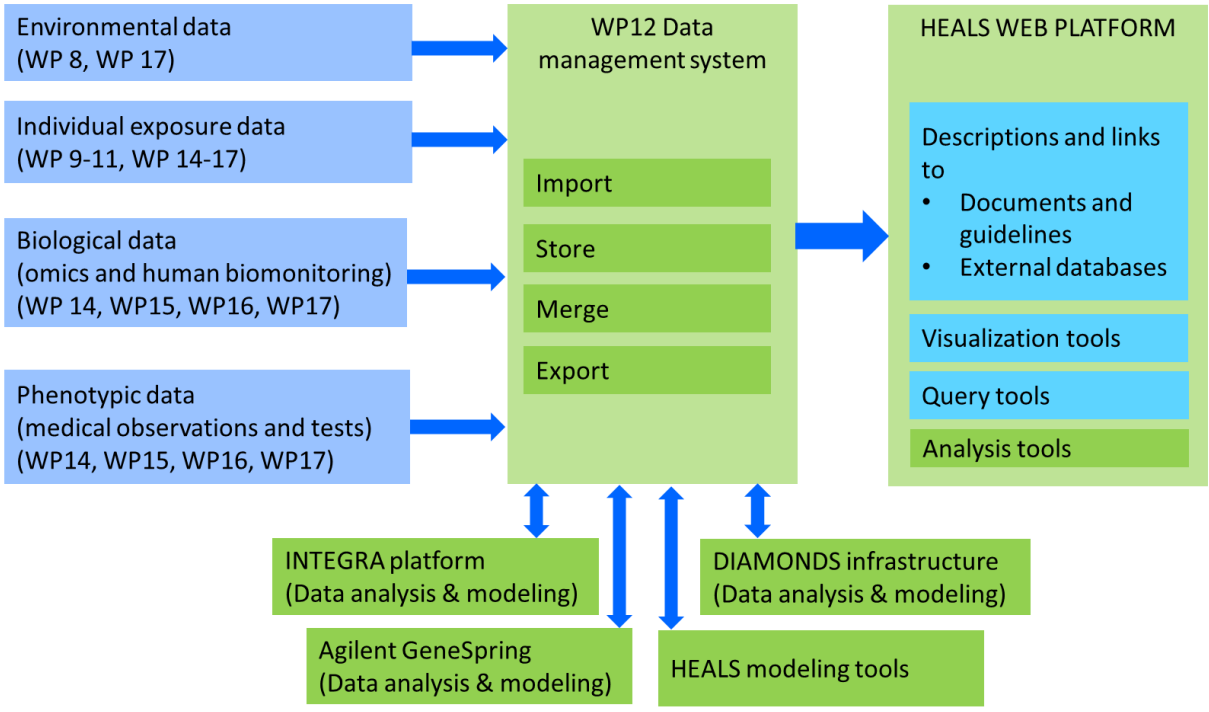

Figure 1 Components of HEALS GeoDatabase

3.1.2 Web-based platform

The HEALS GeoDatabase will be implemented as a web service in address http://heals.vtt.fi and it can be accessed using all modern web-browsers. The functions are implemented so that they can be used using a web browser.

3.1.3 Flexible and interactive platform

The HEALS platform will be flexible in supporting different data formats for import and export. It will also allow flexible interoperability with other systems like the Environment Data Management System developed in WP8.

The users will have interactive tools for managing the data, doing basic data analysis and visualisation. Most of the functions are developed for HEALS researchers, but selected visualisations will be available also for the public.

3.2 Data Contents

The contents of the HEALS geodatabase platform can be divided into three main categories: 1) data collected in or developed for the HEALS project, 2) a library of documents and guidelines relevant for the exposome studies and 3) a library of external databases relevant for the HEALS and other exposome studies.

3.2.1 Data

The data to be stored in the HEALS geodatabase platform consists of four main types of data as depicted in Figure 1:

1. Environmental data (WP8, WP17)
2. Individual exposure data (WP9-11, WP14-17)
3. Biological data including omics and human biomonitoring data (WP14-17)
4. Phenotypic data (medical observations, medical tests, etc.) (WP14-17)

3.2.2 Documents and guidelines

To support the exposome studies, a library containing significant documents and guidelines will be available on the HEALS platform. This section will contain documents written in the HEALS project, as well as national, EU-wide and worldwide guidelines, etc. The documents will be indexed for easy finding. The current list of documents and guidelines is attached to this deliverable (Appendix B: Documents and Guidelines**Errore. L'origine riferimento non è stata trovata.**). The initial list will be updated during the project.

3.2.3 External databases

In exposome studies, the collected data is often analysed together with already existing datasets. The existing datasets can be open data like air quality data available on the web, or it can be certain stressor measurements done within a previous study. Therefore, the HEALS platform will also contain data of and links to a number of external databases. As the environmental data sets were already collected into the EDMS in HEALS WP8 (see D8.1), the WP12 HEALS platform will collect external data sets on areas that are not covered with other work packages, such as: physico-chemical,

physiological, metabolic, molecular biology/biochemistry data and clinical datasets. The current list of external databases can be found in "Appendix A: External Databases". Each external database description includes the database name, a short description and a web link to the web site of the external database. Later, as the library of external databases develops, more data on each database can be added, e.g. spatial and temporal coverage and spatial and temporal resolution, data format, and data access methods.

External data sets on other web sites are often available only after user registration. Thus, direct access via the HEALS geodatabase platform is in most cases not possible, but the idea is to point the researchers to good quality existing databases. The researchers, who find the information relevant to their studies, may then register to the sites and use the data in their studies. Our current plan is to offer the the external database information to all HEALS GeoDatabase users, but obviously, if the data provider so wishes, we can limit the access to a smaller group of researchers as well (e.g., only to HEALS researchers).

3.3 Data Import

The data import functionality allows users to add new data to the HEALS geodatabase platform. The data can be imported programmatically from one database to another, using application programming interfaces (APIs), when available. Another option is to import existing documents to the HEALS database as files. With help of metadata and indexing, content from the data can be found effectively in the HEALS GeoDatabase platform.

3.3.1 Data import from HEALS EXHES study and HEALS cohort studies

Data collected in the HEALS EXHES study by WP17 and in the HEALS cohort studies by WP14, WP15 and WP16 will be transferred to HEALS GeoDatabase platform as simple tabular files (e.g., CSV and TSV). There will be at least two data formats, one for instantaneous measurements containing one row per subject and one column per measured variable. For more continuous measurements like with the individual exposure measurements, the time series data will be saved in subject-wise files, where the rows represent time and columns represent the different measured variables. WP12 will develop parsers to read the different data files of known formats and interpret them. The interpreted data can be pre-processed and converted to more suitable formats for data analysis in WP12. Select data are also visualized on the HEALS web platform.

3.3.2 Data import from EDMS and ODK survey databases

WP8 is developing an environmental data management system (EDMS) integrating already existing environmental databases (See deliverable D8.1). The EDMS will be part of the HEALS platform. In addition, digital surveys collected in the frame of WP9 and stored in an Open Data Kit (ODK) database will be imported to the HEALS platform. HEALS GeoDatabase can access these data via web services provided by the databases.

3.3.3 Data import from individual exposure database

WP9 is developing a database that stores individual exposure data (e.g., individual step counts, home air quality, etc.). The database is based on TNO's NRC database. The platform is a research platform, which allows both the users and the researchers to access the collected data. It also visualizes the collected data as simple graphs for the user. Snapshots of the individual's data can be exported from the system as files. HEALS GeoDatabase platform will access the data via a web service and OAuth2

authentication. Individual data will be anonymized before it is made available on HEALS GeoDatabase platform.

3.3.4 Data import from omics tool (Agilent)

Omics data will be processed through Genespring bioinformatics infrastructure which provides statistical tools for data analysis and visualization. GeneSpring offers an environment that supports understanding of transcriptomics, metabolomics, proteomics and next-generation sequencing (NGS) data within a biological context.

HEALS GeoDatabase platform will provide the data for the analysis and read the analysis results.

3.3.5 Data import from computational modelling tools

HEALS GeoDatabase platform will be able to import the modelling results from analysis tools. One such tool is the INTEGRA platform.

The INTEGRA computational platform is a modelling tool developed by AUTH that integrates environmental fate, exposure and internal dose dynamically in time in a unified computational platform. The INTEGRA platform includes a multimedia model, a dietary contamination module, micro-environmental modelling for indoor locations and life-stage changing mother-foetus generic PBTK model which incorporate multi-route exposure and detailed compartmental description to derive internal doses of parent chemicals and metabolites in human target tissues so as to cover the full chain from chemical releases to internal doses allowing to move forward from the classical epidemiological methodology toward a biologically-based mechanistic approach.

The API to enable data import from INTEGRA is currently being implemented to the INTEGRA platform. Researchers will also be able to import their other data analysis results on the HEALS GeoDatabase as files.

3.3.6 Data import from external databases

There are several external databases that provide useful data for an exposome study data analysis. HEALS GeoDatabase platform will support access to such data, either by linking to the external databases or by accessing the databases directly programmatically, when possible.
External databases on environmental data are already available in WP8 EDMS database. More external databases on biological and phenotype data will be collected to the HEALS GeoDatabase platform. A listing of such databases and other relevant external databases is provided in this deliverable (Appendix A: External Databases). The listing will also be put on the HEALS web platform for easy access for the exposome data analysis.

3.4 Data Export

Data Export functionality of the HEALS GeoDatabase platform will allow the user to export data from the HEALS GeoDatabase platform to 1) files or 2) to an external platform. The files will be in a simple tabular file format (e.g., CSV).

The researchers may further analyse the exported data files in other SW tools. The external platforms will be platforms like the INTEGRA that take data as input to the modelling. In the first phase, the data will be input to INTEGRA using its existing user interface, but during the project we seek to find ways to export data directly from the HEALS GeoDatabase platform to the INTEGRA platform, without the need to manually input the data.

3.5 Modelling support

As an example of data modelling tools, an external and internal exposure modeling platform called INTEGRA will be used for modelling. The INTEGRA platform provides modelling tools for assessing external and internal exposure, supported by algorithms for the backward calculations necessary for biomonitoring data assimilation. The INTEGRA computational platform is based on the existing platform developed in the LRI-B4 INTERA and LRI-B5 TAGS projects. The computational platform was further developed in the project INTEGRA. Further refinements of the INTEGRA platform and coupling with –omics data will be performed in WP6 of HEALS. HEALS GeoDatabase will allow data import for reading the modelling results into the HEALS GeoDatabase platform after the modelling. The results of INTEGRA modelling will be returned as JSON files.

Modelling will be done also in other tools (e.g., Agilent Genespring and DIAMONDS). DIAMONDS an infrastructure with statistical and text mining tools that allow characterization of toxicological properties of new chemical molecules by combining and analysing data from different expertise (computational chemistry, toxicokinetics, systems biology/bio-informatics, statistics, and toxicological risk assessment) coupled with alternative experimental models/assays for biological verification. The name DIAMONDS comes from “Data Infrastructure for Applying Models ON Design and Safety”. Its goal is to effectively assess the toxicological profile of a chemical molecule.

Another modelling tool will be based on the framework to estimate external exposure for population groups that will be developed in Stream 3. It combines the probabilistic individual exposure modelling framework and fuses results with population-specific characteristics. It will be applied to the population studies conducted within Stream 5. The requirements for data import from this tool will be analysed, specified and validated to allow the assessment of the different chemical and physical stressors relevant for the population studies. This will also include meta-information on uncertainty ranges of the relevant data.

3.6 Data queries

Data queries will allow the users to easily find and access data on the HEALS GeoDatabase platform, e.g., for data analysis purposes. The query allows searching, e.g., certain geographical areas, certain time range, keywords, etc.

3.7 Data analysis

Data analysis supported on the HEALS GeoDatabase platform will include both pre-processing functions to clean the data and basic descriptive statistics of the data. Other possible data analysis functions include frequency histograms, map algebra, etc.

3.8 Data visualisation

HEALS GeoDatabase platform will also support simple visualisation of select data in various ways, including spatial representation through open-source GIS tools. Data visualisation is mainly targeted for visualisation of select data to the public. For example certain measured values from blood samples can be displayed as colours on the map to do ‘hot spot’ analysis. Other possible visualisation tools include use of support to image layers, zooming and scrolling tools, etc.

3.9 Data formats

HEALS GeoDatabase platform will store the data both in raw and in processed formats. The raw data format ensures that the original collected data is available and intact for further analysis, when

necessary. Many of the raw data formats have to be converted to other formats to be able to analyse or visualize the data together with other data sets.

The supported data formats will cover both data sets with and without a geo-reference.

3.10 Compatibility with standards

3.10.1 INSPIRE directive

The INSPIRE directive aims to form a spatial data infrastructure for the European Union. It will enable better sharing of environmental spatial data between organisations. The INSPIRE directive came into force in 2007 and its full implementation is required by 2019. The directive includes a wide variety of topical and technical themes.

The INSPIRE directive suggests several common principles: 1) data should be collected only once and kept where it can be maintained most effectively, 2) it should be possible to combine seamless spatial information from different sources across Europe and share it with many users and applications, 3) it should be possible for information collected at one level to be shared with all levels (thus being detailed enough for thorough investigations, and general enough for strategic purposes), 4) geographic information needed for good governance at all levels should be readily and transparently available, 5) easy to find what geographic information is available, how it can be used to meet a particular need, and under which conditions it can be acquired and used.

The directive requires that common implementing rules are adopted in following areas: 1) Metadata – descriptions of available information (spatial data sets, series and services), 2) Data specifications – agreements on how data should be defined and presented, or modelled into virtual reality (e.g., width of highway on mapping), 3) Network services – discovery, view, download transformation and invoke services, and 4) Sharing – obliges authorities to share information.

The HEALS GeoDatabase platform will follow the INSPIRE directive suggestions where applicable.

3.10.2 IPChem

European Commission is developing a single access point for locating and retrieving chemical monitoring data collections that are managed and available to European Commission, European Agencies, Member States, international and national organisations and researchers. This platform has been named IPCheM – The Information Platform for Chemical Monitoring.

The platform supports collecting storing, and accessing monitoring data on chemicals and chemical mixtures, in humans and in the environment. It is a de-centralised system, providing remote access to existing information systems and data providers.

The IPCheM platform relies heavily on the INSPIRE directive. At the time of writing, the IPCheM specification is not yet publicly available, but the HEALS GeoDatabase platform aims to collaborate with the IPCheM platform in the future.

3.11 User groups

In HEALS GeoDatabase platform, there will be several user groups, having different access rights. The user groups are defined in section 4.2.

3.12 Language

The HEALS GeoDatabase will be using English language only.

4 Implementation of the HEALS platform

The HEALS geodatabase platform will be available at the URL http://heals.vtt.fi/. At the moment of writing this deliverable an early prototype is accessible there, providing only limited functionality and not providing public access.

Figure 2 depicts the main components and data flows for the HEALS platform site design. To keep the level of detail reasonable the diagram is somewhat simplified: in particular some "boxes" in the diagram indicate a collection of multiple related modules rather than a single component.

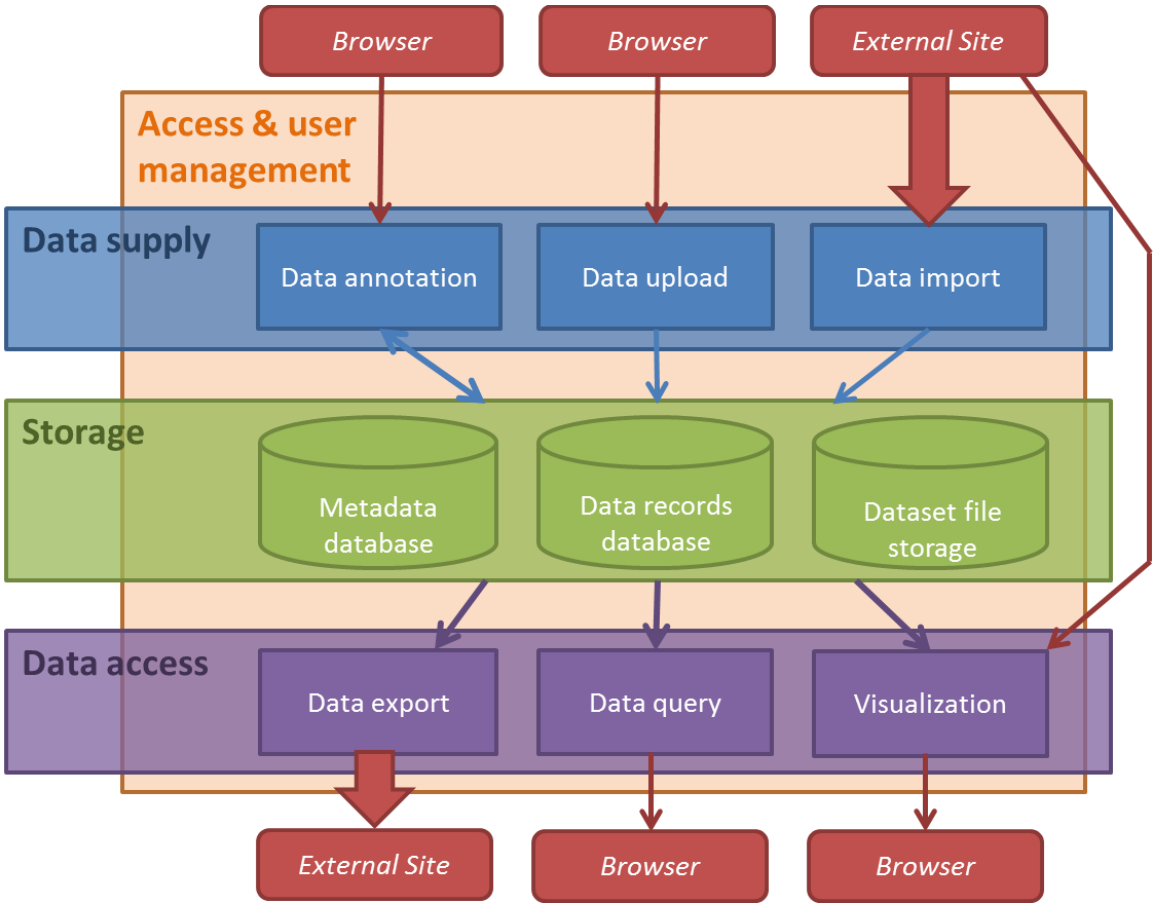

Figure 2 HEALS platform system design and data flows diagram

4.1 Storage

At the center of the system (green colored in the diagram) is the data storage subsystem. Since the system needs to store different kinds of data, different types of storage mechanisms are supported.

1. The ***Dataset file storage*** module is used to store files. This includes raw files for actual data sets, but can also include documents or other auxiliary data. The implementation of this module works directly on the server's filesystem, and interacts with the *metadata database* module to support advanced querying scenarios.

2. The ***Metadata database*** module stores information about the data stored in the system. This includes annotations, properties and tags associated with data. Some of these are automatically assigned; others can be freely added and edited. This is the information used to provide a flexible and rich query experience. The implementation of this module is based on NoSQL database technology.
3. The ***Data records database*** module is a traditional SQL database providing relational data querying and access. Since the layout of data tables is not known until later in the project the implementation of this component will follow at a later stage. In the meantime the file storage component allows storing data in a raw form, that later can be extracted into relational form where needed.

4.2 User management and access control

The HEALS platform supports a pervasive user management and access control system (depicted by the orange box in Figure 2)

4.2.1 Roles

As mentioned in the requirements there are several kinds of "roles" a user of the system can have, and the access or non-access to certain parts of the system depends on this role. The following common roles can be identified:

1. ***Public***. This is a pseudo-role, implied by not logging in and therefore not having any role set.
2. ***User***. This is the role that allows reading data including some non-public data.
3. ***Contributor***. This role additionally allows contributing and modifying data.
4. ***Partner***. This is an extension of the *Contributor* role implying a HEALS project partner. Existence of this role allows marking data as only accessible to HEALS project partners. It is quite possible that in practice there will be no Contributors other than Partners, but having both roles in the system design allows making the distinction should the need arise.
5. ***Administrator***. Administrators can create new users and assign roles to users. Since they can assign roles to themselves, they effectively have all roles.

The HEALS platform uses these roles for basic access control, but implements a richer non-linear role-based system. Note that each user can have multiple roles; for example in the case of the basic roles mentioned above, each role also implies all roles listed above it. In addition to the roles mentioned above the following helper roles are used:

1. ***Enabled***. This is a role that each logged in user must have. Absence of this role indicates a disabled account. An administrator can retract this role for a user to disable an account without deleting the account (and its history), for instance in case an account is compromised.
2. ***Demo***. This is a special "anti-role" set for demonstration accounts, which actively disables some functionalities of the platform. In particular, accounts with this role cannot change their password.

4.2.2 Users

The "user" concept used in the HEALS platform is fairly standard:

- Each person using the system has their own account and their own user name. Accounts are not intended to be shared. This allows keeping track of who supplied what data and allows a fine grained access control system.
- A user is identified by their e-mail address.
- For user interface purposes a user can also have a separate "name". This can for instance be used to indicate the author of a file without divulging that user's e-mail address.
- As mentioned above, each user has a set of "roles" that define their access rights to various components of the platform.

4.3 Data supply

Data can be supplied to the system in a few different ways (depicted by the blue boxes in Figure 2).

4.3.1 Data upload

A user in the "contributor" role can upload raw data files using a web interface. Uploading is a 3 step process:

1. First the user uploads the file to their personal "staging area". While in the staging area the data is on the server, but not yet visible to other users.
2. The user can add or modify metadata to the staged file, to make the file easier to find later on. This is similar to the metadata *editing* capability described next.
3. The user then "publishes" the staged file, making the file visible to other users, and freeing up the user's staging area for further uploads.

The initial prototype of the system will only support uploading raw data or document files (to the *dataset file storage*). Later iterations will add capabilities to parse data content into separate records and insert these into the *data records database*.

4.3.2 Data annotation

Users in the "contributor" role can edit the metadata of datasets via a web interface. Metadata is information that is used to search the collection of datasets in the system. Providing more metadata helps making the dataset easier to find while reducing "false hits" from queries. Metadata is stored in the "metadata database" component of the storage subsystem.

The following types of metadata are supported:

- ***Properties***. A "property" is a key-value pair associated with the target object. As an example, a dataset could be given "latitude" and "longitude" properties to indicate the location where the dataset applies. Or alternatively a dataset could be given a more generic "city" property which also indicates the location, but at a coarser scale. Each property key must be unique for the target object; for example: there can be only one value for "city", and attempting to add another one will just replace the existing one. Property keys in the HEALS platform must be "words", in the sense that they can only contain letters and digits. Property values can be any string value.
- ***Pure Tags***. A "pure tag" is essentially a property with no value. They are used in queries to search for all datasets having (or not having) a specific tag.

- ***Valued tag***. A "valued tag" is similar to a *property* in that it has a key and a value, but unlike a property the key does not need to be unique; only the *combination* of key and value needs to be unique. Another way to look at this is that the key of a valued tag can identify a *set* of zero or more values.

The design of the metadata system is flexible and pervasive. It is not only used to annotate files uploaded to the *dataset file storage*, but can be used to annotate other entities in the system. For instance, internally the metadata system is also used to attach free-form data to user account records (only accessible by administrators).

4.3.3 Data import

"Data Import" is in concept similar to data upload, but refers to data obtained automatically or semi-automatically from other sites rather than data manually uploaded by a user.

"Data Import" can be done in two modes:

- In ***push*** mode the external site calls the HEALS platform *data import Web Service* to supply data.
- In ***pull*** mode the HEALS platform accesses the external web site via their Web Service or plain web link to retrieve data.

As mentioned in the requirements, the HEALS system must be able to communicate with several other systems, and the "data import" module as actually a set of modules tuned for each of these other systems. Some of these specific modules may be combined with a "data export" module (described below) for the same target site.

4.4 Data access

Data in the system is accessed in a few different ways, as depicted in Figure 2 by the purple boxes.

4.4.1 Data query

The "Data Query" module provides functionalities to use a web interface to query for a set of data and expose that data directly in the web interface or make the results downloadable in a variety of data formats, e.g. CSV or TSV files. "Data query" is used here in a generic way; the module actually contains multiple modules, providing different search methods and different ways of returning the results. For example, this module also allows searching for and downloading of raw data files and documents, in addition to actual data content querying. Other query submodules of note are the ones handling the requirements regarding document library (requirement 2.2) and link database (requirement 2.3).

In the initial prototype of the platform the querying will be based on the tags and properties defined in metadata. In a later version queries making use of the capabilities of the databases will be added.

4.4.2 Data export

"Data Export" is similar to "Data Query", but describes machine-to-machine communication rather than a human user querying data. Like "Data Import", "Data Export" can also work in a "push" or a "pull" mode, depending on which party contacts the other. And like "Data Import", this module is actually a group of related modules, each of them handling data export for the different sites identified in the requirements.

4.4.3 Data visualization

The "Data Visualization" module builds on the query engine to obtain data, possibly adding external data, but uses the obtained data for web based visualization purposes. Example visualizations include interactive geographical map displays, histograms, bar charts, etc. This module is not limited to just pure "visualization" but also includes handles operating on data to aid basic data analysis (requirement 7.1).

Even more than other modules, the "Data Visualization" is actually a collection of several modules, and those are likely to be tightly integrated to "Data Query" functionality.

4.5 Technologies used

The platform is being built using the following technologies:

- Operating System: Windows Server 2012 R2
- Web Server: IIS 8.5
- Web server framework: ASP.NET MVC 5 (using C# as implementation language).
- Web service framework: ASP.NET Web API 2 (using C# as implementation language). Web services are used in the system for data import and export.
- Metadata storage: MongoDB (a NoSQL database) (tentative)
- Record storage: SQL Server Express (tentative)
- The libraries to be used for visualization have not been decided upon yet, but will leverage JavaScript/AJAX based technologies on the client side.

As mentioned at the start of this chapter, a prototype of the platform is running on http://heals.vtt.fi/ ; this prototype will be further developed into the final system over the duration of Work Package 12.

5 Appendix A: External Databases

HEALS GeoDatabase platform will also include a library of links to external databases. Primarily, we need data to support the EXHES study data analysis and external cohort study data analysis.

5.1 Data location

The data can be Europe-wide, country-wide, area-wide or city-wide. This data should be of good resolution and quality.

HEALS sensor pilot measurements (WP9) were performed in the following cities:

1. Edinburgh, Great Britain
2. Utrecht, the Netherlands
3. Delft, the Netherlands
4. Thessaloniki, Greece
5. Athens, Greece

The cities and towns involved in the EXHES study are:

1. Paris, France
2. London, Great Britain
3. Athens, Greece
4. Thessaloniki, Greece
5. Ljubljana, Slovenia
6. Zagreb, Croatia
7. Porto, Portugal
8. Regensburg, Germany
9. Tarragona, Spain
10. Pisa, Italy
11. Palermo, Italy
12. Roma, Italy
13. Lodz, Poland

However, also data from other countries, areas and cities are collected, since we want the HEALS GeoDatabase platform to support exposome studies in the whole of Europe.

5.2 Data time range

Primarily the data time range should cover the EXHES study (years 2015-2018). In addition, to address pre-existing population studies covered in WP14-WP16 data from earlier years are necessary. Therefore, all data collected since the year 1950 will be taken into account.

5.3 Data on health measurements

For exposome studies, the main purpose is to get a holistic view of all stressors that affect human health. Environmental databases were already collected into EDMS in HEALS WP8. The collection of external databases in WP12 will focus on health, biological and phenotype data. WP12 will thus focus

on databases that contain "health measurements", not the exposure/stressor data. These health outcome measures include:

- untargeted whole genome mRNA expression,
- metabolomics,
- adductomics,
- proteomics,
- DNA methylation profiling,
- targeted SNP profiling,
- human biomonitoring,
- phenotype data.

In HEALS WP11 the primary stressors and their pathways were defined to be: **Outdoor exposures:** PM2.5, PM10, NOx, SO2, NMVOC, NH3; **Indoor exposures:** PM2.5, PM2.5-10, NO2, formaldehyde/acetaldehyde, mold and allergens, Hg, naphtaline, benzene, Benzo[a]pyrene; **Ingestion via food:** Heavy metals: As, Cd, Pb, Hg; POPs: dioxins, DL-PCBs, PFOA/PFOS, pesticides; **Pharmaceuticals; Noise:** Traffic noise; **Phthalates,** DMP, DEP, DiBP, DnBP, BBzp, DEHP, DINP, DIDP; **Radiation:** Radon, EMF; Others: Green space; Socio-economic status; Heat stress. The stressors have been described in more details in the HEALS deliverable D4.2

5.4 List of external databases

5.4.1 Chemical, physical and toxicological data

1. **IPCHeM**
   Information Platform for Chemical Monitoring is a single access point for locating and retrieving chemical monitoring data collections managed and available to 'European Commission, European Agencies, Member States, international and national organisations and researchers. It includes four modules: Environmental Monitoring data (access to data in key environmental matrices (water, air, soil biota, etc.)); Human Bio-Monitoring; Product and Indoor-Air data (indoor and outdoor sources of air pollution including chemical emissions from construction and consumer products; Food and Feed. The platform is not accessible yet. A public version will be released during April 2015.

   Main contact: Silvia Dalla Costa (silvia.dalla-costa@jrc.ec.europa.eu) and for IT issues Alberto Cusinato alberto.cusinato@ext.jrc.ec.europa.eu.

2. **Tox-Hub**
   http://www.heroic-toxhub-platform.es/V1/publica/HRCP00V4_Main.php
   Tox-Hub includes physical/chemical and toxicological properties. Tox-hub platform is an interactive internet platform enabling the simultaneous search and retrieval of information from already existing toxicological and ecotoxicological databases. Tox-Hub is publicly accessible at: www.heroic-toxhub-platform.es. When performing a search the user must specify three input fields: 1.) Searching scope: Title or Full document (referred to the original external databases).2.) Dictionary: referred to the internally automatically generated (built in) dictionary, or alternatively, to the use of an external one (IUPAC). 3.)Words: a specific keyword related to the topic of interest should be selected from the drop-down menu. User

manual can be found at http://heroic-fp7.eu/en/content/Users-Manual.54/. Tox-Hub is freely available without registration.

3. **ToxCast Phase I and II**
   http://www.epa.gov/ncct/toxcast/
   ToxCast is a multi-year effort launched in 2007 that uses automated chemical screening technologies (called "high-throughput screening assays") to expose living cells or isolated proteins to chemicals. The cells or proteins are then screened for changes in biological activity that may suggest potential toxic effects and eventually potential adverse health effects. ToxCast has evaluated over 2,000 chemicals from a broad range of sources including: industrial and consumer products, food additives, and potentially "green" chemicals that could be safer alternatives to existing chemicals. Chemicals were evaluated in over 700 high-throughput assays that cover a range of high-level cell responses and approximately 300 signaling pathways.

   Phase I: The "Proof of Concept" completed in 2009 profiled roughly 300 well studied chemicals (primarily pesticides). The chemicals included in Phase I have over 30 years of existing toxicity data since they have already been tested using traditional toxicology methods (primarily animal studies). This animal study data can be searched and queried using EPA's Toxicity Reference Database (ToxRefDB) that stores nearly $2 billion worth of studies. Phase II: Screened 1,800 chemicals from a broad range of sources including: industrial and consumer products, food additives, touted "green" products, nanomaterials and drugs that never made it to the market. The chemicals were screened in more than 800 in vitro high-throughput screening assays. The most updated publicly available ToxCast data can be downloaded from http://www.epa.gov/ncct/toxcast/data.html. The data is organized into different data sets and includes: descriptions of ToxCast chemicals and assays as well as files summarizing the screening results from ToxCast (high-throughput data from ~1,800 chemicals), a MySQL database to download and run locally on a computer, EPA's analysis of the chemicals screened

4. **TOXNET**
   http://toxnet.nlm.nih.gov/
   TOXNET® (TOXicology Data NETwork) is a group of databases covering chemicals and drugs, diseases and the environment, environmental health, occupational safety and health, poisoning, risk assessment and regulations, and toxicology. It is managed by the Toxicology and Environmental Health Information Program (TEHIP) in the Division of Specialized Information Services (SIS) of the National Library of Medicine (NLM) . Information in the TOXNET databases covers:
   - Specific chemicals, mixtures, and products
   - Chemical nomenclature
   - Unknown chemicals
   - Special toxic effects of chemicals in humans and/or animals
   - Citations from the scientific literature.

5. **Toxin and Toxin Target Database (T3DB)**
   http://www.t3db.ca/

The *Toxin and Toxin Target Database (T3DB)*, or, soon to be referred as, the *Toxic Exposome Database*, combines detailed toxin data with comprehensive toxin target information. The database currently houses 3 673 toxins described by 41 733 synonyms, including pollutants, pesticides, drugs, and food toxins, which are linked to 2 086 corresponding toxin target records. Altogether there are 42 433 toxin, toxin target associations. Each toxin record (ToxCard) contains over 90 data fields and holds information such as chemical properties and descriptors, toxicity values, molecular and cellular interactions, and medical information. This information has been extracted from over 18 132 which include other databases, government documents, books, and scientific literature.

The focus of the T3DB is on providing mechanisms of toxicity and target proteins for each toxin. This dual nature of the T3DB, in which toxin and toxin target records are interactively linked in both directions, makes it unique from existing databases. It is also fully searchable and supports extensive text, sequence, chemical structure, and relational query searches. It is both modelled after and closely linked to the Human Metabolome Database (HMDB) and DrugBank. Potential applications of T3DB include toxin metabolism prediction, toxin/drug interaction prediction, and general toxin hazard awareness by the public, making it applicable to various fields. Overall, the variety and accessibility of the T3DB make it a valuable resource for both the casual user and the advanced researcher.

T3DB is offered to the public as a freely available resource. Use and re-distribution of the data, in whole or in part, for commercial purposes requires explicit permission of the authors and explicit acknowledgment of the source material (T3DB) and the original publication. Users who download significant portions of the database have to cite the T3DB paper in any resulting publications. T3DB Data Fields are provided in CSV Format and/or JSON Format; Toxin Structures in SDF Format and; Toxin Target Protein/Gene Sequences in FASTA Format.

References:

- Wishart D, Arndt D, Pon A, Sajed T, Guo AC, Djoumbou Y, Knox C, Wilson M, Liang Y, Grant J, Liu Y, Goldansaz SA, Rappaport SM. *T3DB: the toxic exposome database.* Nucleic Acids Res. 2015 Jan;43(Database issue):D928-34.
- Lim E, Pon A, Djoumbou Y, Knox C, Shrivastava S, Guo AC, Neveu V, Wishart DS. *T3DB: a comprehensively annotated database of common toxins and their targets.* Nucleic Acids Res. 2010 Jan 38(Database issue):D781-6.

6. **IUCLID International Uniform Chemical Information Database**
   http://iuclid.eu/index.php?fuseaction=home.iuclidHome
   IUCLID is a software application to capture, store, maintain and exchange data on intrinsic and hazard properties of chemical substances. Distributed free of charge IUCLID is the key tool for chemical industry to fulfill data submission obligations under REACH. It include information on chemical substances, namely their:
   - Composition
   - Reference information, like CAS number, IUPAC name and other identifiers
   - Classification and labelling
   - Physical/chemical properties
   - Toxicological properties
   - Eco-toxicological properties

- Any report relevant to the substance (e.g. study result, assessment)

The OECD and the European Commission have agreed on a standard XML format, called OECD Harmonised Templates (OHTs), in which most of the aforementioned data are stored for easy data exchange. IUCLID can be downloaded upon user registration from http://iuclid.eu/index.php?fuseaction=home.menuNOTSignedUp&page=home.download56

7. **European Chemicals Agency, Chemical Substances Search**

http://echa.europa.eu/information-on-chemicals/registered-substances

Database contains 13,052 unique substances and contains information from 50,405 Dossiers. For each chemical registered under REACH the database includes the following group of data:

- General Information
- Identification
- Compositions
- Classification and Labelling
- Manufacture, Use & Exposure
- PBT assessment
- Physical and chemical properties
- Environmental fate and pathways
- Ecotoxicological Information
- Toxicological information
- Guidance on safe use
- Reference substances

The database can be queried online at http://echa.europa.eu/information-on-chemicals/registered-substances**.**

8. **OECD: The Global Portal to Information on Chemical Substances**

http://www.echemportal.org/echemportal/index?pageID=0&request_locale=en

eChemPortal provides free public access to information on properties of chemicals:

- Physical Chemical Properties
- Ecotoxicity
- Environmental Fate and Behaviour
- Toxicity

eChemPortal allows simultaneous searching of reports and datasets by chemical name and number and by chemical property. Direct links to collections of chemical hazard and risk information prepared for government chemical review programmes at national, regional and international levels are obtained. Classification results according to national/regional hazard classification schemes or to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) are provided when available. In addition, eChemPortal provides also exposure and use information on chemicals. Almost 60 Databases all over the world are currently participating in eChemPortal. The database can be queried online at http://www.echemportal.org/echemportal/page.action?pageID=0

9. **PubChem database**

http://pubchem.ncbi.nlm.nih.gov/#

PubChem is a database of chemical molecules and their activities against biological assays. The system is maintained by the National Center for Biotechnology Information (NCBI), a component of the National Library of Medicine, which is part of the United States National

Institutes of Health (NIH). PubChem can be accessed for free through a web user interface. Millions of compound structures and descriptive datasets can be freely downloaded via FTP. PubChem contains substance descriptions and small molecules with fewer than 1000 atoms and 1000 bonds. More than 80 database vendors contribute to the growing PubChem database. Searching the databases is possible for a broad range of properties including chemical structure, name fragments, chemical formula, molecular weight, XLogP, and hydrogen bond donor and acceptor count. PubChem contains its own online molecule editor with SMILES/SMARTS and InChI support that allows the import and export of all common chemical file formats to search for structures and fragments. Each hit provides information about synonyms, chemical properties, chemical structure including SMILES and InChI strings, bioactivity, and links to structurally related compounds and other NCBI databases like PubMed. PubChem is organized as three linked databases. These are PubChem Substance, PubChem Compound, and PubChem BioAssay. PubChem also provides a fast chemical structure similarity search tool. PubChem and its all components are freely available without registration.

- PubChem BioAssay Database (http://www.ncbi.nlm.nih.gov/pcassay). The PubChem BioAssay Database contains bioactivity screens of chemical substances described in PubChem Substance. It provides searchable descriptions of each bioassay, including descriptions of the conditions and readouts specific to that screening procedure.
- PubChem Substance Database http://www.ncbi.nlm.nih.gov/pcsubstance The PubChem Substance Database contains descriptions of samples, from a variety of sources, and links to biological screening results that are available in PubChem BioAssay. If the chemical contents of a sample are known, the description includes links to PubChem Compound
- PubChem Substance Database http://www.ncbi.nlm.nih.gov/pccompound/. The PubChem Compound Database contains validated chemical depiction information provided to describe substances in PubChem Substance. Structures stored within PubChem Compounds are pre-clustered and cross-referenced by identity and similarity groups.

10. DrugBank - Open Data Drug & Drug Target Database (version 4.2)

http://www.drugbank.ca

The DrugBank database is a unique bioinformatics and cheminformatics resource that combines detailed drug (i.e. chemical, pharmacological and pharmaceutical) data with comprehensive drug target (i.e. sequence, structure, and pathway) information. The database contains 7759 drug entries including 1600 FDA-approved small molecule drugs, 160 FDA-approved biotech (protein/peptide) drugs, 89 nutraceuticals and over 6000 experimental drugs. Additionally, 4282 non-redundant protein (i.e. drug target/enzyme/transporter/carrier) sequences are linked to these drug entries. Each DrugCard entry contains more than 200 data fields with half of the information being devoted to drug/chemical data and the other half devoted to drug target or protein data.

11. EpiSuite

http://www.epa.gov/opptintr/exposure/pubs/episuite.htm

EpiSuite is a Windows-based suite of QSAR programs for estimating physical/chemical properties and environmental fate parameters developed by the EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC). Epi-Suite provides users with

screening-level estimates of physical/chemical (melting point, water solubility, etc.) and environmental fate properties (breakdown in water or air, etc.). These properties are the building blocks of exposure assessment and for PBTK model parametrization. Includes PHYSPROP, a database of measured p/chem and fate properties for >40,000 chemicals. EpiSuite includes several modules to estimate the following properties:

- MPBPWINTM–melting point, boiling point, and vapor pressure
- KOWWINTM–octanol/water partition coefficient
- WS/KOWWINTM–water solubility from Kow
- WATERNTTM –water solubility based on a fragment constant method
- HENRYWINTM–air/water partition coefficient
- PCKOCWINTM–ability to sorb to the organic portion of soil and sediment
- BCFWINTM–ratio of a chemical's concentration in the tissue of an aquatic organism to the concentration in the ambient water
- HYDROWINTM–acid and base-catalyzed hydrolysis
- AEROWINTM–fraction of airborne substance sorbed to airborne particulates
- AOPWINTM –atmospheric persistence
- BIOWINTM–aerobic and anaerobic biodegradation
- BioHCWIN–biodegradation half-life for compounds containing only carbon and hydrogen (e.g., hydrocarbons)
- KOAWIN –octanol/air partition coefficient

EpiSuite is downloadable from http://www.epa.gov/oppt/exposure/pubs/episuitedl.htm (size ca 94 Mb - installed) together with its user manual.

12. **OECD QSAR toolbox**
http://www.qsartoolbox.org/
OECD QSAR toolbox is a Windows software application intended to be used to fill gaps in (eco)toxicity data needed for assessing the hazards of chemicals. The Toolbox incorporates information and tools from various sources into a logical workflow. It includes databases with results from experimental studies, tools to estimate missing experimental values by read-across, by trend analysis (i.e. interpolating (preferred) or extrapolating from a trend (increasing, decreasing, or constant) from tested to untested chemicals within a category) and/or by (Q)SAR models. Is available free of charge. Download instructions and free training material are available online at http://www.qsartoolbox.org/.

5.4.2 Biological data

13. **The Human Metabolome Database (HMDB)**
http://www.hmdb.ca/
HMDB is a freely available electronic database containing detailed information about small molecule metabolites found in the human body. It is intended to be used for applications in metabolomics, clinical chemistry, biomarker discovery and general education. The database is designed to contain or link three kinds of data: 1) chemical data, 2) clinical data, and 3) molecular biology/biochemistry data. The database contains 41,992 metabolite entries. Additionally, 5,688 protein sequences are linked to these metabolite entries. Each MetaboCard entry contains more than 110 data fields with 2/3 of the information being devoted to chemical/clinical data and the other 1/3 devoted to enzymatic or biochemical data. Many data fields are hyperlinked to other databases (KEGG, PubChem, MetaCyc, ChEBI,

PDB, UniProt, and GenBank) and a variety of structure and pathway viewing applets. The HMDB database supports extensive text, sequence, chemical structure and relational query searches. Four additional databases, DrugBank, T3DB, SMPDB and FooDB are also part of the HMDB suite of databases. DrugBank contains equivalent information on ~1600 drug and drug metabolites, T3DB contains information on 3100 common toxins and environmental pollutants, SMPDB contains pathway diagrams for 440 human metabolic and disease pathways, while FooDB contains equivalent information on ~28,000 food components and food additives.

Protein/Gene Sequences are provided in FASTA Format (text-based format for representing either nucleotide sequences or peptide sequences, in which nucleotides or amino acids are represented using single-letter codes); metabolite structures are provide in SDF format (structure-data file) and Metabolite and Protein Data are provided in XML format.

14. **MetaCyc**

http://metacyc.org/

MetaCyc includes information on pathways involved in both primary and secondary metabolism. MetaCyc is a curated database of experimentally elucidated metabolic pathways from all domains of life. It contains 2260 pathways from 2600 different organisms. MetaCyc contains pathways involved in both primary and secondary metabolism, as well as associated metabolites, reactions, enzymes, and genes. The goal of MetaCyc is to catalog the universe of metabolism by storing a representative sample of each experimentally elucidated pathway. MetaCyc applications include: online encyclopedia of metabolism; prediction of metabolic pathways in sequenced genomes; support metabolic engineering via enzyme database; metabolite database aids metabolomics research.

The software/database bundle can be downloaded from http://metacyc.org/download.shtml. Data files only are free, software/database bundle are provided upon a compete license free to academics for research purposes. Information on data format can be retrieved from http://bioinformatics.ai.sri.com/ptools/flatfile-format.html

15. **SMPDB (The Small Molecule Pathway Database)**

http://smpdb.ca/

SMPDB is an interactive, visual database containing more than 618 small molecule pathways found in humans. More than 70% of these pathways (>433) are not found in any other pathway database. SMPDB is designed specifically to support pathway elucidation and pathway discovery in metabolomics, transcriptomics, proteomics and systems biology. It is able to do so, in part, by providing exquisitely detailed, fully searchable, hyperlinked diagrams of human metabolic pathways, metabolic disease pathways, metabolite signaling pathways and drug-action pathways. All SMPDB pathways include information on the relevant organs, subcellular compartments, protein_complex cofactors, protein_complex locations, metabolite locations, chemical structures and protein_complex quaternary structures. Each small molecule is hyperlinked to detailed descriptions contained in the HMDB or DrugBank and each protein_complex or enzyme complex is hyperlinked to UniProt. All SMPDB pathways are accompanied with detailed descriptions and references, providing an overview of the pathway, condition or processes depicted in each diagram. The database is easily browsed and supports full text, sequence and chemical structure searching. Users may query SMPDB with lists of metabolite names, drug names,

genes/protein_complex names, SwissProt IDs, GenBank IDs, Affymetrix IDs or Agilent microarray IDs. These queries will produce lists of matching pathways and highlight the matching molecules on each of the pathway diagrams. Gene, metabolite and protein_complex concentration data can also be visualized through SMPDB's mapping interface. All of SMPDB's images, image maps, descriptions and tables are downloadable from http://smpdb.ca/downloads. Sequences are provided in FASTA format while structure in SDF format.

5.4.3 Genetic data

16. **GenBank®**

http://www.ncbi.nlm.nih.gov/genbank/

GenBank® is the NIH genetic sequence database, an annotated collection of all publicly available DNA sequences. GenBank is part of the International Nucleotide Sequence Database Collaboration, which comprises the DNA DataBank of Japan (DDBJ), the European Molecular Biology Laboratory (EMBL), and GenBank at NCBI.

GenBank releases consist of a set of ASCII text files, most of which contain sequence data. A few supplemental files are also supplied, containing lists of new, modified, and deleted sequence records. The line-lengths of these files is variable. The complete release notes for the current version of GenBank are available on the NCBI ftp site (ftp://ftp.ncbi.nih.gov/genbank/gbrel.txt). A new release is made every two months. An annotated sample GenBank record for a Saccharomyces cerevisiae gene demonstrates many of the features of the GenBank flat file format (http://www.ncbi.nlm.nih.gov/genbank/samplerecord/).

17. **Entrez Gene**

www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene

Entrez Gene is NCBI's database for gene-specific information. It does not include all known or predicted genes; instead Entrez Gene focuses on the genomes that have been completely sequenced, that have an active research community to contribute gene-specific information, or that are scheduled for intense sequence analysis.

The content of Entrez Gene represents the result of curation and automated integration of data from NCBI's Reference Sequence project (RefSeq), from collaborating model organism databases, and from many other databases available from NCBI. Records are assigned unique, stable and tracked integers as identifiers. The content (nomenclature, genomic location, gene products and their attributes, markers, phenotypes and links to citations, sequences, variation details, maps, expression, homologs, protein domains and external databases) is available via interactive browsing through NCBI's Entrez system, via NCBI's Entrez programming utilities (E-Utilities) and for bulk transfer by FTP.

Access to this information either through the Entrez Gene website or by flat files via NCBI's ftp site can be time consuming and limiting in regards to the number of and what questions you can ask about the data. A better solution for intense data mining is to create a relational database. The bioinformatics and research computing (http://jura.wi.mit.edu/entrez_gene/) offers their MySQL based database and data parsing/loading scripts as an easy-to-implement solution to this problem. While the ER diagram describes the database created, a SQL syntax

for both the tables and indexes id also provided. The scripts will automatically download Entrez Gene data files, parse them, and load them into a MySQL database.

18. **The EMBL Nucleotide Sequence Database**
http://www.ebi.ac.uk/embl/
The EMBL, maintained at the European Bioinformatics Institute (EBI), incorporates, organizes and distributes nucleotide sequences from public sources. The database is a part of an international collaboration with DDBJ (Japan) and GenBank (USA). Data are exchanged between the collaborating databases on a daily basis to achieve optimal synchrony. The web-based tool, Webin, is the preferred system for individual submission of nucleotide sequences, including Third Party Annotation (TPA) and alignment data. Automatic submission procedures are used for submission of data from large-scale genome sequencing centres and from the European Patent Office. Database releases are produced quarterly. The latest data collection can be accessed via FTP, email and WWW interfaces. The EBI's Sequence Retrieval System (SRS) integrates and links the main nucleotide and protein databases as well as many other specialist molecular biology databases. For sequence similarity searching, a variety of tools (e.g. FASTA and BLAST) are available that allow external users to compare their own sequences against the data in the EMBL Nucleotide Sequence Database, the complete genomic component subsection of the database, the WGS data sets and other databases. All available resources can be accessed via the EBI home page at http://www.ebi.ac.uk.

19. **CAS Registry Database**
http://www.cas.org/content/chemical-substances
CAS Registry Database contains information on more than 93 million organic and inorganic substances, and more than 64 million protein and DNA sequences - more than any other database. The sequence information comes from CAS and GenBank, produced by the National Institutes of Health. The chemical information is produced by CAS, and is prepared by the CAS Registry System, which identifies each compound with a specific CAS registry number, index name, and graphic representation of its chemical structure. The assignment of chemical names is done according to the chemical nomenclature rules for CA index names, which is slightly different from the internationally standard IUPAC names, according to the rules of IUPAC.

20. **KEGG (Kyoto Encyclopedia of Genes and Genomes)**
http://www.genome.jp/kegg/kegg1.html
KEGG is a database resource for understanding high-level functions and utilities of the biological system, such as the cell, the organism and the ecosystem, from genomic and molecular-level information. Gene catalogs from completely sequenced genomes are linked to higher-level systemic functions of the cell, the organism and the ecosystem KEGG is a computer representation of the biological system, consisting of molecular building blocks of genes and proteins (genomic information) and chemical substances (chemical information) that are integrated with the knowledge on molecular wiring diagrams of interaction, reaction and relation networks (systems information). It also contains disease and drug information (health information) as perturbations to the biological system.

KEGG is an integrated database resource consisting of the seventeen main databases shown below. They are broadly categorized into systems information, genomic information, chemical information and health information.

Category	Database	Content
Systems information	KEGG PATHWAY	KEGG pathway maps
	KEGG BRITE	BRITE functional hierarchies
	KEGG MODULE	KEGG modules of functional units
Genomic information	KEGG ORTHOLOGY	KEGG Orthology (KO) groups
	KEGG GENOME	KEGG organisms with complete
	KEGG GENES	Gene catalogs of complete
	KEGG SSDB	Sequence similarity database for
Chemical information	KEGG COMPOUND	Metabolites and other small
	KEGG GLYCAN	Glycans
	KEGG REACTION	Biochemical reactions
	KEGG RPAIR	Reactant pair chemical
	KEGG RCLASS	Reaction class defined by RPAIR
	KEGG ENZYME	Enzyme nomenclature
Health information	KEGG DISEASE	Human diseases
	KEGG DRUG	Drugs
	KEGG DGROUP	Drug groups
	KEGG ENVIRON	Crude drugs and health-related s

21. **HIstome: The Histone Infobase**
http://www.actrec.gov.in/histome/histone_main.php
The Histone Infobase is an online database that provides detailed information about human histones, their post-translational modifications and enzymes responsible for addition and removal of these modifications.

22. **EpiGenie**
http://epigenie.com/epigenetic-tools-and-databases/
EpiGenie is a web page containing links to tools and databases relevant for epigenetics researchers.

23. **Human Brain Transcriptome**
http://hbatlas.org
The HBT (Human Brain Transcriptome) project at the Department of Neurobiology Yale University School of Medicine is a public database containing transcriptome data and associated metadata for the developing and adult human brain. In the first stage of this project, we provide genome-wide, exon-level transcriptome data generated using the Affymetrix GeneChip Human Exon 1.0 ST Arrays from over 1,340 tissue samples sampled from both hemispheres of postmortem human brains. Specimens range from embryonic development to adulthood and are representative of both males and females from multiple ethnicities. A total of 16 brain regions were sampled: the cerebellar cortex, mediodorsal nucleus of the thalamus, striatum, amygdala, hippocampus, and 11 areas of the neocortex. Genome-wide genotyping data for 2.5 million markers (Illumina Human Omni 2.5-Quad Bead Chips) is available for all specimens upon request. The HBT project is funded by the National

Institute of Health (U01MH081896). Additional data will be incorporated into the database as it becomes available.

5.4.4 Other biological data

24. PopGen

http://xnet.hsl.gov.uk/popgen/

PopGen includes anatomical, physiological and clearance/elimination kinetics data. PopGen aims to generate data that predict realistic anatomical and physiological variation in human populations. Organ volumes and blood flows are determined for virtual individuals from both *a priori* distributions of anthropometric parameters such as body mass, height, and body mass index, and from measured data from existing studies. It requires user registration (just email address). Typical data retrieved are: tissues mass, tissues blood flow, cardiac output, V_{max} (Michaelis-Menten maximum velocity and CL_{int} (intrisic hapatic clearence). Data can be downloaded in various formats (XML, CSV, TXT).

25. Endocrine Active Substances Information System (EASIS)

https://eurl-ecvam.jrc.ec.europa.eu/databases/eas_database

Database covers 428 substances suspected of having the potential for endocrine disruption. Although it has no normative or pre-normative implications, this database has proven useful in providing stakeholders with a significant amount of information on potential endocrine disrupters. However, one of the limitations of the database in its current form is that it is static in nature, and does not allow information to be introduced or updated. New updateable version is under development.

26. UniProt

http://www.uniprot.org

The Universal Protein Resource, is produced by the UniProt Consortium, formed by the Swiss Institute of Bioinformatics (SIB), the European Bioinformatics Institute (EBI) and the Protein Information Resource (PIR). UniProt provides a comprehensive, high-quality and freely accessible resource of protein sequence and functional information. The centrepiece of the UniProt databases is the UniProt knowledge base (UniProtKB), which comprises 2 sections: manually annotated UniProtKB/Swiss-Prot and automatically annotated UniProtKB/TrEMBL. Taken together, these 2 sections give access to all publicly available protein sequences.

UniProtKB/Swiss-Prot is a high quality manually annotated (reviewed) and non-redundant protein sequence database, which brings together experimental results and computed features. Although Swiss-Prot provides annotated entries for all species, it focuses on the annotation of proteins from model organisms of distinct taxonomic groups to ensure the presence of high quality annotation for representative members of all protein families. Protein families and groups of proteins are continuously reviewed to keep up with current scientific findings.

Each Swiss-Prot entry contains information about one or more protein sequence(s) derived from one gene in one species (usermanual: http://www.uniprot.org/manual/).

UniProtKB/Swiss-Prot includes protein sequences and description of alternative protein products (due to alternative splicing, alternative promoter usage, alternative initiation, RNA

editing); protein and gene names using standardised official nomenclature and synonyms used in the literature and other databases; protein function; enzyme-specific information (catalytic activity, cofactors, metabolic pathway, regulation); biologically relevant domains and sites; PTMs; subcellular location(s); tissue expression; expression during embryonic development and /or cell differentiation; secondary and quaternary structure information; polymorphisms; similarities to other proteins; involvement in diseases; cross-references to numerous databases; controlled vocabularies in several (sub)sections; qualifiers for predicted or propagated data.

Complete data sets in the original flat file format, FASTA format, XML or RDF format, are freely downloadable from www.uniprot.org/downloads.

27. **Protein Data Bank (PDB)**
http://www.rcsb.org/pdb/home/home.do
This resource is powered by the Protein Data Bank archive-information about the 3D shapes of proteins, nucleic acids, and complex assemblies that help students and researchers understand all aspects of biomedicine and agriculture, from protein synthesis to health and disease.

As a member of the wwPDB, the RCSB PDB curates and annotates PDB data. The RCSB PDB builds upon the data by creating tools and resources for research and education in molecular biology, structural biology, computational biology, and beyond.

5.4.5 Population data

28. **Eurostat Database**
http://ec.europa.eu/eurostat/data/database
In the eurostat database statistical information about a large variety of data (such as environment, population, social conditions, agricultural among other) is available. Different Database Eurostat's mission: to be the leading provider of high quality statistics on Europe.

29. **OECD Statistics**
http://stats.oecd.org
OECD Statistics database includes data and metadata for OECD countries and selected non-member economies. There are statistics about population, finance, health, democracy, education, environment, industry, labour, productivity etc.

30. **European Social Survey (ESS)**
http://www.europeansocialsurvey.org
The European Social Survey (ESS) is an academically driven cross-national survey that has been conducted every two years across Europe since 2001.
Following an application to the European Commission which was submitted by the UK on behalf of 14 other countries, the ESS was awarded ERIC status on 30th November 2013.
The survey measures the attitudes, beliefs and behaviour patterns of diverse populations in more than thirty nations. The main aims of the ESS are:
- to chart stability and change in social structure, conditions and attitudes in Europe and to interpret how Europe's social, political and moral fabric is changing

- to achieve and spread higher standards of rigour in cross-national research in the social sciences, including for example, questionnaire design and pre-testing, sampling, data collection, reduction of bias and the reliability of questions
- to introduce soundly-based indicators of national progress, based on citizens' perceptions and judgements of key aspects of their societies
- to undertake and facilitate the training of European social researchers in comparative quantitative measurement and analysis
- to improve the visibility and outreach of data on social change among academics, policy makers and the wider public

Prior to becoming an ERIC, funding for the ESS has been received from the European Commission's Framework programmes, from the European Science Foundation, and from national funding councils in participating countries. Funding of the ESS ERIC is via Member and Observer contributions to central costs and to national participation costs.

Data are available at http://www.europeansocialsurvey.org/data/.

31. **European Health Examination Survey (EHES)**
http://www.ehes.info
The European Health Examination Survey (EHES) is a collaboration to collect nationally representative, high quality health data which are comparable between countries and over time.
    - All countries should cover at least the age group 25-64 years. Extending the age group to people 65+ years is recommended. Also people living in institutions should be included whenever feasible.
    - Sample should be nationally representative probability sample of at least 4000 people.
    - Core measurements, which all countries should at least include, are height, weight, waist circumference, blood pressure, total and HDL-cholesterol, fasting glucose or HbA1c and questionnaire(s). Countries can include additional measurements based on national needs, interests and resources.
    - Health examination survey (HES) is complementary to health interview survey (HIS) and administrative registers. Together these form a good basis for the health monitoring in the countries.

EHES can provide information, not available from other data sources, on key health indicators. This will facilitate evidence-based planning and evaluation of public health policies and actions.

"This project has received funding from the European Union's Seventh Programme for research, technological development and demonstration under grant agreement N°603946

HEALS

32. Twin registries

Several twin registries have already been collected around Europe. There are shortly summarized in

Table 1.Summary of European twin studies

Twin data / registry	Organization	Established	Nbr of people	Temporal coverage (birth)	Web site/reference
Finnish Twin Cohorts	THL/University of Helsinki	1975 1991 1994	13888 twins 5563 twins 2724 families	-1958 1974-1979 1983-1987	www.twinstudy.helsinki.fi • Jaakko Kaprio, "The Finnish twin cohort study: an update", Twin Research and Human Genetics, 2013. • Jaakko Kaprio, "Twin studies in Finland 2006", Twin Research and Human Genetics, 2006.
Norwegian Twin Registry (NTR)	Norwegian Institute of Public Health (NIPH)	2009	47989 (31440 with consent to participate in research)	1895-1960 1967-1979	http://www.fhi.no/twins Thomas S. Nilsen et al, "The Norwegian Twin Registry", Twin Research and Human Genetics, 2012.
Swedish Twin Registry (STR)	Karolinska Institute	1961	89000 twin pairs (65000 pair with both twins alive)	1886-1925, 1926-1958, 1959-1990	http://ki.se/en/research/the-swedish-twin-registry-1 http://ki.se/sites/default/files/policy_swedish_twin_registry_collaboration_2013.pdf P. Lichtenstein et al, "The Swedish Twin Registry: a unique resource for clinical, epidemiological and genetic studies", Journal of Internal Medicine, 2002.
Danish Twin Registry	Faculty of Health Sciences, University of Southern Denmark	1950s	> 88000 twin pairs	1870-2009	http://www.sdu.dk/en/om_sdu/institutter_centre/ist_sundhedstjenesteforsk/centre/dtr • Axel Skytthe et al, "The Danish Twin Registry: 127

	(SDU)				Birth Cohorts of Twins", Twin Research, 2002. • Axel Skytthe et al, "The Danish Twin Registry: Linking Surveys, National Registers, and Biological Information", Twin Research and Human Genetics, 2012.
Netherlands Twin Register (NTR)	Vrije Universiteit in Amsterdam	1987	> 88000 twin pairs (62000 under age 18, 25000 of age > 18)		http://www.tweelingenregister.org/en/ • Dorret I. Boomsma et al, "Netherlands Twin Register: From Twins to Twin Families", Twin Research and Human Genetics, 2006. • Dorret I. Boomsma et al, "Netherlands Twin Register: A Focus on Longitudinal Research", Twin Research, 2002.
UK twin registry (TwinsUK)	Department of Twin Research, King's College London	1993	5488 twin pairs (ages 16-98)		Tim D. Spector et al, "The UK Adult Twin Registry (TwinsUK)", Twin Research and Human Genetics, 2006.
Australian Twin Registry (ATR)	University of Melbourne	1981	> 33000 twin pairs		http://www.twins.org.au/ John L. Hopper et al, "Australian Twin Registry: 30 Years of Progress", Twin Research and Human Genetics, 2012.
Italian Twin Register (ITR)	National Institute of Health	2001	24962	1912-	http://www.gemelli.iss.it/ • MA Stazi et al, "The Italian Twin Project: from the personal identification number to a national twin registry", Twin Res., 2002. • Sonia Brescianini et al, "An Update on the Italian Twin Register: Advances in Cohort Recruitment, Project Building and Network Development", Twin Research and Human Genetics, 2012.

"This project has received funding from the European Union's Seventh Programme for research, technological development and demonstration under grant agreement N°603946

5.4.6 Other databases

33. **Microbial volatile organic compound database**
    http://bioinformatics.charite.de/mvoc/
    Database gathers together information regarding microbial volatile compounds (mVOC). There are several possibilities to search for mVOCs: PubChem ID, name several molecular properties or species. Information about the volatile emitters and how these volatiles influence other organisms are integrated. Furthermore, KEGG pathways that map the volatile compounds to pathways of the fungal or bacterial organisms can be visualized for biological interpretation.

    Reference: Lemfack MC, Nickel J, Dunkel M, Preissner R, Piechulla B. mVoC: a database of microbial volatiles. Nucleic Acids Res. 2014 Jan 1;42(1):D744-8.

34. **IRIS database for risk assessment**
    http://www.epa.gov/iris/index.html)
    EPA's Integrated Risk Information System (IRIS) is a human health assessment program that evaluates information on health effects that may result from exposure to environmental contaminants. Through the IRIS Program, EPA provides the highest quality science-based human health assessments to support the Agency's regulatory activities. The IRIS database is web accessible and contains information on more than 550 chemical substances

35. **The EFSA Comprehensive European Food Consumption Database**
    http://www.efsa.europa.eu/en/datexfoodcdb/datexfooddb.htm
    The EFSA Comprehensive Food Consumption Database contains information on food consumption (chronic and acute) across the European Union. It contains detailed data for a number of EU countries. EFSA used its food classification system 'FoodEx' to categorise all foods and beverages included in the Comprehensive Database.

36. **Fineli® - Finnish Food Composition Database**
    http://www.fineli.fi/?lang=en
    Fineli® contains information about Finnish food composition. It is maintained by National Institute for Health and Welfare. It contains information about over 3700 foods and 55 nutrient factors. Nutrient values are the average concentrations of Finnish foods. The data are publicly available at http://www.fineli.fi/showpage.php?page=opendata&lang=en.

37. **FooDB**
    http://foodb.ca
    FooDB is resource on food constituents, chemistry and biology. It provides information on both macronutrients and micronutrients, including many of the constituents that give foods their flavor, color, taste, texture and aroma. Each chemical entry in the FooDB contains more than 100 separate data fields covering detailed compositional, biochemical and physiological information (obtained from the literature). This includes data on the compound's nomenclature, its description, information on its structure, chemical class, its physico-chemical data, its food source(s), its color, its aroma, its taste, its physiological effect, presumptive health effects (from published studies), and concentrations in various foods. Users are able to browse or search FooDB by food source, name, descriptors, function or concentrations.

FooDB is offered to the public as a freely available resource. Use and re-distribution of the data, in whole or in part, for commercial purposes requires explicit permission of the authors and explicit acknowledgment of the source material (FooDB). Data can be downloaded as CSV or SQL file at http://foodb.ca/downloads.

38. **EU Pesticides Database**
http://ec.europa.eu/sanco_pesticides/public/index.cfm?event=homepage&language=EN
The database provides information on the active substances approved in Europe; references to EU legislation for each substance; and toxicological information and maximum residue levels in food and feed.

39. **Household Products Database**
http://hpd.nlm.nih.gov/index.htm
U.S. Department of Health & Human Services provides Household Product Database that describes health and safety information on different household products.

40. **International Information System on Occupational Exposure to Carcinogens - CAREX**
http://www.ttl.fi/en/chemical_safety/carex/pages/default.aspx
CAREX is a MS Access database which contains estimated of the numbers of workers occupationally exposed to carcinogens by industry in 15 previous countries of the European Union (exposure data from 1990-1993) and in four of the ten countries that joined EU in 2004 (exposure data from 1997). CAREX contains also information on industrial distribution of the employed, summarised exposure data, numbers of exposed by occupation, definitions of carcinogenic exposure, descriptions of the estimation procedures and bibliographic references.

6 Appendix B: Documents and Guidelines

6.1 Guidelines by World Health Organization (WHO)

1. **Parma Ministerial Declaration and Commitment to Act – WHO 2010**
   http://www.euro.who.int/__data/assets/pdf_file/0011/78608/E93618.pdf
   The Parma Declaration on Environment and Health is based on a joint declaration by the Ministers and Representatives of Member States in the European Region of the World Health Organization (WHO) responsible for health and the environment, the WHO Regional Director for Europe, the European Commissioners for Health and Consumer Policy and for the Environment, the Executive Secretary of the United Nations Economic Commission for Europe (UNECE) and the Regional Director for Europe of the United Nations Environment Programme (UNEP) to act on the key environment and health challenges including: (a) the health and environmental impacts of climate change and related policies; (b) the health risks to children and other vulnerable groups posed by poor environmental, working and living conditions (especially the lack of water and sanitation); (c) socioeconomic and gender inequalities in the human environment and health, amplified by the financial crisis; (d) the burden of non-communicable diseases, in particular to the extent that it can be reduced through adequate policies in areas such as urban development, transport, food safety and nutrition, and living and working environments; (e) concerns raised by persistent, endocrine-disrupting and bio-accumulating harmful chemicals and (nano)particles; and by novel and emerging issues; (f) insufficient resources in parts of the WHO European Region.

2. **Health and environment: communicating the risks, WHO 2013**
   http://www.euro.who.int/__data/assets/pdf_file/0011/233759/e96930.pdf
   Based on workshop, jointly organized by the WHO European Office for Investment for Health and Development in Venice and the WHO European Centre for Environment and Health in Bonn, held in Trento, Italy with the aim of sharing experiences in the management and communication of environmental risks; this report builds on the presentations and discussions. It presents series of key messages useful to regional and local authorities, as well as to risk managers in general.

3. **Draft guidance document on characterizing and communicating uncertainty in exposure assessment – WHO 2006**
   http://www.inchem.org/documents/harmproj/harmproj/harmproj6.pdf
   This guidance has been developed as a basis for transparently characterizing uncertainty in chemical exposure assessment to enable its full consideration in regulatory and policy decision-making processes. Uncertainties in exposure assessment are grouped under three categories—namely, parameter, model and scenario—with the guidance addressing both qualitative and quantitative descriptions. Guidance offered here is consistent with other projects addressing exposure in the WHO/IPCS Harmonization Project, including a monograph on IPCS Risk Assessment Terminology, which includes a glossary of key exposure assessment terminology, and a monograph on Principles of Characterizing and Applying Human Exposure Models. The framework described in this monograph is considered applicable across a full range of chemical categories, such as industrial chemicals, pesticides, food additives and others. It is intended primarily for

use by exposure assessors who are not intimately familiar with uncertainty analysis. The monograph aims to provide an insight into the complexities associated with characterizing uncertainties in exposure assessment and suggested strategies for incorporating them during human health risk assessments for environmental contaminants. This is presented in the context of comparability with uncertainties associated with hazard quantification in risk assessment.

4. **Combined or multiple exposure to health stressors in indoor built environments (WHO 2013)** http://www.euro.who.int/__data/assets/pdf_file/0020/248600/Combined-or-multiple-exposure-to-health-stressors-in-indoor-built-environments.pdf?ua=1
The objective of this study was to undertake, summarize, and present a systematic review of literature and project reports presenting evidence on multiple or combined risk exposure in indoor built environments. The review covered safety threats and injuries, indoor air pollution, use of household chemicals, noise, damp and mould, thermal conditions, crowding, inadequate hygiene standards, and harmful building and equipment/furnishing materials. In terms of indoor settings the review covered: (a) residential buildings, as well as (b) day care and school settings. Occupational and medical settings were excluded. In addition to searching the published literature through a number of international online databases (Scopus, PubMed, Medline, Google Scholar), results, reports, and databases on the subject that are not necessarily available through journal databases were included to the extent possible (EnVIE, LARES, INTARESE, HEIMTSA, INTERA, SILC, EQLS etc.). The PRISMA methodology was followed for the systematic review in view of the large number of entries found in these databases and the need for a well-targeted methodology to ensure identified publications are relevant to the task. There is a lot of evidence and studies on non-occupational indoor risks. However, the focus is mainly on health outcomes from single stressor exposure and often multiple risks are related to confounding in epidemiological studies. As a consequence, these studies—although rich in data—do not necessarily provide a good overview of multiple exposure to these health stressors and their association to adverse health outcomes per se. In fact, aside from simple additivity of effects and some specific cases of exposure to at most two simultaneous stressors, which may enhance or counteract each other, there is limited actual evidence available on health effects of co-exposure to multiple stressors. The summary report describes the main findings of the studies and projects on multiple exposure in indoor settings, separated by the three settings (home, school, day care). Additionally, the report indicates the most frequent combinations of risk exposure and reveals the impact of combined/multiple exposure on risk ratios for reported outcomes when data on the latter are available.

5. **Biomarkers In Risk Assessment: Validity And Validation, WHO (2001)**
http://www.inchem.org/documents/ehc/ehc/ehc222.htm
This report presents the use of biomarkers in risk assessment since they allow decision-makers to answer important public health questions by being used in research or risk assessments in a way that contributes useful information that cannot be obtained better by other approaches, such as questionnaires, environmental measurements or record reviews. Validity of biomarkers refers to a range of characteristics that is the best approximation of the truth or falsehood as it is a function of intrinsic qualities of the biomarker and characteristics of the analytic procedures used. Although biomarkers have a long history in medicine and public health, the systematic development,

validation and application of biomarkers is a relatively new field in environmental health. This report governs the gap and builds on the findings of biological monitoring in occupational health.

6. **WHO Regional Office for Europe (2010). "Indoor Air Quality Guidelines: Selected Pollutants". Copenhagen, WHO Regional Office for Europe. ISBN 978 92 890 0213 4**
http://www.euro.who.int/__data/assets/pdf_file/0009/128169/e94535.pdf
This book presents WHO guidelines for the protection of public health from risks due to a number of chemicals commonly present in indoor air. The substances considered in this review, i.e. benzene, carbon monoxide, formaldehyde, naphthalene, nitrogen dioxide, polycyclic aromatic hydrocarbons (especially benzo[a]pyrene), radon, trichloroethylene and tetrachloroethylene, have indoor sources, are known in respect of their hazardousness to health and are often found indoors in concentrations of health concern. The guidelines are targeted at public health professionals involved in preventing health risks of environmental exposures, as well as specialists and authorities involved in the design and use of buildings, indoor materials and products. They provide a scientific basis for legally enforceable standards.

7. **WHO guidelines for indoor air quality – dampness and mould – WHO 2009**
http://www.euro.who.int/__data/assets/pdf_file/0017/43325/E92645.pdf
This document presents World Health Organization (WHO) guidelines for the protection of public health from health risks due to dampness, associated microbial growth and contamination of indoor spaces. The guidelines are based on a comprehensive review and evaluation of the accumulated scientific evidence by a multidisciplinary group of experts studying health effects of indoor air pollutants as well as those specialized in identification of the factors that contribute to microbial growth indoors.

8. **WHO Regional Office for Europe (2006). "Air quality guidelines. Global update 2005. Particulate matter, ozone, nitrogen dioxide and sulfur dioxide." Copenhagen, Denmark.**
http://www.euro.who.int/__data/assets/pdf_file/0005/78638/E90038.pdf
This guideline is neither standards nor legally binding criteria, it is designed to offer guidance in reducing the health impacts of air pollution based on expert evaluation of current scientific evidence. They are intended to be relevant to the diverse conditions of all WHO's regions, and to support a broad range of policy options for air quality management. Knowledge about the hazardous properties of the pollutants and indication of the risk related to exposure, summarized by the guidelines, provide an essential scientific contribution to the development of strategies for air quality management. Authorities preparing national strategies, especially in those countries that lack the necessary scientific infrastructure and resources to conduct their own assessments in support of public policy, will find the guidelines an essential resource. This updated guideline comprises 13 chapters. Chapters 1–9 consist of background material, providing a concise yet comprehensive review of the issues affecting the application of the WHO air quality guidelines in risk assessment and policy development.

9. **WHO Regional Office for Europe (2000). "Air Quality Guidelines – Second Edition". Copenhagen, WHO Regional Office for Europe.**
http://www.euro.who.int/__data/assets/pdf_file/0005/74732/E71922.pdf
The guidelines presented in this document are a WHO contribution to HEALTH21, the health for all policy framework for the WHO European Region. This states that, 'by the year 2015, people in the Region should live in a safer physical environment, with exposure to

contaminants hazardous to health at levels not exceeding internationally agreed standards'. These revised air quality guidelines are used as a starting point for the derivation of legally binding limit values in the framework of the EU Air Quality Directive. The aim of the guidelines are to provide a basis for protecting public health from adverse effects of air pollutants and to eliminate or reduce exposure to those pollutants that are known or likely to be hazardous to human health or wellbeing. Hence the guidelines are intended to provide background information and guidance to (inter)national and local authorities in making risk assessment and risk management decisions. In establishing pollutant levels below which exposure – for life or for a given period of time – does not constitute a significant public health risk, the guidelines provide a basis for setting standards or limit values for air pollutants. This guide includes an introduction on the nature of the guidelines and the methodology used to establish guideline values for a number of air pollutants. In addition, it describes the various aspects that need to be considered by national or local authorities when guidelines are transformed into legally binding standards. For the pollutants addressed, the sections on "Health risk evaluation" and "Guidelines" describe the most relevant considerations that have led to the recommended guideline values. For detailed information on exposure and on the potential health effects of the reviewed pollutants, the reader is referred to the Regional Office's web site, where the background documents on the individual air pollutants can be accessed.

10. **Environmental burden of disease associated with inadequate housing. A method guide to the quantification of health effects of selected housing risks in the WHO European Region. Summary report (WHO, 2011).**
http://www.euro.who.int/en/publications/abstracts/environmental-burden-of-disease-associated-with-inadequate-housing.-summary-report
The report provides evidence that the health consequences of inadequate housing are substantial. Improving housing in a way that removes or at least minimizes the negative impact on health and safety and promotes a healthier living environment is good for the residents and beneficial for society. Reducing the burden of responding to the demands on the health system attributable to inadequate housing should therefore be seen as an obvious public health priority, but also as something that makes economic sense. The findings set out in the report provide ample justification for the principle that health should be at the centre of housing policy. Making housing healthy, affordable and sustainable should be a prime objective of all professionals and policy-makers involved in any aspect of housing and of health, and the significant contribution of adequate housing to a healthy lifestyle should be more widely recognized.

11. **Guidelines for Community Noise – WHO 1999**
http://www.who.int/docstore/peh/noise/guidelines2.html
This report by WHO presents guidelines for community noise in order to consolidate actual scientific knowledge on the health impacts of community noise and to provide guidance to environmental health authorities and professional trying to protect people from the harmful effects of noise in non-industrial environments. The health risk to humans from exposure to environmental noise is evaluated and guidelines values derived. The issue of noise control and health protection is briefly addressed.

12. **WHO Regional Office for Europe (2009b). "Night Noise Guidelines for Europe." Copenhagen, WHO Regional Office for Europe.**
http://www.euro.who.int/__data/assets/pdf_file/0017/43316/E92845.pdf
This guidelines document reviews the health effects of night time noise exposure, examines exposure-effects relations, and presents guideline values of night noise exposure to prevent harmful effects of night noise in Europe. Although these guidelines are neither standards nor legally binding criteria, they are designed to offer guidance in reducing the health impacts of night noise based on expert evaluation of scientific evidence in Europe. The aim of this document is to present the conclusions of the WHO working group responsible for preparing guidelines for exposure to noise during sleep. This document can be seen as an extension of the WHO Guidelines for community noise (1999). The need for "health-based" guidelines originated in part from the European Union Directive 2002/49/EC relating to the assessment and management of environmental noise (commonly known as the Environmental Noise Directive and abbreviated as END) which compels European Union Member States to produce noise maps and data about night exposure from mid-2007.

13. **International Classification of Diseases (ICD-10)**
http://www.who.int/classifications/icd/en/
The International Classification of Diseases (ICD) is the standard diagnostic tool for epidemiology, health management and clinical purposes. This includes the analysis of the general health situation of population groups. It is used to monitor the incidence and prevalence of diseases and other health problems, proving a picture of the general health situation of countries and populations. ICD is used by physicians, nurses, other providers, researchers, health information managers and coders, health information technology workers, policy-makers, insurers and patient organizations to classify diseases and other health problems recorded on many types of health and vital records, including death certificates and health records. In addition to enabling the storage and retrieval of diagnostic information for clinical, epidemiological and quality purposes, these records also provide the basis for the compilation of national mortality and morbidity statistics by WHO Member States. Finally, ICD is used for reimbursement and resource allocation decision-making by countries.

14. **Evaluation and use of epidemiological evidence for environmental health risk assessment Guideline Document, WHO 2000**
http://www.euro.who.int/__data/assets/pdf_file/0006/74733/E68940.pdf
The purpose of this project is to develop guidelines, which identify a set of processes and general approaches to assess available epidemiological information in a clear, consistent and explicit manner. The guidelines should also help in the evaluation of epidemiological studies with respect to their ability to support risk assessment and, consequently, risk management. Conducting expert reviews according to such explicit guidelines would make health risk assessment, and subsequent risk management and risk communication processes, more readily understood and likely to be accepted by policy-makers and the public. From WHO's standpoint, it would also make the conclusions reached by reviews more readily acceptable as a basis for future WHO guidelines and other recommendations, and would provide a more rational basis for setting priorities for future research. This project focuses only on approaches to the evaluation and use of epidemiological evidence for health risk assessment. However, this should not be interpreted as implying that only epidemiological studies are important. The Working

Group, and WHO, appreciate that data from toxicological, clinical, and other areas of research often play vital roles in both the characterization of health hazards and the estimation of risks to health, and may, in the absence of suitable epidemiological data, provide the sole basis for such activities.

15. **WHO. 2011. "Biomarkers & human biomonitoring - Children's Health and the Environment - WHO Training Package for the Health Sector."**
http://www.who.int/ceh/capacity/biomarkers.pdf
This is a presentation by WHO on Biomarkers and human biomonitoring, where the objectives are:
    - to understand how biomarkers are used to assess environmental exposures
    - to understand when and why biomarkers may be appropriate tools for specific situations
    - to understand the advantage, limitations and challenges of biomonitoring
    - to be able to give examples of how biomonitoring has been used effectively to improve environmental public health policy.

16. **Children's environmental health - Training modules and instructions the Health Sector WHO, 2011** http://www.who.int/ceh/capacity/training_modules/en/index.html
This site includes all training modules and instructions for health care providers including a number of training modules including, Indoor air pollution, Outdoor air pollution, Chemicals, Lead, Mercury, Other heavy metals, Pesticides, POPs, Water, Sanitation and Hygiene, Food safety, Global climate change, Noise, Radiation, Mycotoxins, Second-hand tobacco smoke, Biomarkers and human biomonitoring, Injuries, Occupational exposure, Cancer, Respiratory diseases, Neurodevelopmental disorders, Endocrine disorders, Immune diseases, Developmental and environmental origins of adult disease, Children's Environmental Health Indicators, Paediatric environmental history.

17. **Summary of Principles for Evaluating Health Risks in Children Associated with Exposure to Chemicals, WHO, 2011**
http://www.who.int/ceh/publications/health_risks_exposure_chemicals/en/
This summary document explains that children are among the most vulnerable of the world's population and environmental factors can affect children's health quite differently from adults' health. It provides a summary of the findings from Environmental Health Criteria 237, Principles for Evaluating Health Risks in Children Associated with Exposure to Chemicals, and was prepared for use by a wider audience.

18. **WHO Regional Office for Europe (2007). "Large analysis and review of European housing and health status (LARES). Preliminary overview." Copenhagen.**
http://www.euro.who.int/__data/assets/pdf_file/0007/107476/lares_result.pdf
The LARES Survey (Large Analysis and Review of European Housing and Health Status), coordinated by the European Centre for Environment and Health, Bonn Office of the WHO Regional Office for Europe was designed to achieve the following objectives:
    - to improve knowledge of the impacts of existing housing conditions on health and mental and physical well-being;
    - to assess the quality of the housing stock in a holistic way and to identify housing priorities in each of the surveyed cities, and possibly common trends;

- to develop an "easy to use" tool to assess the impact of housing on health in any city or region in Europe;
- to prepare the fourth Ministerial Conference on Environment and Health (June 2004, Hungary).

This is survey provides evidence that housing and health is a complex interaction, and covers a variety of health-relevant housing factors that have so far been neglected or underestimated. In each city as well as for the whole sample, there are important and health relevant trends (accessibility and ageing, noise and sleep, mental health, accidents, heating and fuel poverty, allergies, perceived safety, indoor air and moulds, physical activity etc.) that need to be considered in both public health and housing policies.

19. **WHO Regional Office for Europe (2009a). "Social inequalities and their influence on housing risk factors and health." Copenhagen,**
http://www.euro.who.int/__data/assets/pdf_file/0013/113260/E92729.pdf
Since housing conditions have an influence on residents' health, different financial capacities - or social determinants in general - may lead to different housing conditions, they can be a potential source of inequalities. The WHO LARES data set was used, to provide data on housing and health for 8519 individuals in 3373 households compiled from 8 European cities. This study was used an exploratory design and identified the magnitude of inequality for a selected number of social determinants, housing factors, and health outcomes. Within the LARES survey, less affluent residents are more exposed to and affected by inadequate housing conditions. It is shown that inadequate housing conditions have a significant impact on several health outcomes, and that there is a social gradient for both the housing quality and the housing-related exposure, and for housing-associated health outcomes. Within the social category groups, increased exposure to environmental risks was often but not always associated with an increased health outcome. Multiple exposure scores showed the strongest associations. Housing conditions must be considered as one of the mechanisms through which social inequality translates into health inequality. For the LARES cities, these results indicate a strong need for policymakers and local stakeholders to intervene and develop programmes to overcome such inequalities and provide adequate housing conditions for everyone.

20. **WHO Regional Office for Europe (2012). "Environmental health inequalities in Europe. Assessment report." Copenhagen, WHO Regional Office for Europe.**
http://www.euro.who.int/__data/assets/pdf_file/0010/157969/e96194.pdf
The objective of the report is to provide an initial baseline assessment of environmental health inequalities in the WHO European Region. It is based on available statistical data from national or international databases. To undertake the assessment, a set of 14 environmental health inequality indicators was developed, categorized into three inequality dimensions:
    1. Housing-related inequalities (Inadequate water supply; Lack of a flush toilet; Lack of a bath or shower; Overcrowding; Dampness in the home; Inability to keep the home adequately warm)
    2. Injury-related inequalities (Work-related injuries; Fatal road traffic injuries; Fatal poisonings; Fatal falls)
    3. Environment-related inequalities (Noise exposure at home; Lack of access to green/ recreational areas; Second-hand smoke exposure at home; Second-hand smoke exposure at work)

21. **Human health in areas with industrial contamination, WHO 2014**
http://www.euro.who.int/__data/assets/pdf_file/0006/264813/Human-Health-in-Areas-with-Industrial-Contamination-Eng.pdf?ua=1
The scope of this document is to outline a framework for integrated assessment of the impacts of large industrial activities. The framework is supported by examples related to the adverse effects on environment and health of petrochemical industries, based on the results of a research project carried out in Sicily, southern Italy, by the WHO Regional Office for Europe.

22. **WHO guidelines. Electromagnetic fields (EMF)**
http://www.who.int/peh-emf/standards/en/
A number of national and international organizations have formulated guidelines establishing limits for occupational and residential EMF exposure. The exposure limits for EMF fields developed by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) - a non-governmental organization formally recognised by WHO, were developed following reviews of all the peer-reviewed scientific literature, including thermal and non-thermal effects. The standards are based on evaluations of biological effects that have been established to have health consequences. The main conclusion from the WHO reviews is that EMF exposures below the limits recommended in the ICNIRP international guidelines do not appear to have any known consequence on health.

The International EMF Project has compiled a worldwide standards database limiting exposure to EMF. Because disparities in EMF standards around the world has caused increasing public anxiety about EMF exposures from the introduction of new technologies, WHO commenced a process of harmonization of electromagnetic fields (EMF) standards worldwide. With 54 participating countries and 8 international organizations involved in the International EMF Project, it provides a unique opportunity to bring countries together to develop a framework for harmonization of EMF standards and to encourage the development of exposure limits and other control measures that provide the same level of health protection to all people.

6.2 European Commission (EC) policies and legislation

6.2.1 Directives

23. **INSPIRE**
http://inspire.ec.europa.eu/
The INSPIRE directive is based on the infrastructures for spatial information established and operated by the 28 Member States of the European Union. The Directive addresses 34 spatial data themes needed for environmental applications, with key components specified through technical implementing rules. This makes INSPIRE a unique example of a legislative “regional” approach. The 34 spatial data themes includes 3 annexes: annex 1 (coordinate reference systems, geographical grid systems, geographical names, administrative units, addresses, cadastral polices, transport networks, hydrography and protected sites), annex 2 (elevation, land cover, orthoimaginary, geology), annex 3 (statistical units, buildings, soil, land use, human health and safety, utility and government services, environmental monitoring facilities, production and industrial facilities, agricultural and aquacultural facilities, population distribution – demography, area management/restriction/ regulation zones and reporting units, natural risk zones, atmospheric conditions, meteorological geographical conditions, sea regions, bio-geographical regions, habitats and biotopes, species distribution, energy resources and mineral resources).

24. **EU Directive on ambient air quality and cleaner air for Europe (CAFE) (2008/50/EC)**
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32008L0050:EN:NOT
The CAFE Directive has been transposed into national legislation by the Air Quality Standards Regulations in 2011, which revoked and replaced three earlier statutory instruments (SI 33 of 1999, SI 271 of 2002 and SI 53 of 2004). These regulations set limit values/target values for the following pollutants: sulphur dioxide, nitrogen dioxide and oxides of nitrogen, particulate matter (PM10 and PM2.5), lead, benzene, carbon monoxide and ozone. The CAFE Directive did not change existing air quality standards but did introduce new obligations relating to fine particulate matter (PM2.5), which is considered to be especially harmful to human health. All Member States were required to calculate the current exposure of their population to PM2.5 and to take steps to reduce this exposure by 2020. Hence CAFE replaces the air framework directive and includes the following key elements: the merging of most of existing legislation into a single directive (except for the fourth daughter directive) with no change to existing air quality objectives, the new air quality objectives for PM2.5 (fine particles) including the limit value and exposure related objectives – exposure concentration obligation and exposure reduction target, the possibility to discount natural sources of pollution when assessing compliance against limit values, the possibility for time extensions of three years (PM10) or up to five years (NO2, benzene) for complying with limit values, based on conditions and the assessment by the European Commission.

25. **EU Industrial Emissions Directive (IED) (2010/75/EU)**
http://ec.europa.eu/environment/air/pollutants/stationary/ied/legislation.htm
The EU Industrial Emissions Directive (IED) (2010/75/EU) summarized directive 2008/1/EC and six others in a unified one, with regard to the industrial emissions. This Directive contains specific provisions for the following facilities: combustion plants (≥ 50 MW), incineration and co-incineration of waste, certain installations and activities using organic solvents, titanium dioxide production plants. Furthermore, according to the directive every industrial establishment must meet certain basic requirements including, preventive measures against pollution; application of best available techniques (BAT); avoid causing significant pollution; limitation, recycling or disposal of waste in a way to cause the least possible pollution; maximizing energy efficiency; prevention of accidents and limitation of their impact; remediation after the end of activities. Industrial installations must use the BAT, that the most effective techniques to achieve a high general level of environmental protection as a whole. These techniques developed on a scale which allows implementation in the relevant industrial sector, under economically and technically viable conditions. The European Commission should adopt conclusions on BAT, which will include emission levels associated with BAT. These findings serve as a basis for setting permit conditions. The permits must provide the necessary measures to ensure compliance with the basic obligations of the operator as well as environmental quality standards. Such measures shall include at least the following:
    - emission limit values for pollutants;
    - requirements to ensure the protection of soil, water and air;
    - measures for monitoring and management of waste;
    - requirements regarding the emission calculation methodology, the receive frequency data and the evaluation process;
    - obligation to inform the competent authority at least once a year on the results of the monitoring;
    - requirements for maintenance and control of soil and groundwater,

- measures relating to abnormal operating conditions (leaks, malfunctions, temporary suspension or permanent closure, etc.);
- provisions on the minimization of transboundary pollution or pollution over a long distance;
- conditions for assessing compliance with the emission limit values;

26. **Directive 2001/80/EC on the limitation of emissions of certain pollutants into the air from Large Combustion Plants**
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32001L0080
Directive 2001/80/EC focused on the limitation of emissions of certain pollutants into the air from Large Combustion Plants. The Directive entered into force in November 2001 and applied to combustion plants with rated thermal input equal to or greater than 50 MW, irrespective of the type of fuel used. The pollutants concerned in the Directive include SO2, NOx and dust.

27. **Council Directive 94/66/EC amending Directive 88/609/EEC on the limitation of emissions of certain pollutants into the air from large combustion plants**
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31994L0066
The Council Directive 94/66/EC entered into force in December 1994. The Directive amended Directive 88/609/EEC by setting limit values for plants with a rated thermal input of between 50 and 100 MW. Directive 88/609/EEC, published in December 1988, focused on the limitation of emissions of SO2, NOx and dust into the air from existing and new combustion plants with rated thermal input equal to or greater than 50 MW, irrespective of the type of fuel used.

28. **EU Directive on measures to be taken against air pollution by emissions from motor vehicles** (2001/100/EC)
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32001L0100:en:NOT
This Council Directive 70/220/EEC adapts on the approximation of the laws of the Member States on measures to be taken against air pollution by emissions from motor vehicles.

29. **EU Directive Measures to be taken against the emission of gaseous and particulate pollutants from compression-ignition engines for use in vehicles, and the emission of gaseous pollutants from positive-ignition engines fuelled with natural gas or liquefied petroleum gas for use in vehicles (2001/27/EC)**
This directive adapts to the technical progress Council Directive 88/77/EEC on the approximation of the laws of the Member States relating to measures to be taken against the emission of gaseous and particulate pollutants from compression-ignition engines for use in vehicles, and the emission of gaseous pollutants from positive-ignition engines fuelled with natural gas or liquefied petroleum gas for use in vehicles

30. **Directive 2001/81/EC on national emissions ceilings for certain atmospheric pollutants**
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32001L0081
Directive 2001/81/EC entered into force in November 2001. The aim of this Directive is to limit emissions of acidifying and eutrophying pollutants and ozone precursors in order to improve the protection in the Community of the environment and human health against risks of adverse effects from acidification, soil eutrophication and ground-level ozone and to move towards the long-term objectives of not exceeding critical levels and loads and of effective protection of all people against recognized health risks from air pollution by establishing national emission ceilings, taking the years 2010 and 2020 as benchmarks.

31. **Directive 98/70/EC of the European Parliament and of the Council of 13 October 1998 relating to the quality of petrol and diesel fuels and amending Council Directive 93/12/EEC**
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31998L0070
Directive 98/70/EC amended the Council Directive 93/12/EEC and entered into force in December 1998. This Directive sets technical specifications on health and environmental grounds for fuels to be used for vehicles equipped with positive-ignition and compression-ignition engines. In December 2000, Commission Directive 2000/71/EC were brought into force to adapt the measuring methods laid down in Directive 98/70/EC to technical progress. Emendations related to the quality of petrol and diesel fuels were made by Directive 2003/17/EC.

32. **EU Directive Certain components or characteristics of two or three-wheel motor vehicles (97/24/EC)**
http://ec.europa.eu/enterprise/sectors/automotive/documents/directives/directive-97-24-ec_en.htm
This directive has been implemented to reduce two and three wheels vehicles air pollutant emissions: standards have been adopted in two steps for mopeds and one step for motorcycles. This Directive foresees that stricter standards (for motorcycles only) should be implemented in the two years following the date of compliance with stage I (i.e.: 1999).

33. **Council Directive 96/62/EC on ambient air quality assessment and management (Air Quality Framework Directive)**
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31996L0062
Council Directive 96/62/EC on ambient air quality assessment and management (Air Quality Framework Directive) entered into force in November 1996. The general objective of this Directive is to define the basic principles of a common strategy to:
    - define and establish objectives for ambient air quality in the Community designed to avoid, prevent or reduce harmful effects on human health and the environment as a whole;
    - assess the ambient air quality in Member States on the basis of common methods and criteria;
    - obtain adequate information on ambient air quality and ensure that it is made available to the public, inter alia by means of alert thresholds;
    - maintain ambient air quality where it is good and improve it in other cases.

34. **Council Directive 1999/30/EC relating to limit values for sulphur dioxide, nitrogen dioxide and oxides of nitrogen, particulate matter and lead in ambient air (First Daughter Directive)**
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31999L0030
Council Directive 1990/30/EC (First Daughter Directive) related to limit values for sulphur dioxide, nitrogen dioxide and oxides of nitrogen, particulate matter and lead in ambient air. It entered into force in July 1999. The objectives of this Directive include:
    - establish limit values and, as appropriate, alert thresholds for concentrations of sulphur dioxide, nitrogen dioxide and oxides of nitrogen, particulate matter and lead in ambient air intended to avoid, prevent or reduce harmful effects on human health and the environment as a whole;

- assess concentrations of sulphur dioxide, nitrogen dioxide and oxides of nitrogen, particulate matter and lead in ambient air on the basis of common methods and criteria;
- obtain adequate information on concentrations of sulphur dioxide, nitrogen dioxide and oxides of nitrogen, particulate matter and lead in ambient air and ensure that it is made available to the public;
- maintain ambient-air quality where it is good and improve it in other cases with respect to sulphur dioxide, nitrogen dioxide and oxides of nitrogen, particulate matter and lead.

35. **Directive 2000/69/EC of the European Parliament and of the Council relating to limit values for benzene and carbon monoxide in ambient air (Second Daughter Directive)**
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32000L0069
The Directive 2000/69/EC of the European Parliament and of the Council (Second Daughter Directive) is related to benzene and carbon monoxide in ambient air. Member states were demanded to bring into force the laws, regulations and administrative provisions necessary to obey the Directive by 13 December 2002. The objectives of the Directive are:
    - to establish limit values for concentrations of benzene and carbon monoxide in ambient air intended to avoid, prevent or reduce harmful effects on human health and the environment as a whole;
    - to assess concentrations of benzene and carbon monoxide in ambient air on the basis of common methods and criteria;
    - to obtain adequate information on concentrations of benzene and carbon monoxide in ambient air and ensure that it is made available to the public;
    - to maintain ambient air quality where it is good and improve it in other cases with respect to benzene and carbon monoxide.

36. **Directive 2002/3/EC of the European Parliament and of the Council relating to ozone in ambient air (Third Daughter Directive)**
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32002L0003
Directive 2002/3/EC (Third Daughter Directive) focused on ozone in ambient air and entered into force in March 2002. The purpose of this Directive is:
    - to establish long-term objectives, target values, an alert threshold and an information threshold for concentrations of ozone in ambient air in the Community, designed to avoid, prevent or reduce harmful effects on human health and the environment as a whole;
    - to ensure that common methods and criteria are used to assess concentrations of ozone and, as appropriate, ozone precursors (oxides of nitrogen and volatile organic compounds) in ambient air in the Member States;
    - to ensure that adequate information is obtained on ambient levels of ozone and that it is made available to the public;
    - to ensure that, with respect to ozone, ambient air quality is maintained where it is good, and improved in other cases;

    to promote increased cooperation between the Member States, in reducing ozone levels, use of the potential of transboundary measures and agreement on such measures.

37. **Directive 2004/107/EC of the European Parliament and of the Council relating to arsenic, cadmium, mercury, nickel and polycyclic aromatic hydrocarbons in ambient air (Fourth Daughter Directive)**

http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32004L0107
Directive 2004/107/EC (Fourth Daughter Directive) entered into force in January 2005 with focus on arsenic, cadmium, mercury, nickel and polycyclic aromatic hydrocarbons in ambient air. The objectives of the Directive are:

- establish a target value for the concentration of arsenic, cadmium, nickel and benzo(a)pyrene in ambient air so as to avoid, prevent or reduce harmful effects of arsenic, cadmium, nickel and polycyclic aromatic hydrocarbons on human health and the environment as a whole;
- ensure, with respect to arsenic, cadmium, nickel and polycyclic aromatic hydrocarbons, that ambient air quality is maintained where it is good and that it is improved in other cases;
- determine common methods and criteria for the assessment of concentrations of arsenic, cadmium, mercury, nickel and polycyclic aromatic hydrocarbons in ambient air as well as of the deposition of arsenic, cadmium, mercury, nickel and polycyclic aromatic hydrocarbons;
- ensure that adequate information on concentrations of arsenic, cadmium, mercury, nickel and polycyclic aromatic hydrocarbons in ambient air as well as on the deposition of arsenic, cadmium, mercury, nickel and polycyclic aromatic hydrocarbons is obtained and ensure that it is made available to the public.

38. **Council Directive 80/779/EEC of 15 July 1980 on air quality limit values and guide values for sulphur dioxide and suspended particulates, as last amended by Directive 89/427/EEC**
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31980L0779
Council Directive of 15 July 1980 focused on air on air quality limit values and guide values for sulphur dioxide and suspended particulates. The objective of this Directive is to fix limit values and guide values for sulphur dioxide and suspended particulates in the atmosphere and the conditions for their application in order to improve the protection of human health and the environment. This Directive was last amended by Directive 89/427/EEC.

39. **Council Directive 85/203/EEC of 7 March 1985 on air quality standards for nitrogen dioxide, as last amended by Council Directive 85/580/EEC**
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31985L0203
Council Directive of 7 March 1985 focused on air quality standards for nitrogen dioxide. The main purpose of this Directive is to:

- fix a limit value for nitrogen dioxide in the atmosphere specifically to help protect human beings against the effects of nitrogen dioxide in the environment,
- lay down guide values for nitrogen dioxide in the atmosphere in order to improve the protection of human health and contribute to the long-term protection of the environment.

The Directive was last amended by Council Directive 85/580/EEC.

40. **EU Directive on the energy performance of buildings (2010/31/EU)**
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32010L0031:EN:NOT
http://europa.eu/legislation_summaries/internal_market/single_market_for_goods/construction/en0021_en.htm
The EU Directive on the energy performance of buildings (2010/31/EU) entered force in July 2010. Its key elements included: minimum energy performance requirements, cost optimal

methodology, requirements for technical building systems, energy performance certificates, inspection of heating and cooling systems, independent experts and quality control, introduction of nearly zero energy in building, voluntary common EU certification scheme.

41. EU Environmental Noise Directive (END) (2002/49/EC)

http://ec.europa.eu/environment/noise/directive.htm

The objective of the directive is to define a common approach across the EU to avoid, prevent or reduce on a prioritised basis the harmful effects of environmental noise. The harmful effects include: health effect, speech interference, annoyance. It is noted that environmental noise is defined as the unwanted or harmful outdoor sound created by human activities including road, rail, air traffic and Industry. The general aims of directive include: to harmonise noise indicators and assessment methods, to enable comparison of noise levels/affected areas between Member States, to heighten public awareness of noise as an environmental issue, to recognise noise as a significant pollutant. It is noted that this directive represents an experiment in noise legislation and is likely to the beginning of EU legislative initiatives in this area.

42. EU Water Framework Directive (WFD) (2000/60/EC)

http://ec.europa.eu/environment/water/water-framework/

The Water Framework Directive required that all inland and coastal waters within defined river basin districts must reach at least good status by 2015 and defined how this should be achieved through the establishment of environmental objectives and ecological targets for surface waters. The result will be a healthy water environment achieved by taking due account of environmental, economic and social considerations. The key features of the Directive are:

- The concept of river basin management is introduced to all Member States through the establishment of river basin districts as the basic management units. For international rivers these river basin districts (RBDs) will transcend national boundaries (Article 3).
- For each river basin district a river basin management plan must be developed, including a programme of measures3, and these will form the basis for the achievement of water quality protection and improvement (Articles 11 and 13).
- Although its prime aims are environmental, the Directive embraces, all three principles of sustainable development. Environmental, economic and social needs must all be taken into account when river basin management plans are being developed (Article 9).
- The river basin management plans will not allow further deterioration to existing water quality. With certain defined exceptions, the aim is to achieve at least good status for all water bodies in each river basin district. Geographical factors are allowed for when good status is defined and the principle of subsidiarity allows Member States some freedom within the overall requirements of the Directive (Article 4).
- The two previously competing concepts of water quality management, the use of environmental quality standards and the use of emission limit values are brought together by the Directive in a new dual approach (Article 10).
- To overcome the previously piecemeal nature of water environment regulation, a number of existing directives will be replaced when new local standards are developed to meet the Directive requirements. These local standards must be at least as stringent as those being replaced. Daughter directives will be introduced to deal with groundwater quality and for priority substances (formerly known as dangerous substances) (Article 16).

- Measures to conserve water quantity are introduced as an essential component of environmental protection. Unless minimal, all abstractions must be authorised and, for groundwater, a balance struck between abstraction and the recharge of aquifers (Article 11).
- The polluter pays principle is incorporated through a review of measures for charging for water use, including full environmental cost recovery (Article 9).
- Public participation and the involvement of stakeholders is a key requirement of the river basin management planning process, thus satisfying this aspect of Agenda 21

43. EU Groundwater Directive (GWD) (2006/118/EC)

http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32006L0118:EN:NOT

The Groundwater Directive (GWD, 2006/118/EC) on the protection of groundwater against pollution and deterioration was one of the daughter directives of the WFD and established criteria for the assessment of good chemical status. These include groundwater quality standards set at Community level and threshold values. This Directive lays down measures to prevent and control groundwater pollution, including: (a) criteria for the assessment of good groundwater chemical status; and (b) criteria for the identification and reversal of significant and sustained upward trends and for the definition of starting points for trend reversals. Moreover, the Directive complements the provisions preventing or limiting inputs of pollutants into groundwater contained in Directive 2000/60/EC, and aims to prevent the deterioration of the status of all bodies of groundwater.

44. EU Waste Water Treatment Directive 91/271/EEC

http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31991L0271:EN:NOT

The 91/271/EEC is a directive concerning the "collection, treatment and discharge of urban waste water and the treatment and discharge of waste water from certain industrial sectors". Its objective is to protect the environment from the adverse effects of urban waste water discharges and discharges from certain industrial sectors. The directive requires the collection and treatment of waste water. In agglomerations with a population equivalent (PE) of over 2000, and more advanced treatment in agglomerations with a population equivalent greater than 10,000 in sensitive areas.

45. Directive 2008/105/EC of the European Parliament and of the Council of 16 December 2008 on environmental quality standards in the field of water policy

http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32008L0105&from=EN

The Directive 2008/105/EC refers to the need to improve the knowledge and data available on sources of priority substances and ways in which pollution occurs in order to identify targeted and effective control options. In particular, this includes reliable long-term trend analysis of those priority substances that tend to accumulate in sediment and/or biota. In particular it gives particular considerations to strongly accumulative priority substances including: anthracene, brominated diphenylether, cadmium and its compounds, chloroalkanes, di[2-ethylhexyl]-phthalate, fluoranthene, hexachloro-benzene, hexachloro-butadiene, hexachloro-cyclohexane, lead and its compounds, mercury and its compounds, pentachloro-benzene, polyaromatic hydrocarbons: benzo[a]pyrene, benzo([b]fluor-anthene, benzo[k]fluor-anthene, benzo[g,h,i]-perylene, Indeno[1,2,3-cd]-pyrene) and tributyltin compounds.

46. **Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption**
http://eur-lex.europa.eu/legalcontent/EN/TXT/PDF/?uri=CELEX:31998L0083&from=EN
The European Drinking Water Directive (DWD), Council Directive 98/83/EC concerns the quality of water intended for human consumption and forms part of the regulation of Water supply and sanitation in the European Union. The Directive is intended to protect human health by laying down healthiness and purity requirements which must be met by drinking water within the Community (see water quality). It applies to all water intended for human consumption apart from natural mineral waters and waters which are medicinal products. All Member States ensure that such drinking water:
    - does not contain any concentration of micro-organisms, parasites or any other substance which constitutes a potential human health risk;
    - meets the minimum requirements (microbiological and chemical parameters and those relating to radioactivity) laid down by the directive.
    - They will take any other action needed in order to guarantee the healthiness and purity of water intended for human consumption.

47. **Directive 2006/7/EC of the European Parliament and of the Council of 15 February 2006 concerning the management of bathing water quality and repealing Directive 76/160/EEC**
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:064:0037:0051:EN:PDF
Since the 1970s, the EU has had rules in place to safeguard public health and clean bathing waters. The new Bathing Water Directive (BWD) of 2006 updated and simplified these rules. It requires Member States to monitor and assess the bathing water for at least two parameters of (faecal) bacteria. In addition, they must inform the public about bathing water quality and beach management, through the so-called bathing water profiles. These profiles contain for instance information on the kind of pollution and sources that affect the quality of the bathing water and are a risk to bathers' health (such as waste water discharge).

48. **Directive 2008/56/EC of the European Parliament and of the Council of 17 June 2008 establishing a framework for community action in the field of marine environmental policy (Marine Strategy Framework Directive)**
http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32008L0056&from=EN
The Marine Directive aims to achieve Good Environmental Status (GES) of the EU's marine waters by 2020 and to protect the resource base upon which marine-related economic and social activities depend. It is the first EU legislative instrument related to the protection of marine biodiversity, as it contains the explicit regulatory objective that "biodiversity is maintained by 2020", as the cornerstone for achieving GES.

49. **Directive 2012/33/EU of the European Parliament and of the Council of 21 November 2012 amending Council Directive 1999/32/EC as regards the sulphur content of marine fuels**
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32012L0033:EN:NOT
The Directive establishes limits on the maximum sulphur content of gas oils, heavy fuel oil in land-based applications as well as marine fuels for which it serves as the EU legal instrument to incorporate the sulphur provisions of the MARPOL Annex VI. The Directive also contains some additional fuel-specific requirements for ships calling at EU ports, obligations related to the use of fuels covered by the Directive, and the placing on the market of certain fuels (e.g. marine gas oils). The Directive does not contain provisions to regulate ship emissions of NOx or PM.

50. EU Cosmetics Directive (76/768/EEC)

http://ec.europa.eu/consumers/sectors/cosmetics/documents/directive/

The directive defines a "cosmetic product" as "any substance or preparation intended for placing in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or principally to cleaning them, perfuming them or protecting them in order to keep them in good condition, change their appearance or correct body odours." The main part of the directive is the different lists of substances in the annexes:

1. substances that are banned from use in cosmetics
2. substances that are subject to restrictions on their use (Annex III): such substances might only be permitted for certain types of cosmetics, or in certain concentrations, or subject to warning labels, etc.
3. permitted colourings
4. permitted preservatives
5. permitted UV filters.

51. Directive 2003/98/EC of the European Parliament and of the Council of 17 November 2003 on the Re-use of Public Sector Information

http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2003:345:0090:0096:EN:PDF

The directive focuses on the economic aspects of re-use of information rather than on the access of citizens to information. It encourages the Member States to make as much information available for re-use as possible. It addresses material held by public sector bodies in the Member States, at national, regional and local levels, such as ministries, state agencies, municipalities, as well as organisations funded for the most part by or under the control of public authorities (e.g. meteorological institutes). The directive covers written texts, databases, audio files and film fragments; it does not apply to the educational, scientific, broadcasting and cultural sectors.

52. Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work

http://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX:31998L0024

Purpose of the directive is to lay down minimum requirements for the protection of workers from risks to their safety and health arising, or likely to arise, from the effects of chemical agents that are present at the workplace or as a result of any work activity involving chemical agents.

53. Council Directive 2008/1/EC of 15 January 2008 concerning integrated pollution prevention and control

http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32008L0001

Council Directive of 15 January 2008 entered into force in February 2008 and concerned integrated pollution prevention and control. The purpose of this Directive is to achieve integrated prevention and control of pollution arising from the industrial activities. It lays down measures designed to prevent or, where that is not practicable, to reduce emissions in the air, water and land from the abovementioned activities, including measures concerning waste, in order to achieve a high level of protection of the environment taken as a whole, without prejudice to Directive 85/337/EEC and other relevant Community provisions.

54. **Directive 2000/76/EC of the European Parliament and of the Council of 4th December 2000 on the incineration of waste**
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32000L0076
Directive 2000/76/EC entered into force in December 2000. The objectives of the Directive is to prevent or to limit as far as practicable negative effects on the environment, in particular pollution by emissions into air, soil, surface water and groundwater, and the resulting risks to human health, from the incineration and co-incineration of waste. This aim shall be met by means of stringent operational conditions and technical requirements, through setting emission limit values for waste incineration and co-incineration plants within the Community and also through meeting the requirements of Directive 75/442/EEC on waste.

55. **Directive 94/63/EC of the European Parliament and of the Council on the control of VOC emissions resulting from the storage of petrol and its distribution from terminals to service stations**
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31994L0063
The VOC emissions from the system for storage and distribution of petrol represent some 500 000 tons per year or some 5 % of the total emissions of man-made VOCs in the Community. In order to reduce the emissions, the Directive set requirements concerning operations, installations, vehicles and vessels used for storage, loading and transport of petrol. The Directive was published in December 1994 and Member States were demanded to bring into force the laws, regulations and administrative provisions necessary to comply with this Directive by 31 December 1995.

56. **Council Directive 1999/13/EC on the limitation of emissions of volatile organic compounds due to the use of organic solvents in certain activities and installations**
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31999L0013
The purpose of this Directive is to prevent or reduce the direct and indirect effects of emissions of volatile organic compounds into the environment, mainly into air, and the potential risks to human health, by providing measures and procedures to be implemented for certain activities and installations. The Directive listed the activities and installations that give rise to VOC emissions, as well as the corresponding solvent consumption threshold and emission limit values. The Directive entered into force in March 1999 and requires Member States to bring into force the laws, regulations and administrative provisions necessary to comply with this Directive not later than April 2001.

57. **Directive 1999/32/EC on reduction of sulphur content of certain liquid fuels**
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31999L0032
The purpose of this Directive is to prevent or reduce the direct and indirect effects of emissions of volatile organic compounds into the environment, mainly into air, and the potential risks to human health, by providing measures and procedures to be implemented for certain activities and installations. The Directive listed the activities and installations that give rise to VOC emissions, as well as the corresponding solvent consumption threshold and emission limit values. The Directive entered into force in March 1999 and requires Member States to bring into force the laws, regulations and administrative provisions necessary to comply with this Directive not later than April 2001.

6.2.2 Regulations

58. EU Cosmetic Products Regulation No 1223/2009

http://europa.eu/legislation_summaries/consumers/product_labelling_and_packaging/co0013_en.htm

Regulation (EC) 1223/2009 replaced Directive 76/768/EEC, it lists restricted and banned substances, and provides positive lists of preservatives, colorants and UV filters. These provisions are largely unchanged from Directive 76/768/EEC. In addition, Regulation (EC) 1223/2009 clarifies the role of a 'responsible person' and a distributor in ensuring compliance with the relevant obligations, requires all cosmetic products to be notified to the European Commission rather than to national authorities and more clearly describes the product information file. It also introduces a concept of Serious Undesirable Effects, which have to be reported, and defines nanomaterials, which also have to be reported. Regulation (EC) 1223/2009 is directly applicable in all Member States, meaning that no domestic regulation is required in order for the obligations to have effect. However, domestic regulation is needed in order to enforce Regulation (EC) 1223/2009, in relation to offences and penalties. Regulation (EC) 1223/2009 also requires Member States to provide additional labelling rules for non-pre-packaged goods.

59. EU Regulation No 305/2011 on construction products

http://ec.europa.eu/enterprise/sectors/construction/legislation/index_en.htm

Construction Products Regulation (the CPR) was used to ensure reliable information on construction products in relation to their performances. This was achieved by providing a "common technical language", offering uniform assessment methods of the performance of construction products. These methods have been compiled in harmonised European standards (hEN) and European Assessment Documents (EAD). The provisions of the new Regulation seek to: clarify the affixing of CE marking to construction products for which the manufacturer has made a declaration of performance; introduce simplified procedures enabling cost reductions for businesses, especially the Small and medium-sized enterprises and impose stricter designation for organisations responsible for assessing the performance of construction products and verifying their consistency. This common technical language was applied by: the manufacturers when declaring the performance of their products, the authorities of Member States when specifying requirements for them and their users (architects, engineers, constructors…) when choosing the products most suitable for their intended use in construction works.

60. Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs, EC, 2006

http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02006R1881-20140701&from=EN

This regulation sets maximum levels for certain contaminants (such as metals, mycotoxins, nitrates, PAHs, PCDD/Fs, PCB) in order to reduce their presence in foodstuffs to the lowest possible levels, reasonably possible in good manufacturing or agricultural practices. The aim is to achieve a high level of protection of public health, especially for sensitive groups of the population: children, allergy sufferers, etc.

61. Regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

http://ec.europa.eu/enterprise/sectors/chemicals/reach/index_en.htm

REACH addresses the production and use of chemical substances and their potential impacts on both human health and the environment. It was proposed under dual reasoning: protection of human health and protection of the environment. REACH requires all companies manufacturing or importing chemical substances into the European Union in quantities of one tonne or more per year to register these substances with a new European Chemicals Agency (ECHA). REACH also addresses the continued use of chemical substances of very high concern (SVHC) because of their potential negative impacts on human health or the environment. One of the major elements of the REACH regulation is the requirement to communicate information on chemicals up and down the supply chain. This ensures that manufacturers, importers and also their customers are aware of information relating to health and safety of the products supplied. For many retailers the obligation to provide information about substances in their products within 45 days of receipt of a request from a consumer is particularly challenging. Having detailed information on the substances present in their products will allow retailers to work with the manufacturing base to substitute or remove potentially harmful substances from products. The list of harmful substances is continuously growing and requires organizations to constantly monitor any announcements and additions to the REACH scope.

62. **Classification, Labelling and Packaging Regulation (CLP)**
http://echa.europa.eu/regulations/clp
The CLP regulation aligns the European Union system of classification, labelling and packaging chemical substances and mixtures to the Globally Harmonised System (GHS). It facilitates global trade and the harmonised communication of hazard information of chemicals and promotes regulatory efficiency. It complements the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Regulation (EC No 1907/2006) and replaced the system contained in the Dangerous Substances Directive (67/548/EEC)[and the Dangerous Preparations Directive (1999/45/EC). The hazard of a substance or mixture is the potential for that substance or mixture to cause harm. It depends on the intrinsic properties of the substance or mixture. In this connection hazard evaluation is the process by which information about the intrinsic properties of a substance or mixture is assessed to determine their potential to cause harm. In cases where the nature and severity of an identified hazard meets the classification criteria, hazard classification is the assignment of a standardised description of this hazard of a substance or a mixture causing harm to human health or the environment. Hazard labelling allows for the communication of hazard classification to the user of a substance or mixture, to alert the user to the presence of a hazard and the need to avoid exposures and the resulting risks.

6.2.3 Other

63. **Environment and Health Action Plan (2004-2010) – European Commission**
http://ec.europa.eu/health/healthy_environments/policy/health_environment/actionplan_en.htm
As a follow-up to the strategy, the Commission presented the European Environment and Health Action Plan 2004-2010. The plan comprised 13 action points aimed at improving the co-ordination between the health, environment, and research sectors. The actions are divided into the three following areas:
- Monitoring: Developing indicators to measure the link between environment and health and understand the routes pollutants take from their source to the human body. This

would for example include 'biomonitoring' (taking regular samples of blood, urine or hair) to measure human exposure to environmental pollutants.

- Research: Focusing research on four priority diseases (asthma/allergy, neuro developmental disorders, cancers and endocrine disrupting effects) to 'fill the knowledge gap'.
- Communication: Developing citizen's awareness to help them make informed health choices. Other actions include training to health professionals to make sure they are alert about environment and health interactions.

64. 7th Environment Action Programme (EAP) – European Commission

http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32013D1386.

The programme, entitled 'Living well, within the limits of our planet', lists nine priority objectives and what the EU needs to do to achieve them by 2020. These are: 1. to protect, conserve and enhance the Union's natural capital, 2. to turn the Union into a resource-efficient, green, and competitive low-carbon economy, 3. to safeguard the Union's citizens from environment-related pressures and risks to health and wellbeing, 4. to maximise the benefits of the Union's environment legislation by improving implementation, 5. to increase knowledge about the environment and widen the evidence base for policy, 6. to secure investment for environment and dimate policy and account for the environmental costs of any societal activities, 7. to better integrate environmental concerns into other policy areas and ensure coherence when creating new policy, 8. to make the Union's cities more sustainable, 9. to help the Union address international environmental and climate challenges more effectively.

65. 6th Environment Action Programme 2002-2012

http://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX:32002D1600

The sixth Environment Action Programme (6th EAP), adopted in 2002, is the EU's ten-years (2002-2012) policy programme for the environment. It identified four key environmental priorities: climate change, nature and biodiversity, environment and health, and natural resources and waste. The 6th EAP (entitled "Environment 2010: Our future, our choice") "proposed five priority avenues of strategic action: improving the implementation of existing legislation; integrating environmental concerns into other policies; working closer with the market; empowering people as private citizens and helping them to change behaviour; and taking account of the environment in landuse planning and management decisions. Based on a 2007 review, the 6th EAP, the EU was still not on the way to sustainable development, it was stated that the domestic legislation of the MSs was influenced by the EU law at least to an extent of 80% and the major conclusion was that there is an urgent need for better integration, and environmental policy must be revised in 2012.

66. Commission Communication: Strategy on Environment and Health (SCALE)

http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:52003DC0338

The Commission presented an Action Plan on the increasing effects of environmental pollution on people's health which focused on the most vulnerable groups, particularly children. It was stressed that some chemicals that are harmless to adults may bring permanent damage to the developing bodies of children. In addition, despite the differences between adults and children, most environmental legislation is based on adult standards and norms. This is partially due to the considerable lack of data on the effects chemicals and other pollutants in the environment have on children. The strategy (known as 'SCALE' for Science, Children, Awareness, Legislation and Evaluation) has five key features:

- it is based on science and look at the complex interactions between different pollutants and the body;
- it focuses on children: the Commission will launch pilot actions on pollutants with specific relevance to children, such as dioxins, heavy metals and endocrine disruptors;
- it aims to raise awareness from stakeholders and the general public;
- EU legislation will complement national laws and be reviewed to reflect children's special situation and needs;
- actions taken will undergo constant evaluation procedures.

67. Technical Guidance Document on Risk Assessment – ECHA European Commission 2003
Part I http://echa.europa.eu/documents/10162/16960216/tgdpart1_2ed_en.pdf
Part II https://echa.europa.eu/documents/10162/16960216/tgdpart2_2ed_en.pdf
Part III https://echa.europa.eu/documents/10162/16960216/tgdpart3_2ed_en.pdf
This Technical Guidance Document is presented in four separate, easily manageable parts: part I including the general discussion and risk assessment for human health, part II including environmental risk assessment, part III including the use of quantitative structure activity relationships (QSARs), the use of categories and risk assessment report reporting format. It is noted that part IV includes the emission scenario documents and is excluded from this recommendation list.

68. Toxicity and Assessment of Chemical Mixtures – SCHER, SCENIHR, SCCS (2011)
http://ec.europa.eu/health/scientific_committees/environmental_risks/docs/scher_o_155.pdf
This report presents the decision tree for evaluating the risk of chemical based on a number of conclusions suggested by the European Commission. This includes:

4. Under certain conditions, chemicals will act jointly in a way that the overall level of toxicity is affected.
5. Chemicals with common modes of action will act jointly to produce combination effects that are larger than the effects of each mixture component applied singly. These effects can be described by dose/concentration addition.
6. For chemicals with different modes of action (independently acting), no robust evidence is available that exposure to a mixture of such substances is of health or environmental concern if the individual chemicals are present at or below their zero effect levels.
7. Interactions (including antagonism, potentiation, and synergies) usually occur at medium or high dose levels (relative to the lowest effect levels). At low exposure levels, they are either unlikely to occur or are toxicologically insignificant.
8. In view of the almost infinite number of possible combinations of chemicals to which humans and environmental species are exposed, some form of initial filter to allow a focus on mixtures of potential concern is necessary. Several criteria for such screening are offered.
9. With regard to the assessment of chemical mixtures, a major knowledge gap at the present time is the lack of exposure information and the rather limited number of chemicals for which there is sufficient information on their mode of action. Currently, there is neither an agreed inventory of mode of actions, nor a defined set of criteria how to characterise or predict a mode of action for data-poor chemicals.

10. If no mode of action information is available, the dose/concentration addition method should be preferred over the independent action approach. Prediction of possible interaction requires expert judgement and hence needs to be considered on a case-by-case basis.

69. State of the Art Report on Mixture Toxicity European Commission 2009
http://ec.europa.eu/environment/chemicals/effects/pdf/report_mixture_toxicity.pdf
This report details the findings of a project on mixture toxicology and ecotoxicology commissioned by the European Commission, DG Environment. It describes the scientific state of the art in the field, and gives an account of the regulatory state of the art for dealing with combined exposures in the European Union, in major competing economies, including the USA and Japan and in international bodies.

70. ePSIplatform: Europe's One-Stop Shop on Public Sector Information (PSI) Re-use
http://www.epsiplatform.eu/
The ePSIplatform is a European Commission (DG CONNECT) initiative with the objective of promoting a dynamic Public Sector Information (PSI) and Open Data re-use market across the European Union. The portal highlights: news on European PSI and Open Data developments; legal cases surrounding the re-use of PSI; good practices and examples of new products and services created through Open Data re-use; events, workshops and webinars around Europe.

71. European Commission (2015). Air Quality Standards.
http://ec.europa.eu/environment/air/quality/standards.htm
This web page shows a summary of target and limit values for different pollutants in ambient air.

72. European Commission (2009). Council Recommendation on smoke-free environments.
http://ec.europa.eu/health/tobacco/law/free_environments/index_en.htm
The Recommendation calls on Member States to act in three main fronts:

- adopt and implement laws to fully protect their citizens from exposure to tobacco smoke in enclosed public places, workplaces and public transport as cited in Article 8 of the Framework Convention on Tobacco control, within three years of the adoption of the Recommendation
- Enhance smoke-free laws with supporting measures such as protecting children, encouraging efforts to give up tobacco use and pictorial warnings on tobacco packages.
- Strengthen cooperation at EU level by setting up a network of national focal points for tobacco control.

6.3 Guidelines by United States Environmental Protection Agency (EPA)

73. Guidelines for Exposure Assessment – EPA 1992
http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=15263#Download

The Guidelines for Exposure Assessment describe the general concepts of exposure assessment including definitions and associated units, and by providing guidance on the planning and conducting of an exposure assessment. Guidance is also provided on presenting the results of the exposure assessment and characterizing uncertainty. Although these Guidelines focus on exposures of humans to chemical substances, much of the guidance also pertains to assessing wildlife exposure to chemicals, or human exposures to biological, noise, or radiological agents. The Guidelines include a glossary which helps standardize terminology used by the Agency in exposure assessment. They emphasize that exposure assessments done as part of a risk assessment need to consider the hazard identification and dose-response parts of the risk assessment in the planning stages of the exposure assessment so that these three parts can be smoothly integrated into the risk characterization. The Guidelines discuss and reference a number of approaches and tools for exposure assessment, along with discussion of their appropriate use. The Guidelines also stress that exposure estimates along with supporting information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

74. **Next Generation Risk Assessment: Incorporation of Recent Advances in Molecular, Computational, and Systems Biology, EPA 2014**
http://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=286690#Download
This final report, "Next Generation Risk Assessment: Recent Advances in Molecular, Computational, and Systems Biology", describes new approaches that are faster, less resource intensive, and more robust that can help address the challenges of assessing potential health hazards for large number of chemicals introduced into the environment and to evaluate their safety from the perspective of human health. This report describes how new molecular, computational and systems biology data and approaches (together called "NexGen") could better inform risk assessment. The report summarizes the state of the science and provides prototypes, which are case studies that use available NexGen information.

75. **U.S. EPA. Handbook for Use of Data from the National Health and Nutrition Examination Surveys (NHANES): A Goldmine of Data for Environmental Health Analyses. U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-02/044, 2003.**
ofmpub.epa.gov/eims/eimscomm.getfile?p_download_id=36933
This Handbook provides descriptive background information and general guidance on how to access and use data from the National Health and Nutrition Examination Surveys (NHANES). This is an enormous human database that can be used to develop information suitable for use in risk assessments, and to support regulatory and policy needs of EPA. For more than 30 years, EPA has been one of many collaborating agencies that help plan and support funding of data collection through NHANES. Because only a limited number of Agency managers and staff are aware of the content and availability of this rich database, this Handbook was developed to familiarize staffs with NHANES and foster increased use of the data to support EPA needs. Despite the limitations and complex design of this survey, it is clear that NHANES is a unique, rich database that offers a tremendous amount of human health, nutrition, and exposure information, and will continue to do so into the future. It is hoped that by informing staff about NHANES, this

Handbook will encourage efforts to "mine" the data to support Agency needs across the program offices. It is also hoped that innovative approaches (e.g., using geographic information systems; linking NHANES to available databases such as the National Death Index), will be developed to analyze the data in new ways that produce information that is useful to the mission of the Agency. Now that the National Center for Health Statistics (NCHS) has established their Research Data Center, it should be possible to conduct studies that were impossible in the past because of lack of access to sensitive data. Finally, more thought should be given to designing and conducting studies that make use of subjects' biological samples (blood, urine, saliva) stored by NCHS. These samples offer a rare opportunity to study potential biomarkers of exposure and/or effects on a national sample of the U.S. population and link the data to health, nutrition, exposure and socioeconomic data collected in the baseline surveys.

76. Child-specific exposure factors handbook, EPA 2002
http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=55145#Download
CEA has published the Exposure Factors Handbook in 1997 (EPA/600/P-95/002Fa-c), that include exposure factors and related data on both adults and children, the EPA Program Offices identified the need to consolidate all children exposure data into one document. The goal of the Child-Specific Exposure Factors Handbook is to fulfill this need. The document provides a summary of the available and up-to-date statistical data on various factors assessing children exposures. These factors include drinking water consumption, soil ingestion, inhalation rates, dermal factors including skin area and soil adherence factors, consumption of fruits and vegetables, fish, meats, dairy products, homegrown foods, breast milk, activity patterns, body weight, consumer products and life expectancy.

77. Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures, EPA 2000
http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=20533
This document is a supplement to the EPA Guidelines for the Health Risk Assessment of Chemical Mixtures of 1986. The 1986 Guidelines represent the Agency's science policy and are a procedural guide for evaluating data on the health risks from exposures to chemical mixtures. The emphasis is on dose-response and risk characterization. The principles and concepts put forth in the Guidelines remain in effect. However, where the Guidelines describe broad principles and include few specific procedures, the present guidance is a supplement that is intended to provide more details on these principles and their applications.

78. Risk Assessment Forum White Paper: Probabilistic Risk Assessment Methods and Case Studies, EPA 2014
http://www2.epa.gov/osa/risk-assessment-forum-white-paper-probabilistic-risk-assessment-methods-and-case-studies
The EPA developed this report to provide a general overview of the value of probabilistic analyses and similar or related methods. Probabilistic risk assessment (PRA), in its simplest form, is a group of techniques that incorporate uncertainty and variability into risk assessments. Variability refers to the inherent natural variation, diversity and heterogeneity across time, space or individuals within a population or life-stage, while uncertainty refers to imperfect knowledge or a lack of precise knowledge of the physical

world, either for specific values of interest or in the description of the system. Variability and uncertainty have the potential to result in overestimates or underestimates of the predicted risk. PRA provides estimates of the range and likelihood of a hazard, exposure or risk, rather than a single point estimate. Stakeholders inside and outside of the Agency have recommended a more complete characterization of risks, including uncertainties and variability, in protecting more sensitive or vulnerable populations and life-stages. PRA can be used to support risk management by assessment of impacts of uncertainties on each of the potential decision alternatives.

79. Microbial Risk Assessment Guideline: Pathogenic Microorganisms with Focus on Food and Water, EPA 2012

http://www2.epa.gov/osa/microbial-risk-assessment-guideline-pathogenic-microorganisms-focus-food-and-water

This document addresses the entire risk assessment process from an introduction to terminology and roles of the participants to planning the risk assessment, identifying and characterizing the hazard, assessing how the size of an outbreak may be affected by the dose (exposure assessment) or how the severity of the disease may be affected by the pathogen and its response within the human host (dose-response assessment). The document describes the importance of addressing the routes of exposure, transport media, uncertainties and assumptions for exposure and the other components of the risk assessment paradigm when characterizing risk, and also provides information about microbial risk management and risk communication.

80. Benchmark Dose Technical Guidance, EPA 2012

http://www2.epa.gov/osa/benchmark-dose-technical-guidance

This document provides guidance on the application of the benchmark dose approach for determining the point of departure for health effects data. This guidance discusses the computation of BenchMark Dose (BMD)s, benchmark concentrations (BMCs) and their confidence limits; data requirements; dose-response analysis; and reporting recommendations that are specific to the use of BMDs or BMCs. The following convention for terminology has been adopted in this document: BMD is used generically to refer to the benchmark dose approach; in the specific cases of characterizing model results, BMD and BMC refer to central estimates. BMDL or BMCL refers to the corresponding lower limit of a one-sided 95% confidence interval on the BMD or BMC, respectively. This is consistent with the terminology introduced by Crump (1995) and with that used in the U.S. EPA's BMD software (BMDS), which is freely available at http://epa.gov/NCEA/bmds/. Despite the similarity in names, this document is not specific to EPA's BMDS software.

81. Documents for Recommended Toxicity Equivalency Factors for Human Health Risk Assessments of Dioxin and Dioxin-Like Compounds, EPA 2012

http://www2.epa.gov/osa/documents-recommended-toxicity-equivalency-factors-human-health-risk-assessments-dioxin-and

These documents describe EPA's updated approach for evaluating the human health risks from exposures to environmental media containing dioxin-like compounds (DLCs). Dioxin and DLCs are structurally and toxicologically related halogenated aromatic hydrocarbons. Traditionally, the Toxic Equivalency Factor (TEF) Methodology, a component mixture method, has been used to evaluate human health risks posed by these mixtures. There are two documents available: 'Recommended Toxicity Equivalency Factors (TEFs) for Human Health Risk Assessments of

Dioxin and Dioxin-Like Compounds: External Review Draft' and 'Recommended Toxicity Equivalence Factors (TEFs) for Human Health Risk Assessments of 2,3,7,8-Tetrachlorodibenzo-p-dioxin and Dioxin-Like Compounds'. The former describes the U.S. Environmental Protection Agency's (U.S. EPA's) updated approach for evaluating the human health risks from exposures to environmental media containing dioxin-like compounds (DLCs). Dioxin and DLCs are structurally and toxicologically related halogenated aromatic hydrocarbons. The latter describes the U.S. Environmental Protection Agency's (EPA's) updated approach for evaluating the human health risks from exposures to environmental media containing dioxin-like compounds (DLCs). 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and DLCs are structurally and toxicologically related halogenated aromatic hydrocarbons.

82. Guidelines for Neurotoxicity Risk Assessment, EPA 1998

http://www2.epa.gov/osa/guidelines-neurotoxicity-risk-assessment

The Guidelines for Neurotoxicity Risk Assessment continue the guidelines development process initiated in 1984. These Guidelines set forth principles and procedures to guide EPA scientists in evaluating environmental contaminants that may pose neurotoxic risks, and inform Agency decision makers and the public about these procedures. These Guidelines are the Agency's first statement on setting principles and procedures to guide EPA scientists in conducting neurotoxicity risk assessments. These Guidelines have been developed by a cross-Agency Technical Panel organized by the Risk Assessment Forum.

A link between human exposure to some chemical substances and neurotoxicity has been firmly established. The Guidelines emphasize that risk assessment will be conducted on a case-by-case basis. They stress that information will be fully presented in Agency risk assessment documents and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions and limitations, as well as the scientific basis and rationale for each assessment.

The Guidelines bridge gaps in risk assessment methodology and data by identifying these gaps and the importance of the missing information to the risk assessment process, encouraging research and analysis that will lead to new risk assessment methods and data. The Guidelines specifically note the special vulnerability of the nervous system of infants and children to environmentally relevant chemicals and provide guidance for the interpretation of data from developmental and reproductive studies involving assessment of nervous system structure and function.

The Guidelines help develop a sound scientific basis for neurotoxicity risk assessment and promote consistency in the Agency's assessment of nervous system effects. As in the case of earlier risk assessment guidelines, the principles articulated in these Guidelines will be incorporated into program-specific guidance and procedures. Risk assessment guidelines are not regulations and do not impose legally binding requirements on EPA, states, or the regulated community.

83. Guidelines for Reproductive Toxicity Risk Assessment, EPA 1996

http://www2.epa.gov/osa/guidelines-reproductive-toxicity-risk-assessment

The guideline describes the procedures that EPA follows in using existing data to evaluate the potential toxicity of environmental agents to the human male and female reproductive systems and to developing offspring. These guidelines focuses on reproductive

system function as it relates to sexual behavior, fertility, pregnancy outcomes, and lactating ability, and the processes that can affect those functions directly. Included are effects on gametogenesis and gamete maturation and function, the reproductive organs, and the components of the endocrine system that directly support those functions. These Guidelines concentrate on the integrity of the male and female reproductive systems as required to ensure successful procreation. They also emphasize the importance of maintaining the integrity of the reproductive system for overall physical and psychological health. The Guidelines for Developmental Toxicity Risk Assessment focus specifically on effects of agents on development and should be used as a companion to these Guidelines.

6.4 Standards

6.4.1 International Organization for Standardization (ISO)

84. **ISO 7730: 2005. Ergonomics of the thermal environment - Analytical determination and interpretation of thermal comfort using calculation of the PMV and PPD indices and local thermal comfort criteria.**
ISO 7730:2005 presents methods for predicting the general thermal sensation and degree of discomfort (thermal dissatisfaction) of people exposed to moderate thermal environments. It enables the analytical determination and interpretation of thermal comfort using calculation of PMV (predicted mean vote) and PPD (predicted percentage of dissatisfied) and local thermal comfort, giving the environmental conditions considered acceptable for general thermal comfort as well as those representing local discomfort.

85. **ISO 9972 Thermal insulation - Determination of building air tightness – Fan pressurization method.**
This International Standard is intended for the measurement of the air permeability of buildings or parts of buildings in the field. It specifies the use of mechanical pressurization or depressurization of a building or part of a building. It describes the measurement of the resulting air flow rates over a range of indoor-outdoor static pressure differences. This International Standard is intended for the measurement of the air leakage of building envelopes of single-zone buildings. For the purpose of this International Standard, many multi-zone buildings can be treated as single-zone buildings by opening interior doors or by inducing equal pressures in adjacent zones. It does not address evaluation of air permeability through individual components.

86. **ISO 11731-1:1998 Water Quality - Detection and enumeration of Legionella.**
This International Standard describes a culture method for the isolation of Legionella organisms and estimation of their numbers in environmental samples. This method is applicable to all kinds of environmental samples including potable, industrial and natural waters and associated materials such as sediments, deposits and slime.

87. **ISO 11731-2:2004 Water Quality - Detection and enumeration of Legionella - Part 2 Direct membrane filtration method for waters with low bacteria counts.**
ISO 11731-2:2004 describes a monitoring method for the isolation and enumeration of Legionella organisms in water intended for human use (e.g. hot and cold water, water used for washing), for human consumption and for treated bathing waters (e.g. swimming pools). It is especially suitable for waters with prospected low numbers of Legionella. As the growth

of Legionella may be inhibited by overgrowth of other bacterial colonies on the membrane the method is only suitable for waters containing low bacterial.

88. BS EN ISO 14464:1 Clean Rooms.

This part of ISO 14644 covers the classification of air cleanliness in cleanrooms and associated controlled environments exclusively in terms of concentration of airborne particles. Only particle populations having cumulative distributions based on threshold (lower limit) sizes ranging from 0,1 µm to 5 µm are considered for classification purposes.

This part of ISO 14644 does not provide for classification of particle populations that are outside of the specified particle size range, 0,1 µm to 5 µm. Concentrations of ultrafine particles (particles smaller than 0,1 µm) and macroparticles (particles larger than 5 µm) may be used to quantify these populations in terms of U descriptors and M descriptors, respectively. This part of ISO 14644 cannot be used to characterize the physical, chemical, radiological, or viable nature of airborne particles.

89. BS EN ISO 14464:2 Clean Rooms.

This part of ISO 14644 specifies requirements for periodic testing of a cleanroom or clean zone to prove its continued compliance with ISO 14644-1 for the designated classification of airborne particulate cleanliness.

These requirements invoke the test described in ISO 14644-1 for classification of a cleanroom or clean zone. Additional tests are also specified, to be carried out in accordance with the requirements of this part of ISO 14644. Optional tests, to be applied at the user's discretion, are also identified.

This part of ISO 14644 also specifies requirements for monitoring of a cleanroom or clean zone (hereafter referred to as an installation) to provide evidence of its continued compliance with ISO 14644-1 for the designated classification of airborne particulate cleanliness.

90. UNE EN ISO 14644-1:1999. Clase ISO 9. Clasificación de la limpieza del aire (PM10 content).

This is the Spanish version of the international standard ISO 14644-1:1999. This part of ISO 14644 covers the classification of air cleanliness in cleanrooms and associated controlled environments exclusively in terms of concentration of airborne particles. Only particle populations having cumulative distributions based on threshold (lower limit) sizes ranging from 0,1 µm to 5 µm are considered for classification purposes. This part of ISO 14644 does not provide for classification of particle populations that are outside of the specified particle size range, 0,1 µm to 5 µm. Concentrations of ultrafine particles (particles smaller than 0,1 µm) and macroparticles (particles larger than 5 µm) may be used to quantify these populations in terms of U descriptors and M descriptors, respectively. This part of ISO 14644 cannot be used to characterize the physical, chemical, radiological, or viable nature of airborne particles.

91. ISO 16000-1:2004 Indoor air - Part 1: General aspects of sampling strategy.

ISO 16000-1:2004 is intended to aid the planning of indoor pollution monitoring. Before a sampling strategy is devised for indoor air monitoring, it is necessary to clarify for what purposes, when, where, how often and over what periods of time monitoring is to be performed. The answers to these questions depend, in particular, on a number of special characteristics of the indoor environments, on the objective of the measurement and, finally,

on the environment to be measured. ISO 16000-1:2004deals with the significance of these factors and offers suggestions on how to develop a suitable sampling strategy. ISO 16000-1:2004 is applicable to indoor environments such as dwellings having living rooms, bedrooms, do-it-yourself rooms, recreation rooms and cellars, kitchens and bathrooms; workrooms or work places in buildings which are not subject to health and safety inspections in regard to air pollutants (for example, offices, sales premises); public buildings (for example hospitals, schools, kindergartens, sports halls, libraries, restaurants and bars, theatres, cinemas and other function rooms), and also cabins of vehicles.

92. **ISO 16000-2:2004 Indoor air - Part 2: Sampling strategy for formaldehyde.**
ISO 16000-2:2004 is intended as an aid to planning formaldehyde indoor pollution measurements. In the case of indoor air measurements, the careful planning of sampling and the entire measurement strategy are of particular significance, since the result of the measurement can have far-reaching consequences, for example, with regard to the need for remedial action or the success of such an action.

93. **ISO 16000-3:2011 Indoor air - Part 3: Determination of formaldehyde and other carbonyl compounds - Active sampling method.**
This part of ISO 16000:
- Specifies a determination of formaldehyde (HCHO) and other carbonyl compounds (aldehydes and ketones) in air. The method is specific to formaldehyde but, with modification, at least 12 other aromatic as well as saturated and unsaturated aliphatic carbonyl compounds (see last paragraph) can be detected and quantified. It is suitable for determination of formaldehyde and other carbonyl compounds in the approximate concentration range 1 µg/m3 to 1 mg/m3. The sampling method gives a time-weighted average (TWA) sample. It can be used for long-term (1 h to 24 h) or short-term (5 min to 60 min) sampling of air for formaldehyde.
- Specifies a sampling and analysis procedure for formaldehyde and other carbonyl compounds that involves collection from air on to adsorbent cartridges coated with 2,4-dinitrophenylhydrazine (DNPH) and subsequent analysis of the hydrazones formed by high performance liquid chromatography (HPLC) with detection by ultraviolet absorption.
- Applies to the determination of: formaldehyde; acetaldehyde; acetone; benzaldehyde; butyraldehyde; valeraldehyde; 2,5-dimethylbenzaldehyde; capronaldehyde; isovaleraldehyde; propionaldehyde; o-tolualdehyde; m-tolualdehyde; p-tolualdehyde.

94. **ISO 16000-4:2011 Indoor air - Part 4: Determination of formaldehyde -- Diffusive sampling method.**
ISO 16000-4:2011 specifies a determination of formaldehyde in indoor air using a diffusive sampler with solvent desorption and high performance liquid chromatography (HPLC). The test method is applicable to the measurement of formaldehyde in indoor air over the range from 0,001 mg/m3 to 1,0 mg/m3 for a sampling period of between 24 h and 72 h. For sampling periods of 24 h, the applicable concentration range is 0,003 mg/m3 to 1 mg/m3, and for 72 h it is 0,001 mg/m3 to 0,33 mg/m3. The method is suitable for measurements in atmospheres with conventional indoor air relative humidity and for monitoring at air velocities as low as 0,02 m/s. The chromatographic step in the method is designed to eliminate potential interferences,

including those due to the presence of other carbonyl compounds. The sampling method gives a time-weighted average result.

95. **ISO 16000-5:2007 Indoor air - Part 5: Sampling strategy for volatile organic compounds (VOCs).**
ISO 16000-5:2007 is intended as an aid to planning volatile organic compound (VOC) indoor pollution measurements. In the case of indoor air measurements, the careful planning of sampling and the entire measurement strategy are of particular significance since the result of the measurement may have far-reaching consequences, for example, with regard to the need for remedial action or the success of such an action. An inappropriate measurement strategy may contribute to the complete uncertainty of the measurement result in a larger extent than the measurement procedure itself.

96. **ISO 16000-6:2011 Indoor air - Part 6: Determination of volatile organic compounds in indoor and test chamber air by active sampling on Tenax TA sorbent, thermal desorption and gas chromatography using MS/FID.**
ISO 16000-6:2011 specifies a method for determination of volatile organic compounds (VOCs) in indoor air and in air sampled for the determination of the emission of VOCs from building products or materials and other products used in indoor environments using test chambers and test cells. The method uses Tenax TAÒ sorbent with subsequent thermal desorption and gas chromatographic analysis employing a capillary column or columns and a flame ionization detector and/or a mass spectrometric detector. The method is applicable to the measurement of non-polar and slightly polar VOCs at concentrations ranging from sub-micrograms per cubic metre to several milligrams per cubic metre. Using the principles specified in this method, an annex describes how some very volatile compounds and semi-volatile organic compounds can also be analysed.

97. **ISO 16000-9:2006 Indoor air - Part 9: Determination of the emission of volatile organic compounds from building products and furnishing -- Emission test chamber method**.
ISO 16000-9:2006 specifies a general laboratory test method for determination of the area specific emission rate of volatile organic compounds (VOCs) from newly produced building products or furnishing under defined climate conditions. The method can also, in principle, be applied to aged products. The emission data obtained can be used to calculate concentrations in a model room. This standard applies to various emission test chambers used for determination of the emission of volatile organic compounds from building products or products. A general description of an emission test chamber is given. ISO 16000-9:2006 is also applicable to wood-based panels and other building products, in order to determine the emission rate of formaldehyde.

98. **ISO 16000-10:2006 Indoor air - Part 10: Determination of the emission of volatile organic compounds from building products and furnishing - Emission test cell method.**
ISO 16000-10:2006 specifies a general laboratory test method for determination of the area specific emission rate of volatile organic compounds (VOCs) from newly produced building products or furnishing under defined climate conditions. The method can also, in principle, be applied to aged products. The emission data obtained can be used to calculate concentrations in a model room. According to the definition of an emission test cell, it is also possible to perform non-destructive emission measurements on building products on-site in buildings. However, the procedure for such measurements is not described in ISO 16000-10:2006. An

example of an emission test cell is described. ISO 16000-10:2006 is also applicable to wood-based panels and other building products, in order to determine the emission rate of formaldehyde.

99. **ISO 16000-11:2006 Indoor air - Part 11: Determination of the emission of volatile organic compounds from building products and furnishing - Sampling, storage of samples and preparation of test specimens.**
Studies of the emission of volatile organic compounds from unused building products or furnishing in test chambers or cells require proper handling of the product prior to testing, and during the testing period. ISO 16000-11:2006 defines three types of building products or furnishing: solid, liquid and combined. For each type, specifications are given for the sampling procedures, transport conditions, storage, and substrate used that can affect emissions of volatile organic compounds. For individual products, the preparation of a test specimen for each type is prescribed.

100. **BS ISO 16000-19:2012 Indoor air – Part 19: Sampling strategy for moulds.**
ISO 16000-19:2012 describes the measurement strategy for the detection of fungi in indoor environments. ISO 16000-19:2012 describes suitable sampling and analysis methods together with a description of the applicability and the interpretation of the measurement results to maximize the comparability of the measured data obtained for a given measurement objective. It does not include details on recording building characteristics or field inspections by qualified professionals which have to take place prior to any microbiological measurement. ISO 16000-19:2012 is not applicable to a detailed description of the building physics- and building-engineering-related procedures applicable to field inspections. The methods and procedures presented do not allow quantitative exposure assessment with regard to the room occupants. The application of ISO 16000-19:2012 presupposes the knowledge of ISO 16000-1.

101. **BS EN ISO 16000-26:2015 Indoor air – Part 26: Sampling strategy for carbon dioxide (CO2).**
ISO 16000-26:2012 specifies the planning of carbon dioxide indoor pollution measurements. In the case of indoor air measurements, the careful planning of sampling and the entire measurement strategy are of particular significance since the result of the measurement can have far-reaching consequences, for example, with regard to ascertaining the need for remedial action or the success of such an action. An inappropriate measurement strategy can lead to misrepresentation of the true conditions or, worse, to erroneous results. ISO 16000-26:2012 is not applicable to the measurement strategy for carbon monoxide (CO).

102. **ISO 16017-1:2000 Indoor, ambient and workplace air - Sampling and analysis of volatile organic compounds by sorbent tube/thermal desorption/capillary gas chromatography - Part 1: Pumped sampling.**
This part of ISO 16017 gives general guidance for the sampling and analysis of volatile organic compounds (VOCs) in air. It is applicable to ambient, indoor and workplace atmospheres and the assessment of emissions from materials in small- or full-scale test chambers.

It is appropriate for a wide range of VOCs, including hydrocarbons, halogenated hydrocarbons, esters, glycol ethers, ketones and alcohols. A number of sorbents 1) are recommended for the sampling of these VOCs, each sorbent having a different range of applicability. Very polar compounds will generally require derivatization, very low boiling compounds will only be partially retained by the sorbents, depending on ambient temperature, and can only be

estimated qualitatively. Semi-volatile compounds will be fully retained by the sorbents, but may only be partially recovered. Compounds for which this part of ISO 16017 has been tested are given in tables. This part of ISO 16017 may be applicable to compounds not listed, but in these cases it is advisable to use a back-up tube containing the same or a stronger sorbent.

This part of ISO 16017 is applicable to the measurement of airborne vapours of VOCs in a concentration range of approximately 0,5 mg/ m3 to 100 mg/m3 individual compound.

The upper limit of the useful range is set by the sorptive capacity of the sorbent used and by the linear dynamic range of the gas chromatograph column and detector or by the sample-splitting capability of the analytical instrumentation used. The sorptive capacity is measured as a breakthrough volume of air, which determines the maximum air volume that shall not be exceeded when sampling.

The lower limit of the useful range depends on the noise level of the detector and on blank levels of analyte and/or interfering artefacts on the sorbent tubes. Artefacts are typically sub-nanogram for well-conditioned Tenax GR and carbonaceous sorbents such as Carbopack/Carbotrap type materials, carbonized molecular sieves and molecular sieves such as Spherocarb, or pure charcoal; at low nanogram levels for Tenax TA and at 5 ng to 50 ng levels for other porous polymers such as Chromosorbs and Porapaks. Sensitivity is typically limited to 0,5 µg/m3 for 10-litre air samples with this latter group of sorbents because of their inherent high background.

The procedure specified in this part of ISO 16017 is applicable to low flowrate personal sampling pumps and gives a time-weighted average result. It is not applicable to the measurement of instantaneous or short-term fluctuations in concentration.

103. ISO 16017-2:2003 Indoor, ambient and workplace air - Sampling and analysis of volatile organic compounds by sorbent tube/thermal desorption/capillary gas chromatography - Part 2: Diffusive sampling.

ISO 16017-2:2003 gives general guidance for the sampling and analysis of volatile organic compounds (VOCs) in air. It is applicable to indoor, ambient and workplace air. This standard is applicable to a wide range of VOCs, including hydrocarbons, halogenated hydrocarbons, ester, glycol ethers, ketones and alcohols. A number of sorbents are recommended for the sampling of these VOCs, each sorbent having a different range of applicability. Very polar compounds generally require derivatisation; very low boiling compounds are only partially retained by the sorbents and can only be estimated qualitatively. Semi-volatile compounds are fully retained by the sorbents, but may only be partially recovered.

ISO 16017-2:2003 is applicable to the measurement of airborne vapours of VOCs in a concentration range of approximately 0,002 mg/m3 to 100 mg/m3 individual organic for an exposure time of 8 h, or 0,3 g/m3 to 300 g/m3 individual organic for an exposure time of four weeks.

The upper limit of the useful range is set by the sorptive capacity of the sorbent used and by the linear dynamic range of the gas chromatograph column and detector or by the sample splitting capability of the analytical instrumentation used. The lower limit of the useful range depends on the noise level of the detector and on blank levels of analyte and/or

interferingartefacts on the sorbent tubes. Artefacts are typically sub-nanogram for well-conditioned Tenax GR and carbonaceous sorbents, carbonized molecular sieves and pure charcoals; at low nanogram levels for Tenax TA and at 5 ng to 50 ng levels for other porous polymers.

104. **BS ISO 16814 Building environment design. Indoor air quality. Methods of expressing the quality of indoor air for human occupancy.**
ISO 16814:2008 is intended to specify methods to express the quality of indoor air suitable for human occupancy, to allow several acceptable target levels of indoor air quality, depending on local requirements, constraints and expectations. ISO 16814:2008 applies to the design of new buildings and their systems and the retrofit of existing buildings and systems, indoor environments where the major concern is that of human occupants, buildings having any combination of mechanical and natural ventilation, commercial and institutional buildings. ISO 16814:2008 does not apply to residential buildings, industrial buildings and hospitals although those parts of such buildings that are similar to commercial buildings are covered. The requirements of ISO 16814:2008 might not achieve acceptable IAQ for all people in all buildings, due to one or more of the following sources of uncertainty. The outdoor air brought into the building can be unacceptable or might not be adequately cleaned. Indoor air has a wide diversity of sources and contaminants. There are many factors that affect occupant perception and acceptance of IAQ, such as air temperature, humidity, noise, odours, lighting and psychological stress. There is a range of susceptibility and preference in the population.

6.4.2 European standards (EN)

105. **SFS-EN 779:en Particulate air filters for general ventilation – Determination of the filtration performance.**
This European Standard refers to particulate air filters for general ventilation. These filters are classified according to their performance as measured in this test procedure. This European Standard contains requirements to be met by particulate air filters. It describes testing methods and the test rig for measuring filter performance. In order to obtain results for comparison and classification purposes, particulate air filters shall be tested against two synthetic aerosols, a fine aerosolfor measurement of filtration efficiency as a function of particle size within a particle size range 0,2 ?m to 3,0 ?m, and a coarse one for obtaining information about test dust capacity and, in the case of coarse filters, filtration efficiency with respect to coarse loading dust (arrestance). This European Standard applies to air filters having an initial efficiency of less than 98 % with respect to 0,4 µm particles. Filters shall be tested at an air flow rate between 0,24 m3/s (850 m3/h) and 1,5 m3/s (5400 m3/h). The performance results obtained in accordance with this standard cannot by themselves be quantitatively applied to predict performance in service with regard to efficiency and lifetime.

106. **SFS-EN 1751:en Ventilation for buildings. Air terminal devices. Aerodynamic testing of dampers and valves.**
This European Standard specifies methods for the testing and rating of dampers and valves used in air distribution systems with pressure differences up to 2 000 Pa. The tests incorporated in this European Standard are: a) leakage past a closed damper or valve; b) casing leakage; c) flow rate/pressure requirement characteristics; d) torque; e) thermal transmittance.

The acoustic testing of dampers and valves is not included in this European Standard. The tests specified above apply to the following: f) measurement of leakage past a closed damper or valve; g) measurement of casing leakage; h) determination of flow rate and pressure requirements; i) measurement of torque characteristics; j) measurement of thermal transfer characteristics to determine insulation properties. Certain aspects of the dynamic performance of dampers or valves are dependent upon the air distribution system to which they are connected and are, therefore, difficult to measure in isolation. Such considerations have led to the omission of these aspects of the dynamic performance measurements from this European Standard. Also, in common with other air distribution components, the results from tests carried out in accordance with this European Standard may not be directly applicable if the damper or valve is situated in an area of non-uniform flow.

107. **CEN CR 1752:1998 Ventilation for buildings: Design criteria for the indoor environment.**
This European Prestandard specifies the requirements for, and methods of expressing the quality of the indoor environment for the design, commissioning, operation and control of ventilation and air-conditioning systems. For the purposes of this prestandard, the indoor environment comprises the thermal environment, the air quality and the acoustic environment. This prestandard covers indoor environments where the major concern is the human occupation but excludes dwellings.

108. **SFS-EN 12097:en Ventilation for buildings. Ductwork. Requirements for ductwork components to facilitate maintenance of ductwork systems.**
This European standard specifies requirements for dimension, shape and location for access panels for cleaning and service in ductwork systems, which conform to EN 1505, EN 1506 and EN 13180. National regulations shall always be followed, even when they deviate from requirements given in this standard.

109. **SFS-EN 12341:2014 Ambient air. Standard gravimetric measurement method for the determination of the PM_{10} or $PM_{2,5}$ mass concentration of suspended particulate matter.**
The aim of this European Standard is to present a harmonized methodology for monitoring the 10 µm and 2,5 µm mass concentrations of suspended particulate matter (PM_{10}, respectively $PM_{2,5}$) in ambient air, following Directive 2008/50/EC on ambient air quality and cleaner air for Europe, which sets the parameters specific to the assessment of ambient concentration levels of particulate matter. EN 12341 contains - a description of a manual gravimetric standard measurement method for PM_{10} or $PM_{2,.5}$ using sequential samplers or single-filter samplers; - a summary of performance requirements of the method; - requirements for suitability testing of facilities and equipment on initial application of the method; - requirements for ongoing quality assurance / quality control when applying the method in the field; - the assessment of measurement uncertainty of the results; - criteria and test methods for the evaluation of the suitability of filters for application using this method.

110. **SFS-EN 12464-1 Light and lighting. Lighting of work places. Part 1: Indoor work places.**
This European Standard specifies lighting requirements for indoor work places, which meet the needs for visual comfort and performance. All usual visual tasks are considered, including Display Screen Equipment (DSE). This European Standard does not specify lighting requirements with respect to the safety and health of workers at work and has not been prepared in the field of application of Artide 137 of the EC treaty, although the lighting requirements, as specified in this standard, usually fulfil safety needs. Lighting requirements

with respect to the safety and health of workers at work may be contained in Directives based on Article 137 of the EC treaty, in national legislation of member states implementing these directives or in other national legislation of member states. This standard neither provides specific solutions, nor restricts the designers freedom from exploring new techniques nor restricts the use of innovative equipment. This standard is not applicable for the lighting of outdoor work places and underground mining.

111. **SFS-EN 13030:en Ventilation for buildings. Terminals. Performance testing of louvres subjected to simulated rain.**
This European Standard specifies a method for measuring the water rejection performance of louvres subject to simulated rain and wind pressures, both with and without air flow through the louvre under test. For the purpose of tests in this standard, a 1000 mm section of weather louvre or the nearest possible blade increment is considered. Weather louvres are designed to restrict the passage of water during rainfall while allowing the passage of air into or from an air distribution system or part of a building. They are used in a wide range of applications, where there may be differences in wind speed and direction, levels of local turbulence, rate and droplet size, distribution of rainfall and surface water flow from the surrounding structure. It is impractical to consider a standard test procedure simulating the whole range of likely conditions, but this standard provides for heavy rainfall directed on to the louvre surface, with simulated wind pressures. This provides a common basis on which to compare the water rejection performance of weather louvres of different designs. This standard is not intended for the evaluation of weather performance of pressure relief dampers. The purpose of tests incorporated in this European Standard is as follows: a) Weather tests: to establish the weather louvre effectiveness when subjected to wind pressure at various air flow rates; and b) Discharge and Entry loss coefficient/Pressure requirements: to establish the air pressure loss through the weather louvre at various air flow rates and by calculation the Discharge and Entry Loss Coefficient.

112. **SFS-EN 13032-2:en. Light and lighting. Measurement and presentation of photometric data of lamps and luminaires. Part 2: Presentation of data for indoor and outdoor work places.**
This document specifies the required data for lamps and luminaires for the verification of conformity to the requirements of EN 12464-1 and prEN 12464-2. It also specifies data that are commonly used for lighting of indoor and outdoor work places. When these data are provided, they should conform to this document.

113. **EN 13098:2000. Workplace atmospheres - Guidelines for measurement of airborne microorganisms and endotoxin.**
This standard provides guidelines for the assessment of workplace exposure to airborne micro-organisms including the determination of total number and culturable number of micro-organisms in the workplace atmosphere. Also provides methods for measurement of airborne endotoxin in the work environment. The standard soes not apply to viruses, specific pathogenic micro-organisms and toxins other than endotoxin, although some of the measurement principles may be the same.

114. **SFS-EN 13779:2007en Ventilation for non-residential buildings. Performance requirements for ventilation and room-conditioning systems.**
This European Standard applies to the design and implementation of ventilation and room conditioning systems for non-residential buildings subject to human occupancy, excluding

applications like industrial processes. It focuses on the definitions of the various parameters that are relevant for such systems. The guidance for design given in this standard and its annexes are mainly applicable to mechanical supply and exhaust ventilation systems, and the mechanical part of hybrid ventilation systems. Applications for residential ventilation are not dealt with in this standard. Performance of ventilation systems in residential buildings are dealt with in CEN/TR 14788. The classification uses different categories. For some values, examples are given and, for requirements, typical ranges with default values are presented. The default values given in this standard are not normative as such, and should be used where no other values are specified. Classification should always be appropriate to the type of building and its intended use, and the basis of the classification should be explained if the examples given in the standard are not to be used. Different standards may express the categories for the same parameters in a different way, and also the category symbols may be different.

115. **SFS-EN 13829:en Thermal performance of buildings. Determination of air permeability of buildings. Fan pressurization method (ISO 9972:1996, modified).**
This standard is intended for the measurement of the air permeability of buildings or parts of buildings in the field. It specifies the use of mechanical pressurization or depressurization of a building or part of a building. It describes the measurement of the resulting air flow rates over a range of indoor-outdoor static pressure differences. This standard is intended for the measurement of the air leakage of building envelopes of single-zone buildings.

116. **SFS-EN 14412:en. Indoor air quality. Diffusive samplers for the determination of concentrations of gases and vapours. Guide for selection, use and maintenance.**
This document gives guidelines for the selection, use and maintenance of diffusive samplers used to analyse gaseous pollutants in indoor air including measurement strategy and planning. This document gives guidelines for the selection, use and maintenance of diffusive samplers used to measure indoor air quality and personal exposure. This document is applicable to indoor air quality assessment because crucial differences to ambient air measurement have to be taken into account concerning environmental parameters, measurement strategy, as well as the nature, number, source and abundance of indoor air pollutants. In contrast to typical ambient air measurements the appearance of unexpected compounds in indoor air environments is quite common. Procedures to calculate specific uptake rates of these compounds are needed more often as there is only a limited number of uptake rates validated by experiments (see EN 13528-2 and EN 13528-3) to assess the respective concentration values. In addition to the general calculation procedure of the individual uptake rate as given in EN 13528-2 and EN 13528 3.

117. **SFS-EN 15251. Indoor environmental input parameters for design and assessment of energy performance of buildings addressing indoor air quality, thermal environment, lighting and acoustics.**
This European Standard specifies the indoor environmental parameters which have an impact on the energy performance of buildings. The standard specifies how to establish indoor environmental input parameters for building system design and energy performance calculations. The standard specifies methods for long term evaluation of the indoor environment obtained as a result of calculations or measurements. The standard specifies criteria for measurements which can be used if required to measure compliance by inspection. The standard identifies parameters to be used by monitoring and displaying the indoor

environment in existing buildings. This standard is applicable mainly in non-industrial buildings where the criteria for indoor environment are set by human occupancy and where the production or process does not have a major impact on indoor environment. The standard is thus applicable to the following building types: single family houses, apartment buildings, offices, educational buildings, hospitals, hotels and restaurants, sports facilities, wholesale and retail trade service buildings. The standard specifies how different categories of criteria for the indoor environment can be used. But it does not require certain criteria to be used. This is up to national regulations or individual project specifications. The recommended criteria in this standard can also be used in national calculation methods, which may be different to the methods referred to here. The standard does not prescribe design methods, but give input parameters to the design of buildings, heating, cooling, ventilation and lighting systems. The standard does not include criteria for local discomfort factors like draught, radiant temperature asymmetry, vertical air temperature differences and floor surface temperatures.

6.4.3 National Standards of EU Member States

National standards and regulations exist for many countries. The harmonization efforts are unifying the different regulations and standards. In Europe, the standards of the member states can be accessed via European Committee of Standardization (CEN) web site (www.cen.eu). By selecting "Members" on the front page, one can access the standards of individual member states.

6.4.4 American Society for Testing and Materials (ASTM) International Standards

118. ASTM E2267-04. Standard Guide for Specifying and Evaluating Performance of Single Family Attached and Detached Dwellings-Indoor Air Quality
http://www.astm.org/Standards/E2267.htm
This guide contains suggested performance statements for single family residential buildings (attached and detached) that address indoor air quality performance including indoor air pollution and thermal comfort. These performance statements are not presented as proposed requirements, but are written in permissive language as suggestions that can be used in developing specifications to satisfy user needs. This guide does not address other aspects of the indoor environment such as lighting and acoustics.

Performance statements addressing building ventilation and ventilation rates are also included in the standard, since it is premature to base performance only on indoor air pollution, that is, airborne contaminant concentrations. When health authorities have established contaminant concentration limits for residential environments, it may be possible to define indoor air quality performance in terms of contaminant concentrations rather than ventilation.

This guide is one in a series of guides containing performance statements for residential buildings that are intended for use in the procurement, specification and evaluation of one- and two-family dwellings. These companion standard guides include those noted in the Introduction above.

This guide also addresses a number of residential indoor air quality issues that cannot be expressed as performance statements at this time. However, they are important enough to include in this guide to at least raise the awareness of those involved in the process of procurement, specification and evaluation.

119. **ASTM D5157-97. Standard Guide for Statistical Evaluation of Indoor Air Quality Models.**
http://www.astm.org/Standards/D5157.htm
This guide provides quantitative and qualitative tools for evaluation of indoor air quality (IAQ) models. These tools include methods for assessing overall model performance as well as identifying specific areas of deficiency. Guidance is also provided in choosing data sets for model evaluation and in applying and interpreting the evaluation tools. The focus of the guide is on end results (that is, the accuracy of indoor concentrations predicted by a model), rather than operational details such as the ease of model implementation or the time required for model calculations to be performed.

120. **ASTM D5791 -95(2012)e1. Standard Guide for Using Probability Sampling Methods in Studies of Indoor Air Quality in Buildings.**
http://www.astm.org/Standards/D5791.htm
This guide covers criteria for determining when probability sampling methods should be used to select locations for placement of environmental monitoring equipment in a building or to select a sample of building occupants for questionnaire administration for a study of indoor air quality. Some of the basic probability sampling methods that are applicable for these types of studies are introduced.

Probability sampling refers to statistical sampling methods that select units for observation with known probabilities (including probabilities equal to one for a census) so that statistically defensible inferences are supported from the sample to the entire population of units that had a positive probability of being selected into the sample.

This guide describes those situations in which probability sampling methods are needed for a scientific study of the indoor air quality in a building. For those situations for which probability sampling methods are recommended, guidance is provided on how to implement probability sampling methods, including obstacles that may arise. Examples of their application are provided for selected situations. Because some indoor air quality investigations may require application of complex, multistage, survey sampling procedures and because this standard is a guide rather than a practice, the references in Appendix X1 are recommended for guidance on appropriate probability sampling methods, rather than including expositions of such methods in this guide.

121. **ASTM D6245-12. Standard Guide for Using Indoor Carbon Dioxide Concentrations to Evaluate Indoor Air Quality and Ventilation**
http://www.astm.org/Standards/D6245.htm
This guide describes how measured values of indoor carbon dioxide (CO_2) concentrations can be used in evaluations of indoor air quality and building ventilation. It also describes the determination of CO_2 generation rates from people as a function of body size and level of physical activity, as well as the experimentally-determined relationship between CO_2 concentrations and the acceptability of a space in terms of human body odor.

This guide defines the following uses of indoor CO_2 concentrations to evaluate building ventilation–mass balance analysis to determine the percent outdoor air intake at an air handler, the tracer gas decay technique to estimate whole building air change rates, and the

constant injection tracer gas technique at equilibrium to estimate whole building air change rates.

This guide discusses the use of continuous monitoring of indoor and outdoor CO2 concentrations as a means of evaluating building ventilation and indoor air quality. This guide discusses some concentration measurement issues, but it does not include or recommend a method for measuring CO2 concentrations. This guide does not address the use of indoor CO2 to control outdoor air intake rates

122. **ASTM D7297-06. Standard Practice for Evaluating Residential Indoor Air Quality Concerns.**
http://www.astm.org/Standards/D7297.htm
This standard practice describes procedures for evaluating indoor air quality (IAQ) concerns in residential buildings. The practice primarily addresses IAQ concerns encountered in single-family detached and attached (for example, townhouse or duplex design) residential buildings. Limited guidance is also included for low- and high-rise multifamily dwellings.

The IAQ evaluation procedures are comprised of interviews with the homeowner or resident(s) (including telephone interviews and face-to-face meetings) and on-site investigations (including walk-through, assessment, and measurements). For practicality in application, these procedures are divided into three separate phases, which may occur over one or more site visits.

The procedures described in this standard practice are aimed at identifying potential causes contributing to the IAQ concern. Such findings should become a basis for recommending corrective measures. This standard practice does not describe problem resolution or corrective measures and the standard is not intended to evaluate the impact of corrective measures.

This practice describes a pathway for characterizing indoor air, though adherence to this practice does not guarantee that an investigator will be able to identify or resolve an IAQ complaint for one or more of the following reasons: (1) the diversity of sources and contaminants in indoor air; (2) other factors that may affect occupant perception and acceptance of indoor air quality, such as air temperature, humidity, noise, lighting, and psychological stress; (3) the range of susceptibility in the population.

Implementation of procedures given in this standard requires the investigator (or investigative team) to have adequate background in several areas: general principles of IAQ; interviewing techniques; building design and construction practices; basic understanding of heating and cooling systems and appliances; use of IAQ measurement equipment; interpretation of IAQ data; and technical report writing.

Although many elements described in this standard practice may be useful in training of IAQ investigators, it should not be used as the sole basis for specifying or conducting such training.

6.5 Other documents and guidelines

123. **ISEE Ethics Guidelines for Environmental Epidemiologists**
http://colinsoskolne.com/documents/Soskolne_Sieswerda_in_Science_Engineering_Ethics.pdf

This paper suggests the infrastructure required to facilitate the development and introduction of a comprehensive ethics program into any particular professional organization if the public interest is to be optimally protected. This suggestion is put forward to provoke discussion on this matter. The example of the ISEE could not have succeeded without the voluntary effort of active members of the profession enjoying the support of the elected officers. If infrastructure and incentives for such efforts were made available in the professions, the approaches taken by ISEE likely would be able to be implemented more painlessly by others in the future.

124. Toxicity Testing in the 21st Century

http://www.nap.edu/openbook.php?record_id=11970

Advances in molecular biology and toxicology are paving the way for major improvements in the evaluation of the hazards posed by the large number of chemicals found at low levels in the environment. This book presents that developing, improving, and validating new laboratory tools based on recent scientific advances could significantly improve our ability to understand the hazards and risks posed by chemicals. This new knowledge would lead to much more informed environmental regulations and dramatically reduce the need for animal testing because the new tests would be based on human cells and cell components. Substantial scientific efforts and resources will be required to leverage these new technologies to realize the vision, but the result will be a more efficient, informative and less costly system for assessing the hazards posed by industrial chemicals and pesticides.

125. Guidance for Laboratory Biomonitoring Programs - Association of Public Health Laboratories (2012)

http://www.aphl.org/AboutAPHL/publications/Documents/EH_2012_Guidance-for-Laboratory-Biomonitoring-Programs.pdf

The goals of this guidance are to outline the infrastructure and expertise needed to develop laboratory capacity for a biomonitoring program and to highlight some of the main considerations chemists should address before beginning a biomonitoring study, which include the need to:

- Define the goals of a biomonitoring study;
- Choose the appropriate biomarker in the appropriate matrix at a sufficient level of sensitivity;
- Identify resource needs and sources of potential funding;
- Collaborate with epidemiologists and toxicologists in the development of the study design and to analyze and communicate biomonitoring data;
- Produce reliable, valid and comparable data;
- Engage the community early in the study design process; and
- Develop an effective communication plan that involves reporting of individual results (if appropriate), aggregate data and access to public health, citizens or medical professionals for results distribution and interpretation.

126. Compendium of Chemical Terminology IUPAC Gold Book

http://goldbook.iupac.org/about.html

The Compendium is popularly referred to as the "Gold Book", in recognition of the contribution of the late Victor Gold, who initiated work on the first edition. It is one of the series of IUPAC "Colour Books" on chemical nomenclature, terminology, symbols and

units and collects together terminology definitions from IUPAC recommendations already published in Pure and Applied Chemistry and in the other Colour Books. Terminology definitions published by IUPAC are drafted by international committees of experts in the appropriate chemistry sub-disciplines, and ratified by IUPAC's Interdivisional Committee on Terminology, Nomenclature and Symbols (ICTNS). In this edition of the Compendium these IUPAC-approved definitions are supplemented with some definitions from ISO and from the International Vocabulary of Basic and General Terms in Metrology; both these sources are recognised by IUPAC as authoritative. The result is a collection of nearly 7000 terms, with authoritative definitions, spanning the whole range of chemistry.

127. **Guidelines on Good Practice for Ground Application of Pesticides, FAO, 2001**
http://www.fao.org/docrep/006/y2767e/y2767e00.htm
This guideline is aimed at decision-makers, managers, field supervisors and spray operatives. However, it must be emphasized that in some countries legislation is already in place to control safe and efficient pesticide use and application. Accordingly, local legislation, or voluntary codes must be the first point of reference with this set of guidelines offered as additional information. This is an important point, as compliance with local legislation may have legal significance in the event of a claim against the poor field performance of a pesticide. For other countries, this guideline might serve as a guide until appropriate legislation is in place.

128. **Best Management Practices for Agricultural Pesticide Use to Protect Water Quality**
http://www.ext.colostate.edu/pubs/crops/xcm177.pdf
This guide addresses Best Management Practices (BMPs) for preventing nonpoint source contamination of water resources by agricultural pesticides. Contamination from normal pesticide application is typically considered nonpoint contamination, since a single point of contamination cannot be identified. Point source contamination would include spills of concentrated chemicals during transportation, or at storage, mixing, or loading sites.

129. **Pesticide and Fertilizer Storage and Handling**
http://www.ext.colostate.edu/pubs/crops/xcm178.pdf
This guide addresses the pesticide and the fertilizer storage and handling in their concentrated forms that pose the highest potential risk to ground or surface water from agricultural chemicals. The guide describes the essential features facilities should have for storage and handling and how these products should be properly sited, designed, constructed, and operated. The ideal management practices include:
- Minimize the amount of agricultural chemicals stored and handled
- Reduce waste such as rinsate, containers, and partially used product
- Maintain good records of all chemical use
- Provide preparation, equipment, and training to respond to emergencies.

130. **Heat stress awareness guide**
http://www.healthandsafetyontario.ca/HSO/media/WSN/Resources/Downloads/Heat_Stress_Guide.pdf?ext=.pdf
This guide aims to help employers and workers learn how to prevent heat stress. It includes, a summary of causes, symptoms, and treatment of heat-related illness, presents a five-step

approach for using the Humidex to assess heat stress hazards and outlines specific actions for managing and controlling heat stress. In addition, the appendices include: a self-audit checklist an example of a heat stress policy an outline of the essential elements of a heat stress program some useful contact information.

131. **Tolerable Upper Intake Levels for Vitamins and Minerals by the Scientific Panel on Dietetic products, nutrition and allergies (NDA) and Scientific Committee on Food (SCF), EFSA 2006**
http://www.efsa.europa.eu/en/ndatopics/docs/ndatolerableuil.pdf
This document presents the scientific opinions developed at the request of the European Commission by the Scientific Committee on Food (SCF) (up to April 2003) and the Scientific Panel on Dietetic Products, Nutrition and Allergies (NDA) of EFSA (May 2003 to 2005). This document is a scientific reference on the safety of micronutrients used in food and food supplements.

132. **Scientific Opinion on establishing Food-Based Dietary Guidelines EFSA 2010 EFSA Journal 2010; 8(3):1460**
http://www.efsa.europa.eu/en/efsajournal/doc/1460.pdf
This scientific opinion of the EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA) provides guidance on the translation of nutrient based dietary advice into guidance, intended for the European population as a whole, on the contribution of different foods or food groups to an overall diet that would help to maintain good health through optimal nutrition (food-based dietary guidelines).

133. **Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment, EFSA Journal 2011;9(3):2097**
http://www.efsa.europa.eu/en/efsajournal/doc/2097.pdf
Present document aims to overview of the Comprehensive Database and to provide guidance on its use for dietary exposure assessments. The EFSA Comprehensive European Food Consumption Database (Comprehensive Database) has been built from existing national information on food consumption at a detailed level. Competent organisations in the European Union's Member States provided EFSA with data from those most recent national dietary survey in their country, at the level of consumption by the individual consumer. Summary statistics of this database are available on the EFSA website (http://www.efsa.europa.eu/en/datexfoodcdb/datexfooddb.htm).

134. **INSPIRE Thematic Working Group Coordinate Reference Systems & Geographical Grid Systems (2014). D2.8.I.1 Data Specification on Coordinate Reference Systems – Technical Guidelines.**
http://inspire.ec.europa.eu/documents/Data_Specifications/INSPIRE_DataSpecification_RS_v3.2.pdf
This document specifies a harmonised data specification for the spatial data theme Coordinate Reference Systems as defined in Annex I of the INSPIRE Directive. This data specification provides the basis for the drafting of Implementing Rules according to Article 7 (1) of the INSPIRE Directive [Directive 2007/2/EC]. The entire data specification is published as implementation guidelines accompanying these Implementing Rules. This document was written by INSPIRE Thematic Working Group Coordinate Reference Systems & Geographical Grid Systems. It does not represent an official position of the European Commission.

135. **CIBSE (Chartered Institution of Building Services Engineers).**
http://www.cibse.org/
CIBSE is the standard setter and authority on building services engineering. It publishes Guidance and Codes which are internationally recognised as authoritative, and sets the criteria for best practice in the profession. The Institution speaks for the profession and so is consulted by government on matters relating to construction, engineering and sustainability. It is represented on major bodies and organisations which govern construction and engineering occupations in the UK, Europe and worldwide.

136. **CIBSE TM26 Hygienic Maintenance of Office Ventilation Ductwork**
http://www.cibse.org/knowledge/cibse-tm/tm26-hygienic-maintenance-of-office-ventilation-du
This publication aims to demonstrate to building managers the importance of ductwork maintenance and to provide practical guidance on the proper procedures for maintaining ductwork systems in a safe and effective state.

Recent publications from the Heating and Ventilation Contractors Association (HVCA) and Building Services Research and Information Association (BSRIA) have provided a general review of the issues of ventilation system hygiene and ductwork cleaning. BSRIA has also produced a standard form of contract for ductwork cleaning, with associated guidance. These documents give specific guidance on good cleaning and maintenance practices for ductwork systems in terms of particulate (dust) contamination only.

The guidance contained in this publication is intended to add to that good practice by providing guidance for managers of buildings that are air conditioned, or otherwise mechanically ventilated, on the issues of assessment and maintenance of the microbiological cleanliness of ductwork systems. For those who are unfamiliar with current practice in air duct systems, a separate section reviews this subject.

This publication gives guidance on the methods to use when obtaining microbial samples from the air in occupied spaces and from the inside surfaces of the ducts. It also indicates the levels of microbial contamination that are likely to be found on undeaned and cleaned duct surfaces, and draws on a body of expert opinion to help the building manager to interpret the results of sampling. The procedure may also be used to assess the residual microbial contamination following a commercial cleaning process, or following disinfection, and as a remote means of assessing the performance of filtration of ventilation air.

137. **CIBSE Guide A: Environmental Design.**
http://www.cibse.org/knowledge/cibse-guide/cibse-guide-a-environmental-design
Environmental criteria for design: this chapter has been extensively revised to include the adaptive approach and thermal comfort criteria based on the outdoor running mean temperature for offices in both the free running mode (naturally ventilated and mixed mode buildings) and for sealed buildings served by heating and cooling systems. Guidance on overheating criteria has also been included.

138. **ECA Report no 6 - Strategy for sampling chemical substances in indoor air**
http://www.buildingecology.com/publications/ECA_Report6.pdf

The document describes the sampling strategies that apply to the case that a certain knowledge of the potential sources and pollutants is available. The document does not cover the procedures to be followed if the reasons for unspecific complaints have to be detected. Developing a sampling strategy means to answer the questions when, how often, for what period of time and where samples should be taken.

The document is divided into two parts: a) Detailed discussion of the dynamics of the indoor environment and of the objectives of indoor pollution measurements is given. In addition, general rules are derived for an optimal sampling strategy to answer the questions when, for what period of time, how often, and where samples should be taken; and b) These rules are applied to those pollutants or pollutant classes which for the time being are considered of major importance. As the same facts had to be viewed at from different angles, some repetition could not be avoided. However, such repetition was accepted to help a better understanding.

However, much of the content of this document may also apply to microbiological indoor pollutants, although in the case of these agents, temperature and relative humidity will probably have a much more pronounced influence on the pollutant level than in the case of chemical substances.

139. **ECA Report no 14 - Sampling strategies for volatile organic compounds (VOCs) in indoor air Luxembourg. 1995 ISBN 92-826-9332-5 © ECSC-EC-EAEC. Brussels – Luxembourg, 1995.**
http://www.inive.org/medias/eca/eca_report14.pdf
This report gives more specific guidance for the development of sampling strategies for volatile organic compounds (VOCs). The report is divided into three sections: a) General considerations which highlight the sampling objectives of indoor VOC measurements, the numerous sources of VOCs and their emission characteristics, the dynamic character of indoor pollution by VOCs, and the interpretation of VOC measurements in relation to health and comfort. These considerations are a prerequisite for the development of sampling strategies; b) Discussion of the elements of sampling strategies for VOCs. These elements include the type and number of objects (buildings) and spaces in which air samples should be taken, the types and status of sources in these spaces, the environmental conditions before and during sampling, the position of the sampler in the selected spaces, the sampling duration, time and frequency, sampling and analytical methods, and quality control and assurance. The common choices of the above mentioned elements are discussed; and c) Outline of sampling strategies, i.e. selections of the above-mentioned elements, for the more frequent sampling objectives.

140. **ECA report no. 24 (2005). Harmonisation of indoor material emissions labelling systems in the EU – Inventory of existing schemes. EUR 21891 EN, ISBN 92-79-01043-3, Office for Official Publications of the European Communities, Luxembourg.**
http://www.inive.org/medias/ECA/ECA_Report24.pdf
This report reviews and discusses recent developments concerning the indoor material labelling schemes at European level. The aim was to discuss the scientific background and practical limitations of material emission declaration and labelling systems, and to identify principles for minimum requirements (e.g. measurement data and criteria) for a generally acceptable labelling system. The main outcome is that - although all of these voluntary systems are for labelling the indoor-related properties of building products, - there are big differences between them, e.g., the criteria and for what kind of materials the systems have

been created. Therefore, a strong need for harmonisation of material labelling systems has been identified. In this report the recent developments concerning the efforts to promote harmonisation of the indoor material labelling schemes at European level are presented and discussed.

141. **Indoor air and its impact on man. Report 18: Evaluation of VOC emissions from building products. Solid Flooring materials. European Collaborative Action (ECA), 1997.**
http://www.inive.org/medias/ECA/ECA_Report18.pdf
This report outlines the principles of a general evaluation procedure for emissions of volatile organic compounds (VOCs) from building materials with respect to their potential effects on health and comfort. Using available knowledge, the principles have been applied to a simplified case, i.e a procedure for the evaluation of VOC emissions from solid flooring materials. The procedure is intended for the classification and/or labelling of these materials and may serve for both voluntary and regulatory purposes. The procedure includes: a) the selection and handling of appropriate test specimens; b) the determination of emission factors of individual VOCs and of TVOC (Total Volatile Organic Compounds) using small test chamber measurements; c) modelling of indoor relevant VOC concentrations; d) their toxicological evaluation; and e) measurements of sensory irritation and odour or perceived air quality of the emissions. An overall scheme of how to combine the different elements of the procedure and rules how to use the information obtained for labelling of building materials have been established.

142. **Indoor air and its impact on man. Report 19: Total Volatile Organic Compounds (TVOC) indoor air investigations. Collaborative Action (ECA), 1997.**
http://www.fhi.no/dav/fb9b469003.pdf
This report recommends a definition of TVOC referring to a specified range of VOCs and it proposes a method for the measurement of this TVOC entity. Within the specified range, the measured concentrations of identified VOCs (including 64 target compounds) are summed up, concentrations of non-identified compounds in toluene equivalents are added and, together with the identified VOCs, they give the TVOC value. The report reviews the TVOC concept with respect to its usefulness for exposure assessment and control and for the prediction of health or comfort effects. Although the report concludes that presently it is not possible to use TVOC as an effect predictor it affirms the usefulness of TVOC for characterizing indoor pollution and for improving source control as required from the points of view of health, comfort, energy efficiency and sustainability.

143. **Indoor air and its impact on man. Report 24: Harmonisation of indoor material emission labelling systems in the EU. Collaborative Action (ECA), 2005.**
http://www.inive.org/medias/ECA/ECA_Report24.pdf
Indoor Air Quality (IAQ) and emissions from building materials have been over the last decades a major challenge for scientists, industry and consumers. In response to the need for improved consumer protection different kinds of labelling systems for material emissions have been developed in many European countries and by industrial organisations. The main purpose is to protect consumers from exposure to chemical pollutants and resulting adverse health effects (i.e., carcinogenic, teratogenic, irritant) or annoyance by bad odours, which could be caused by chemical emissions from materials. This protection can be effectively achieved by supporting the market demand for low emitting materials. The labelling systems developed are typically voluntary for the manufacturers. In spite of a trend towards European harmonisation, most of

these labelling systems are mainly focussed on national markets and often require specific tests. Despite a common market there is no harmonised system for material emission labelling available in Europe. This report reviews and discusses recent developments concerning the indoor material labelling schemes at European level.

144. **Jantunen M., Oliveira Fernandes E., Carrer P., Kephalopoulos S., Promoting actions for healthy indoor air (IAIAQ).(2011) European Commission Directorate General for Health and Consumers. Luxembourg.**
http://ec.europa.eu/health/healthy_environments/docs/env_iaiaq.pdf
The IAIAQ project assessed and in some cases omitted or amended the diseases, agents and sources of the EnVIE tool, re-evaluated the matrix coefficients, and combined the model with a new 26 (31) country European model input database, which greatly improved the comprehensibility and eased the use of the modelling tool.

The EnVIE-IAIAQ modeling tool was first used to quantify the total current European IAQ related burden of disease (BoD) and to attribute it on the diseases, exposure agents and sources included in the model. The given and main focus of IAIAQ was on assessing the public health impacts, i.e. achievable reductions to the above modelled IAQ BoD, of some current European IAQ policies and to predict the potential impacts of some alternative and future IAQ policy scenarios, which in a broad sense were defined in the EAHC tender.

IAIQ made also some attempts to assess the impacts of some EU funded IAQ data compiling projects on indoor air relevant EU legislation and respectively on the potential health impacts of such legislation, as well as on the impacts of some EU funded indoor air research projects on the results of the EU funded data compiling projects (pre-normative projects), and further on the health impacts of the IAQ relevant EU legislation.

145. **EU (2005) Development of horizontal standardised assessment methods for harmonised approaches relating to dangerous substances under the construction products directive (CPD). Emission to indoor air, soil, surface water and ground water. European Commission, M/366.**
http://ec.europa.eu/enterprise/standards_policy/mandates/database/index.cfm?fuseaction=search.detail&id=323#
This mandate details the scope of a standardization mandate issued by the Commission concerning construction products (the Directive or CPD). The mandate deals with the subject of emission of dangerous substances from construction products as defined in the CPD that may have harmful impacts on human health and the environment. The scope of this mandate covers these substances as far as they are relevant with regard to construction products and, due to the risk of harmful impacts, are restricted or banned by any EU and/or Member States notified regulations. The present mandate is intended to provide harmonized European measurement/test standards that are needed in order to make possible the "approximation" of laws, regulations and administrative provisions of the Member States
Harmonized product standards and ETA's will take into account the intended uses of the product, the content and release of regulated dangerous substances, the assessment of conformity and the information accompanying the CE marking, which will contain the values of the characteristics of the product on the basis of the technical specifications.
This standardization mandate refers to products for which the two following conditions are fulfilled:

a) The products are or risk to be subject to technical barriers to trade arising from regulated dangerous substances;
b) The characteristics of the products regarding regulated dangerous substances influence the satisfaction by the construction works, in which they are to be incorporated in a permanent manner, of the essential requirements as laid down in article 3 of the CPD and set out in terms of objectives with regard to hygiene, health and the environment. These works are subject to legislative, regulatory or administrative regulations of Member States covering such essential requirements specifically in the field of dangerous substances.

146. **Kotzias D, Koistinen K, Kephalopoulos S, Schlitt C, Carrer P, Maroni M, Jantunen M, Cochet C, Kirchner S, Lindvall T, McLaughlin J, Mølhave L, de Oliveira Fernandes E, and Seifert B. 2005. Critical Appraisal of the Setting and Implementation of Indoor Exposure Limits in the EU. The INDEX project: Final Report. EUR 21590 EN. EC DG JRC. Institute for Health and Consumer Protection. Physical and Chemical Exposure Unit.**
http://ec.europa.eu/health/ph_projects/2002/pollution/fp_pollution_2002_frep_02.pdf
Scope of INDEX was to identify priorities and to assess the needs for a Community strategy and action plan in the area of indoor air pollution by: a) setting up a list of compounds to be regulated in indoor environments with priority on the basis of health impact criteria; b) providing suggestions and recommendations on potential exposure limits for these compounds; and c) providing information on links with existing knowledge, ongoing studies, legislation etc. at world scale.

Information from the exposure assessment and toxicity assessment were integrated and a risk characterization performed on each chemical. Based on the conclusions of the assessments and on the completeness of individual databases, a priority ranking was arranged with the 14 chemicals assigned to three groups: 1) high priority chemicals (formaldehyde, carbon monoxide, nitrogen dioxide, benzene and naphthalene); 2) second priority chemicals (acetaldehyde, toluene, xylenes and styrene); and 3) chemicals requiring further research with regard to human exposure or dose response (ammonia, limonene and á-pinene).

147. **Oliveira Fernandes, E., H. Gustafsson, O. Seppanen, D. Crump, G. Ventura Silva, J. Madureira, and A. Martins. 2008. WP3 Final Report on Characterization of Spaces and Sources. EnVIE Project. European Comission 6th Framework Programme of Research, Brussels.**
http://paginas.fe.up.pt/~envie/documents/finalreports/Final%20Reports%20Publishable/EnVIE%20WP3%20Final%20Report.pdf
The aim of the EnVIE project is to increase the understanding of the Europe-wide public health impacts of indoor air quality by identifying the most widespread and significant indoor causes for these health impacts and evaluating the existing and optional building and housing related policies for controlling them. It addresses in particular how indoor air quality might contribute to the observed rise in asthma and respiratory allergy, together with other acute and chronic health impacts. The intention is not to conduct new experimental or field research, but rather to build on the broad scientific experience and the wealth of accumulated literature from the domestic and international indoor air research projects as well as the EU, WHO, ISIAQ and CIB committees and expert groups during the past 20 years.

WP3 characterize the spaces and sources in order to understand where and how to act to guarantee good IAQ. From the two strategies for good IAQ, source control and ventilation, the

precautionary principle suggests that first priority shall be given to source control, avoiding, mitigating or simply managing sources of emissions.

148. **Review of evidence on health aspects of air pollution – REVIHAAP Project. Technical Report. 2013. The WHO European Centre for Environment and Health.**
This document presents answers to 24 questions relevant to reviewing European policies on air pollution and to addressing health aspects of these policies. The answers were developed by a large group of scientists engaged in the WHO project "Review of evidence on health aspects of air pollution – REVIHAAP". The experts reviewed and discussed the newly accumulated scientific evidence on the adverse effects on health of air pollution, formulating science-based answers to the 24 questions. Extensive rationales for the answers, including the list of key references, are provided. The review concludes that a considerable amount of new scientific information on the adverse effects on health of particulate matter, ozone and nitrogen dioxide, observed at levels commonly present in Europe, has been published in recent years. This new evidence supports the scientific conclusions of the WHO air quality guidelines, last updated in 2005, and indicates that the effects in some cases occur at air pollution concentrations lower than those serving to establish these guidelines. It also provides scientific arguments for taking decisive actions to improve air quality and reduce the burden of disease associated with air pollution in Europe.

149. **NIOSH Manual of Analytical Methods, 1998.**
http://www.cdc.gov/niosh/docs/2003-154/
NMAM is a collection of methods for sampling and analysis of contaminants in workplace air, and in the blood and urine of workers who are occupationally exposed. These methods have been developed or adapted by NIOSH or its partners and have been evaluated according to established experimental protocols and performance criteria. NMAM also includes chapters on quality assurance, sampling, portable instrumentation, etc.

150. **RITE Real Decreto 1027/2007, de 20 de julio, por el que se aprueba el Reglamento de Instalaciones Térmicas en los Edificios. (*) Para entornos que no cumplan estas condiciones aplicar la norma UNE-EN-ISO 7730 Valores limite RD 486/1997 (temperature and relative humidity).**
http://www.boe.es/buscar/doc.php?id=BOE-A-2007-15820
Regulation of Thermal Installations in Buildings is to establish the requirements for energy efficiency and security to be met by thermal installations in buildings designed to meet the demand for welfare and health of people, during their design and sizing, implementation, maintenance and use, and to determine the procedures for accrediting compliance.

151. **Real Decreto 1073/2002. Valor limite 10% VLA del INSHT (conformance criteria PM10).**
http://www.boe.es/buscar/doc.php?id=BOE-A-2002-20933
This Royal Decree is to define and establish limit values and alert thresholds for concentrations of sulfur dioxide, nitrogen dioxide and oxides of nitrogen, particulate matter, lead, benzene and carbon monoxide in ambient air; Regular evaluation, maintenance and improvement of air quality in relation to such substances, as well as information to the public and the European Commission. This is intended to avoid, prevent and reduce the harmful effects of controlled substances on human health and the environment as a whole.

152. **The Education (School Premises) Regulations (SPR) No 2.**

http://www.nasuwt.org.uk/consum/groups/public/@salariespensionsconditions/documents/nas_download/nasuwt_008968.pdf
This standard ensures that schools are addressing the issue of pupils and staff working in excessively cold or hot temperatures as well as poor ventilation conditions in schools through appropriate enforcement of the current minimum temperature of 18°C and through providing leadership on helping schools save on energy costs through energy-saving mechanisms, such as thermal insulation and improved management of energy use, not by reducing the minimum temperature in classrooms to 16°C as is proposed. Research suggests that specific temperature ranges (between 20-23.3°C) have an impact on reading and mathematics learning, with negative learning effects above 23.3°C.

153. **Building Bulletin 87 Guidelines for Environmental Design in Schools.**
http://www.deapss.org.uk/attachments/article/0/BB87%202nd%20Ed%20Ver%201.pdf?Free%20Publications/Building%20Bulletins/
The intention of this document is to provide advice on the environmental design of schools such that compliance with Requirements of ADL2 2002 and of ADF 1995 of the Building Regulations are achieved, and the energy and environmental performance of new and refurbished school buildings is compatible with current building standards. The design guidance relating to Approved Document L2 2002 is formulated in a format similar to that of ADL2 2002, so that it reflects the three 4 alternative means of compliance with the Energy Efficiency Requirements of Part L2 of the Building Regulations. However, BB87 contains some specific Constructional Standards for school buildings which refine and override the recommendations for compliance with Building Regulations given in ADL2 2002 and ADF 1995. Notwithstanding the obligations required under the Building Regulations it should also be borne in mind that The Education (School Premises) Regulations 1999, SI 1999 No.2 are still in force and contain minimum environmental standards that apply to both new and existing school buildings.

154. **Building Bulletin 101 Ventilation of School Buildings.**
https://www.gov.uk/government/publications/building-bulletin-101-ventilation-for-school-buildings
This Building Bulletin provides the regulatory framework in support of the Building Regulations for the adequate provision of ventilation in schools. It deals with the design of school buildings to meet the ventilation requirements of both The School Premises Regulations and the Building Regulations Part F (Ventilation). This Building Bulletin is quoted in Approved Documents F and L2 (amended 2006) as a means of compliance with Regulations F1 and L of the Building Regulations for school buildings.

155. **EH40/2005: Workplace Exposure Limits 2005**
This edition of EH40 replaces the previous version, first published in 2005, and takes account of new substances and workplace exposure limits (WELs) introduced in 2007 and 2011.
Many people are exposed to a variety of substances at work, eg chemicals, fumes, dusts etc, which can have a harmful effect on their health. If exposure to these hazardous substances is not properly controlled, it may cause ill health in a number of ways.
This book contains advice and guidance about:
- European occupational exposure limits
- workplace exposure limits

- the Control of Substances Hazardous to Health Regulations 2002 (as amended) (COSHH)
- approved workplace exposure limits

156. Workplace (Health Safety and Welfare) Regulations 1992 (L24).

The Workplace (Health, Safety and Welfare) Regulations 1992 cover a wide range of basic health, safety and welfare issues and apply to most workplaces (except those involving construction work on construction sites, those in or on a ship, or those below ground at a mine). The book includes the Regulations in full, as well as the Approved Code of Practice and guidance. It will help employers understand the regulatory requirements on issues such as ventilation, temperature, lighting, cleanliness, room dimensions, workstations and seating, floor conditions, falls or falling objects, transparent and translucent doors, gates and walls, windows, skylights and ventilators, traffic routes, escalators, sanitary conveniences and washing facilities.

This revised and updated version takes account of changes to legislation since the previous edition was published, including:

- Quarries Miscellaneous Health and Safety Provisions Regulations 1995
- Quarries Regulations 1999
- Work at Height Regulations 2005
- Construction (Design and Management) Regulations 2007
- Health and Safety (Miscellaneous Amendments) Regulations 2002

157. Health & Safety Executive's MDHS14/3 for inhalable dusts.

http://www.hse.gov.uk/pubns/mdhs/pdfs/mdhs14-4.pdf

The methods described in this MDHS are suitable for the measurement of exposure to the health-related concentrations of most aerosols in the workplace. In some instances alternative methods exist (e.g. welding fume, colophony and isocyanates) and you should refer to these specific methods. For some materials a specific sampler is required (eg IOM sampler is the preferred sampler for cotton dust) to reliably perform the analysis. The use of alternative methods is acceptable provided that the accuracy and reliability appropriate to the application can be demonstrated.

This procedure describes the analysis of the collected aerosol using the gravimetric technique. After drawing a measured volume of air through the preweighed collection medium (eg filter or foam) mounted in a suitable particle size selective sampler, the mass concentration can then be determined from the mass of the aerosol collected and the sampled air volume. Where further analysis for specific constituents is required, refer to the appropriate methods to ensure the sampling medium is compatible with the analysis technique.

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7 Appendix C: Examples of data

7.1 An example of a common file format

This example shows a fake example of a common file format that can merge data form different studies. Note, the data come from different studies, countries, cities and volunteers.

Study	UniqueID	SchoolCode	ClassCode	City	Country	CountryCode	CommuneCode	...	DateOfBirth	Gender	FamilySeq	...	EverAsthma	DoctorDiagnosedAsthma	AsthmaAttacks12Months	AsthmaGINA	...	PM25	PM10	Benzene	Formaldehyde	CC16	...
Ferma	CDJ365			Pessac	France	FR			22.1.2005	M	1		0	0		0		35.2	65.1	89.1	0.1		
Ferma	BJE968			Clermont-Ferrand	France	FR			31.8.2001	F	1		0			0		23.4	12.4	0.7	0.9		
Ferma	AQM011			St. Urcize	France	FR			16.4.1998	M	1							12.7	14.9	38.4	7.5		
Ferma	PLY957			St. Urcize	France	FR			14.7.1952	M	2		1	1		2			7.8				
Ferma	MMA368			St. Martin d'Hères	France	FR			29.2.1996	F	1		0					26.1	5.9		3.9		
Ferma	SAU445			Sauges	France	FR			17.11.1981	F	1		1	0		1		1.4	54.7	19.6	12.8		
Ferma	REM528			St. Rémy	France	FR			12.8.1966	F	1		0	0				8.2	43.8	21.1			
Ferma	BQP014			Aurillac	France	FR			25.6.1983	M	1		1			3		9		70.5	3.6		
Ferma	FFT422			Finistère	France	FR			11.4.2011	M	1		0			0					6.4		
Ferma	IDE280				France	FR				F	1		0	0		0		7.8	7.9	16.4			
SINPHONIE	IT-S05-C02-P21	IT-S05	IT-S05-C02	Milan	Italy	IT			6.5.2008						0			23.9	0.7				
SINPHONIE	DE-S04-C01-P16	DE-S04	DE-S04-C01	Cologne	Germany	DE			30.10.2007	F				0				14.7	6.3				
SINPHONIE	FR-S01-C04-P03	FR-S01	FR-S01-C04	La Rochelle	France	FR			17.9.2005	M				0	0			23.8	42.1				
SINPHONIE	AU-S02-C03-P27	AU-S02	AU-S02-C03	Salzburg	Austria	AU				F				1	0			7.1					
SINPHONIE	RS-S01-C01-P11	RS-S01	RS-S01-C01	Zagreb	Serbia	RS			19.9.2003	F				1	1			2.3	2.9				
SINPHONIE	FI-S04-C02-P07	FI-S04	FI-S04-C02	Tampere	Finland	FI			4.6.2007	F					1			3.8	6.3				
SINPHONIE	SE-S06-C04-P29	SE-S06	SE-S06-C04	Malmö	Sweden	SE			9.2.2009	M				0									
SINPHONIE	PT-S04-C03-P27	PT-S04	PT-S04-C03	Porto	Portugal	PT			17.3.2010	M				0	0				12.8				
SINPHONIE	PT-S06-C01-P12	PT-S06	PT-S06-C01		Portugal	PT			22.12.2004	F				0	0			6.8	77.8				
SINPHONIE	UK-S01-C03-P08	UK-S01	UK-S01-C03	Leeds	United Kingdom	UK			8.6.2003	M				0	0			17.5					
SINPHONIE	HU-S05-C04-P19	HU-S05	HU-S05-C04	Budapest	Hungary	HU			9.12.2006	M				0	1				18				
SINPHONIE	EE-S04-C01-P24	EE-S04	EE-S04-C01	Tartu	Estonia	EE				F				0				0.7					
ISAAC	6570	3	8	Créteil	France	FR	9810425		7.4.2000	F					0				17.9	12			
ISAAC	6571	3	8	Créteil	France	FR	9810425		18.3.1998					0					5.5	84			
ISAAC	6572	3	8	Créteil	France	FR	9810425			F				0						32.5			
ISAAC	6588	4	6	Créteil	France	FR	9810368		13.5.1995	M					0				6.3	16.4			
ISAAC	6589	4	6	Créteil	France	FR	9810368		30.11.1994	M				1	0				70.4				
ISAAC	6601	8	2	Rouen	France	FR	9710117		1.2.1992	F				1	1				35.9	7.8			
ISAAC	6891	8	3	Rouen	France	FR	9728554		16.9.2001	M					0				44.7	51.7			
ISAAC	6892	8	3	Rouen	France	FR	9728554		10.10.2000	F				0	1				31.2				
ISAAC	2508	1	4	Bordeaux	France	FR	3382207		7.7.1997	M				1	0					0.9			
ISAAC	2546	2	5	Bordeaux	France	FR	3382207		6.4.2009	F									1	0.2			

7.2 Example of previous study questionnaire data coding

This example shows data from the PHIME mother-child population study. The example shows the question codes, questions and answer coding of PHIME brief questionnaire that the volunteers filled in prior to recruitment.

PHIME - Brief questionairre (filled prior to recruitment)

Var name	Variable	Code	type	format
Q1	Mother's name			
Q2	Mother's date of birth		DATE	dd/mm/yyyy
Q3	Mother's place of birth			
Q4	address			
Q5	telephone number			
Q6	Since when have you been living here	year	NUM	
Q7	do you plan to move within the next 2 years?	1=yes, 2=no	NUM	
Q8	Mother's usual occupation held in the past year			
Q9	years of schooling		NUM	
Q10	Number of children		NUM	
Q11	birth date of youngest child		DATE	dd/mm/yyyy
Q12	father's name			
Q13	father's date of birth		DATE	dd/mm/yyyy
Q14	father's current occupation			
Q15	father's years of schooling		NUM	
Q16	due date		DATE	dd/mm/yyyy
Q17	pregnancy problems	1=yes, 2=no	NUM	
Q18	what problems?			
Q19	Are you being treated for any illness)	1=yes, 2=no	NUM	
Q20	what illness?			
Q21	weight before pregnancy	kg	NUM	
Q22	height	cm	NUM	
Q231	smoking before pregnancy	1=yes, 2=no	NUM	
Q232	smoking currently	1=yes, 2=no	NUM	
Q24	number of cigarettes per day		NUM	
Food frequency				
Q251	vegetables	1=never, 2=less than once per month, 3=1-3 times per month, 4=once per week, 5=2 times per week, 6=3 times per week, 7=4 times per week, 8=5 times per week, 9=6 times per week, 10=at least once per day		
Q252	milk and milk products	1=never, 2=less than once per month, 3=1-3 times per month, 4=once per week, 5=2 times per week, 6=3 times per week, 7=4 times per week, 8=5 times per week, 9=6 times per week, 10=at least once per day		
Q253	egg	1=never, 2=less than once per month, 3=1-3 times per month, 4=once per week, 5=2 times per week, 6=3 times per week, 7=4 times per week, 8=5 times per week, 9=6 times per week, 10=at least once per day		
Q254	meat	1=never, 2=less than once per month, 3=1-3 times per month, 4=once per week, 5=2 times per week, 6=3 times per week, 7=4 times per week, 8=5 times per week, 9=6 times per week, 10=at least once per day		
Q255	fresh fish	1=never, 2=less than once per month, 3=1-3 times per month, 4=once per week, 5=2 times per week, 6=3 times per week, 7=4 times per week, 8=5 times per week, 9=6 times per week, 10=at least once per day		
Q256	frozen fish	1=never, 2=less than once per month, 3=1-3 times per month, 4=once per week, 5=2 times per week, 6=3 times per week, 7=4 times per week, 8=5 times per week, 9=6 times per week, 10=at least once per day		
Q257	tinned fish	1=never, 2=less than once per month, 3=1-3 times per month, 4=once per week, 5=2 times per week, 6=3 times per week, 7=4 times per week, 8=5 times per week, 9=6 times per week, 10=at least once per day		
Q258	alcoholic beverages	1=never, 2=less than once per month, 3=1-3 times per month, 4=once per week, 5=2 times per week, 6=3 times per week, 7=4 times per week, 8=5 times per week, 9=6 times per week, 10=at least once per day		
Q261	intake of alcoholic bevarages: before pregnancy	1=yes, 2=no	NUM	
Q262	intake of alcoholic bevarages: currently	1=yes, 2=no	NUM	
Q27	Is your alcohol intake concentrated during certian	1=yes, 2=no	NUM	
Q28	If YES, how many days per week?		NUM	
Q29	were you away from your current home during the	1=yes, 2=no	NUM	
Q30	How long?			
Q301	number of weeks		NUM	
Q302	number of months		NUM	
Q31	where?			
Q32	date of hair sampling		DATE	dd/mm/yyyy

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7.3 Example of human biomonitoring data

This example shows an excerpt of actual human biomonitoring data that contains volunteer ID (an unidentifiable code, blurred for this example), geo-coded location (latitude and longitude) of the volunteers home address, values of different biomonitoring measurements (chemical concentration in different biological matrices, e.g., hair, blood, milk, serum, etc.) and the birth year. Note that the value -9999 is used to represent a missing value. The data file contains a lot of more data from different variables and volunteers. Geo-coding of the home address is important for many exposure assessments.

ID	Latitude	Longitude	M_hair_THg	M_hai_MeHg	M_1mha_THg	Cord_b_THg	Cor_b_MeHg	Cord_bl_Mn	Cord_bl_Cu	Cord_bl_Zn	Cord_bl_As	Cord_bl_Se	Cord_bl_Cd	Cord_bl_Pb	M_milk_THg	M_mlk_MeHg	M_milk_Mn	M_milk_Cu	M_milk_Zn	M_milk_As	M_milk_Se	M_milk_Cd	M_milk_Pb	CB_Seru_Ca	CB_Seru_Mg	CB_S_FeII	CB_Seru_Se	CB_Plasma_Zn	M_birth
#####	#########	#########	192	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	0.12	-9999	2.964581	512.711	2978.968	0.04	20.07876	0.036014	0.4	-9999	-9999	-9999	-9999	-9999	1978
#####	#########	#########		-9999	-9999	1.92	-9999	16.53494	573.3041	1583.556	1.172935	74.30711	0.16312	6.21112	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	2.98	0.81	27.9	42	14.3	-9999
#####	#########	#########		-9999	-9999	0.57	-9999	24.80066	571.9207	1697.783	0.462876	77.15647	0.12	10.18669	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	2.67	0.86	25.2	31	11.8	-9999
#####	#########	#########		-9999	-9999	1.68	-9999	14.73303	455.1714	1304.204	0.796142	55.96149	0.12	5.07417	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	2.69	0.82	26.8	-9999	-9999	-9999
#####	#########	#########		-9999	-9999	3.61	-9999	22.52064	564.8395	2155.673	2.178549	92.5929	0.12	5.882435	0.25	-9999	2.077402	621.9525	897.9968	0.518149	19.7269	0.055092	0.4	2.96	0.76	21	37	12.9	1970
#####	#########	#########	73	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	2.69	0.99	24.7	-9999	-9999	2009
#####	#########	#########		-9999	-9999	0.38	-9999	46.39968	758.9545	3131.75	0.509103	87.44804	0.424853	15.0046	0.098	-9999	1.95023	572.7514	1722.754	0.04	15.2351	0.130118	0.4	2.67	0.93	19.8	39	15.3	1967
#####	#########	#########	343	-9999	-9999	1.61	-9999	29.12524	745.9703	4027.952	1.317288	69.25714	0.135745	7.255646	0.37	-9999	2.175299	732.4421	3247.822	0.199379	17.67405	0.069742	0.404306	2.6	0.74	21.1	-9999	-9999	1977
#####	#########	#########	202	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	1987
#####	#########	#########	202	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	1972
#####	#########	#########	301	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	1974
#####	#########	#########	49	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	1981
#####	#########	#########	98	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	1983
#####	#########	#########	75	-9999	-9999	0.66	-9999	44.72418	610.6219	1867.906	0.294442	61.82885	0.12	9.301917	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	2.98	0.81	27.7	-9999	-9999	1981
#####	#########	#########	275	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	1972
#####	#########	#########	545	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	1978
#####	#########	#########	586	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	1977
#####	#########	#########	54	-9999	-9999	0.68	-9999	24.5618	559.4581	2156.036	0.526965	74.39041	0.12	7.435644	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	2.75	0.75	47.5	-9999	-9999	1981
#####	#########	#########	354	-9999	-9999	1.91	-9999	17.24215	487.4293	1446.383	0.912008	49.67171	0.220112	9.263838	0.7	-9999	3.640709	568.3023	3827.711	0.148846	16.92227	0.092267	0.4	2.58	0.79	19.1	-9999	-9999	1978
#####	#########	#########	85	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	0.48	-9999	1.864401	662.849	3296.273	0.04	17.21411	0.073493	0.4	-9999	-9999	-9999	-9999	-9999	1981
#####	#########	#########	687	-9999	-9999	2.4	-9999	21.31419	494.4254	1449.018	1.199071	73.25916	0.12	4.736768	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	2.59	0.9	38.1	-9999	-9999	1980
#####	#########	#########	397	-9999	-9999	2.94	-9999	22.07382	525.8	1790.657	0.576371	61.20759	0.12	3.339392	2.86	-9999	7.525476	463.3509	1306.793	0.040422	37.61904	0.309367	0.4	2.48	0.73	23.2	36	-9999	1980
#####	#########	#########	389	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	1978
#####	#########	#########	277	-9999	-9999	1.83	-9999	30.18072	488.1537	1689.818	1.661743	80.51471	0.12	4.274998	0.48	-9999	3.208303	631.6569	4152.533	1.724792	11.02872	0.04268	0.4	2.92	0.9	25.7	-9999	-9999	1975
#####	#########	#########	374	-9999	-9999	2.07	-9999	24.82836	452.9674	1731.418	0.524657	79.14384	0.12	15.05382	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	-9999	2.66	0.94	36.1	-9999	-9999	1972
#####	#########	#########	632	-9999	-9999	5.03	-9999	45.22282	644.177	1899.189	1.149061	108.9227	0.12	9.06611	0.27	-9999	1.314123	457.1465	2211.958	0.102156	16.73118	0.044187	0.4	2.78	0.78	43.3	-9999	-9999	1971