Air pollution in high risk sites: risk analysis and health impact

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1. Introduction

During the last century, at the top of industrialization phase, the excessive use of increasingly more complex inorganic and organic chemicals has caused serious environmental contamination all over the world with acute and chronic effects on population health.

The sites considered to be very contaminated and classified as dangerous are very numerous and often belong to industrial centres; in the past years, the contamination of soil and their contribution to air pollution have had an important role.

In countries characterized by a high socio-economic status, the industrial impact on air pollution is certainly less than the weight of traffic and urban heating, while in the developing and emerging countries, industrialization has still an important and unresolved role because of the lack of legislative management and control.

Epidemiological studies represent the scientific basis used to verify the existence of negative health effects caused by air pollution and to quantify the value of these effects, estimating the dose-response relationships. Many studies have demonstrated that air pollution is associated with a wide range of adverse health outcomes. Statistical analyses, conducted on monitoring and biomonitoring data, also show a relationship between the level of air pollution and the rate of mortality and morbidity. Unlike accidents, pollution is not considered a cause of immediate death. Actually, it is thought that it represents a cause of premature death. Air pollution is associated with a great number of illnesses, such as cancer, respiratory, cardiovascular and neurological diseases, and also diabetes and infertility problems.

The estimated cost of pollution becomes an economic evaluation of the risk of getting sick or dying prematurely. but the effects of pollution are particularly difficult to evaluate in terms of quantity and cost. In order to assess the related risk of air pollution, it is certainly very important to establish the effects of pollution on human health, but it is also needful to consider some health determinants such as genetic factors, age, sex and lifestyle habits.

Considering all these aspects, our proposal includes a chapter about atmospheric and urban pollution describing their relative and assessed effects on human health, with a detailed regard on risk assessment. In the last decades a large amount of legislatives are been issued accepting international subscribed agreement, such as Kyoto's protocol, to save public health and restrict the effects of pollution on climate change. We will also focus on indoor pollution, with its undersized data and relative problem and difficulties in management, on methodologies of study and on some case reports.

2. Description of air pollution and characterization of monitored atmospheric pollutants.

According to WHO, air pollution is contamination of the indoor or outdoor environment by any chemical, physical or biological agent that modifies the natural characteristics of the atmosphere. Household combustion devices, motor vehicles, industrial facilities and forest fires are common sources of air pollution. Pollutants of major public health concern include particulate matter, carbon monoxide, ozone, nitrogen dioxide and sulfur dioxide that pose serious health risks [1].

In Europe, emissions of many air pollutants have decreased significantly the last thirty years and air quality has improved across the region. However, excess of air quality standards still occur, especially in metropolitan areas, and air pollutants released in one country may be transported in the atmosphere, polluting or degrading the air quality in neighboring countries. On the bases of this statement air pollution can be considered as a local, pan-European and hemispheric issue [2].

At present particulate matter, nitrogen dioxide and ground-level ozone, are recognized as the most dangerous three pollutants that affect human health, ranging in severity of impact according to long-term and peak exposures. Moreover, benzo(a)pyrene is a carcinogenic substance of increasing concern as its concentrations are above the threshold set to protect human health in several urban areas, especially in central and eastern Europe. Air pollution could also represent a danger for the environment, producing acidification, eutrophication, damage to agriculture.

There are various sources of air pollution, both anthropogenic and of natural origin, in turn divided in stationary and mobile sources. The most common anthropogenic sources of pollutants are combustion processes used for electricity generation, transport, industry and households, industrial processes and solvent use, agricultural crops and livestock, waste incinerator and landfill. A stationary source of air pollution, also known as a point source, refers to a fixed emission source, represented by factories, power plants, dry cleaners, residential wood burners, dry lake beds, and landfills. A mobile source of air pollution refers to a source that is capable of moving under its own power. In general, mobile sources imply "on-road" transportation, which includes vehicles such as cars, sport utility vehicles, and buses. In addition, there is also a "non-road" or "off-road" category that includes gas-powered lawn tools and mowers, farm and construction equipment, recreational vehicles, boats, planes, and trains.

Natural "air pollution" is not caused by people or their activities and emission sources generally comprise volcanic eruptions, windblown dust, sea-salt spray, wild animals in their natural habitat and plants releasing volatile organic compounds [2].

In the evaluation of pollution effects it must keep in mind that dangerous substances can be emitted as primary or secondary pollutants. Primary pollutants are emitted directly into the air from pollution sources, whilst secondary pollutants are formed when primary pollutants undergo chemical changes in the atmosphere. For example NOX and SO2 are directly emitted into the air following fuel combustion or industrial processes. In contrast, O3 and the major part of PM form in the atmosphere following emissions of various precursor species, and their concentrations depend strongly on meteorological conditions, such as high air temperatures and sunlight.
At present the attention of scientist and legislator is focused on the major sources of dangerous substances, represented by urban and industrial activities.
In the evaluation of urban pollution it is important to consider regional pollution, city pollution real and *hot spot* events, determined by peaks of pollutants higher than average followed by gradual restoration of normal limits. Of these three components the first two have direct effects on human and environmental health as they expose population to contaminants for a longer time, causing chronic effects.
As regards industrial pollution, it is due to the full range of unwanted substances and losses generated by industrial activities, including emissions to air or surface waters and the substances sent to sewage treatment plants, deposited in landfills, released or applied to the land, treated, injected underground, controlled through storage, recycled or burned for energy recovery [3].
For this reason to assess significant trends and to discern the effects of reduced anthropogenic precursor emissions, long time-series of measurements and a continuous monitoring of air quality are needed [4].
The application of European Directives contained the emission of many pollutants, consequently reducing their levels in the atmosphere. However, whilst imposed restrictions on industries, developed technologies to reduce pollutants from road transport and continuous monitoring of the most representative substances in the air, air pollution is still a current problem and it is necessary to focus the attention on its effects on human health and on methods to reduce these effects.
At present, based on "*The Clean Air Act",* Quality Standards are set for six common air pollutants, also known as "criteria pollutants". They are particulate matter, ground-level ozone, carbon monoxide, sulfur oxides, nitrogen oxides, and lead. These pollutants can harm human health and the environment, and cause property damage. The set of limits based on human health is called primary standards. Another set of limits intended to prevent environmental and property damage is called secondary standards [5].
The main pollutants measured to characterize and monitor the quality of the environment are shown below.

2.1 Particulate matter (PM)

PM is one of the most important pollutants in terms of potential to harm human health, as it penetrates into low regions of the respiratory system. PM is a complex heterogeneous mixture of solid particles and liquid droplets found in the air, whose size and chemical composition change in time and space, depending on different emission sources and atmospheric and weather conditions. These particles come in many sizes and shapes and can be made up of hundreds of different chemicals. Particulate matter includes both primary and secondary PM; primary PM is the fraction of PM that is emitted directly into the atmosphere from construction sites, unpaved roads, fields, smokestacks or fires, whereas secondary PM forms in the atmosphere following the oxidation and transformation of precursor gases (mainly SO2, NOX, NH3 and some volatile organic compounds (VOCs) that are emitted from power plants, industries and automobiles.

Particle pollution includes "inhalable coarse particles," with diameters larger than 2.5 micrometers and smaller than 10 micrometers and "fine particles," with diameters that are 2.5 micrometers and smaller. Smaller sizes of particulate matter such as PM2.5, with a diameter up to 2.5 μm, are considered particularly harmful due to their greater ability to penetrate deep into the lungs.

2.2 Tropospheric or ground-level ozone (O3)

Ozone (O_3) is a secondary pollutant formed in the troposphere, from complex photochemical reactions following emissions of precursor gases such as NO_X and non-methane volatile organic compounds (NMVOCs), deriving from paint application, road transport, dry-cleaning and other solvent uses. At the continental scale, methane (CH4) and carbon monoxide (CO) also play a role in ozone formation. Ozone is a powerful and aggressive oxidising agent, causing respiratory and cardiovascular problems and leading to premature mortality. High levels of O_3 can also damage plants, leading to reduced agricultural crop yields and decreased forest growth.
Ozone is found at ground level and in the upper regions of the atmosphere. Both types of ozone have the same chemical composition (O_3)., but while upper atmospheric ozone protects the earth from the sun's harmful rays, ground level ozone is one of the main component of smog.
Troposheric, or ground level ozone is created by chemical reactions between oxides of nitrogen (NOx) and volatile organic compounds (VOC) after its emission in the air from industrial facilities and electric utilities, motor vehicle exhaust, gasoline vapors and chemical solvents. Ozone is likely to reach unhealthy levels on hot sunny days in urban environments and can also be transported through long distances by wind so that even rural areas can experience high ozone levels.
Ozone contributes to what we typically experience as "smog" or haze, which still occurs most frequently in the summertime, but can occur throughout the year in some southern and mountain regions. Ground level ozone that we breathe can harm human health, especially affecting people with lung disease, children, older adults, and people who are active outdoors.
Children are at greatest risk from exposure to ozone because their lungs are still developing and they are more likely to be active outdoors when ozone levels are high, which increases their exposure. Ozone also damages vegetation , in

particular trees and plants during the growing season, and ecosystems, including forests, parks, wildlife refuges and wilderness areas.

2.3 Carbon monoxide (CO)

Carbon monoxide (CO) is a colorless, odorless gas emitted from combustion processes. Particularly in urban areas, the majority of CO emissions to ambient air come from mobile sources. CO can cause harmful health effects by reducing oxygen delivery to the body's organs (like the heart and brain) and tissues, and causing death at extremely high levels.

2.4 Sulphur dioxide (SO_2)

Sulphur dioxide (SO_2) is emitted by the combustion of fuels containing sulphur. It contributes to acid deposition and can cause adverse effects on aquatic ecosystems in rivers and lakes, and damage to forests.

Sulfur dioxide (SO_2) is one of a group of highly reactive gasses known as “oxides of sulfur.” The largest sources of SO_2 emissions are from fossil fuel combustion at power plants (73%) and other industrial facilities (20%). Smaller sources of SO_2 emissions include industrial processes such as extracting metal from ore, and the burning of high sulfur containing fuels by locomotives, large ships, and non-road equipment. SO_2 is linked with a number of adverse effects on the respiratory system.

2.5 Nitrogen oxides (NO_X)

Nitrogen oxides (NOX) are emitted during fuel combustion, by industrial facilities and the road transport. contribute. NO_X a contribute to the formation of secondary inorganic particulate matter and tropospheric O_3, to acid deposition and to eutrophication. Of the chemical species that comprise NOx, NO_2 is associated with adverse affects on health, such as inflammation of the airways and reduced lung function.

Nitrogen dioxide (NO_2) is one of a group of highly reactive gasses known as "oxides of nitrogen," or "nitrogen oxides (NOx)." Other nitrogen oxides include nitrous acid and nitric acid. EPA’s National Ambient Air Quality Standard uses NO_2 as the indicator for the larger group of nitrogen oxides. NO2 forms quickly from emissions from cars, trucks and buses, power plants, and off-road equipment. In addition to contributing to the formation of ground-level ozone, and fine particle pollution, NO_2 is linked with a number of adverse effects on the respiratory system. EPA both a primary standard (to protect health) and a secondary standard (to protect the public welfare) for NO_2 at 0.053 parts per million (53 ppb), averaged annually. In January 2010, EPA established an additional primary standard at 100 ppb, averaged over one hour. Together the primary standards protect public health, including the health of sensitive populations, people with asthma, children, and the elderly. No area of the country has been found to be out of compliance with the current NO_2 standards.

2.6 Heavy metals

The main heavy metals in outdoor air are arsenic (As), cadmium (Cd), lead (Pb), mercury (Hg) and nickel (Ni); they are emitted mainly as a result of various combustion processes and industrial activities and generally can reside in or be attached to particulate matter (PM). Heavy metals are persistent in the environment and can be deposited on terrestrial or water surfaces, contaminating soils or sediments and accumulating in food-chains.

2.7 Polycyclic Aromatic Hydrocarbons (PAHs) and Benzo(a)pyrene (BaP)

PAHs are a group of chemicals that are formed during the incomplete burning of coal, oil, gas, wood, garbage, or other organic substances, such as tobacco and charbroiled meat. There are more than 100 different PAHs. PAHs generally occur as complex mixtures. The primary sources of exposure to PAHs are inhalation of the compounds in tobacco smoke, wood smoke and ambient air.

PAHs is a growing health concern in Europe with particular regard toBaP, a polycyclic aromatic hydrocarbon, formed mainly from the incomplete burning of organic material such as wood, and from car exhaust fumes especially from diesel vehicles. It is a known cancer-causing agent in humans. A main source of BaP in Europe is domestic home heating, in particular wood burning, waste burning, coke and steel production and mobile sources. Other sources include outdoor burning and rubber tyre wear. In Europe, BaP pollution is mainly a problem in certain areas such as western Poland, the Czech Republic and Austria where domestic coal and wood burning is common.

The International Agency for Research on Cancer (IARC) considers BaP a known carcinogen. While laboratory studies show that BaP is a known carcinogen in animals, epidemiological studies have only been able to assess the effect of a mixture of PAH, including BaP found in soot, tars and oils. Benzo(a)pyrene is a promutagen, which needs to be metabolised before it can induce mutation. Benzo(a)pyrene can also react with O_3 to produce strong mutagens such as BaP-4,5 oxide. While exposure to C_6H_6 in Europe is limited to a few local areas close to traffic or industrial sources, exposure to BaP pollution is quite significant and widespread. Populations living in central and eastern Europe are exposed to ambient BaP concentrations above the target value. Between 20 % and 29 % of the urban population in the EU was exposed to BaP concentrations above the target value (1 ng/m3) in the period 2008 to 2010. As much as 94 % of the urban population was exposed to BaP concentrations above the calculated WHO reference level [6]. The increase in BaP emissions in Europe over the last years is therefore a matter of concern, as it is aggravating the exposure of the European population to BaP concentrations. Regarding BaP, the Industrial Emissions Directive [7] regulates emissions from a large range of industrial sources.

2.8 BTEX

It is a group of chemical compounds including Benzene, Toluene, Ethylbenzene and Xylenes. BTEX are made up of naturally-occurring chemicals that are found mainly in petroleum products such as gasoline. Most everyone is exposed to small amounts of BTEX compounds in the outdoor air, at work, and in their home. Besides the common daily exposures to BTEX, larger amounts can enter the environment from leaking under-ground storage tanks, overfills of storage tanks, fuel spills from auto accidents and from landfills.
Short-term exposure to gasoline and its components benzene, toluene and xylenes has been associated with skin and sensory irritation, central nervous system-CNS problems and effects on the respiratory system. Chronic exposure to BTEX compounds can affect the kidney, liver and blood systems. Long-term exposure to high levels of the benzene compound can lead to leukemia and cancers of the blood-forming organs [8].

2.9Physical pollution

Physical pollution is pollution caused by colour (change), suspended solids, foaming, temperature conditions or radioactivity and it is characterized by its influence on environmental conditions caused by forces and operations of physics, such as noise, microwave radiation, vibration.

2.10 Microbiological factors

Microbiological factors in the environment represent an underestimated but insidious risk factor which concern has increased with the introduction of advanced technologies in hospitals, industry and agriculture. Microbial agents are transported and diffused in ambient through particular matter [9]. The main sources of microorganisms are Flügge droplets from human airways and conditioning systems, the last containing different bacteria such as *Legionella pneumophila*, virus and mould.
To maintain a healthy environment a strict monitoring must be led for each of the contaminants above mentioned; legislation on environment sets benchmark and provides a series of actions to hold the values of the contaminants within the limits.
As air pollutants can be transported many miles away from the area of their emission, monitoring these substances is more difficult than monitoring contaminants in water or soil, so it was decided to record ambient air quality data focusing on major pollutants. Continuously operating automatic analyzers are the most important information source on air pollution levels [10]. According to current legislation, measurements are taken at permanent sites equipped with physico-chemical monitoring devices even if these stations provide only data on exposure levels which do not facilitate making conclusions on the effects or impacts to human health and the general environment. Moreover spatial coverage and temporal definition of the carried measurements together with meteorological conditions influence the degree of representativeness of the data compared to the real state of pollution of the study area [11] .
Recently innovative technologies have been developed and direct damage of harmful effects can be demonstrated by monitoring living organisms, called biomonitors, which provide a measure of integrated exposure over a certain amount of time taking into account also climatic conditions and enrich the substance to be determined so that the analytical accessibility is improved and the measurement uncertainty reduced. Moreover Sampling is relatively simple and no expensive technical equipment is needed. The field of biomonitoring includes bioindication of effects and bioaccumulation of pollutants [12].
The information provided by mosses, lichens and higher plants on the deposition on the effects of air pollutants are an important complement to the data acquired with automatic systems. Distribution of tree species on a national or supranational lets you draw cheaply and in a short time, maps of diffusion and deposition of persistent pollutants or the effects of tropospheric ozone and other phytotoxic pollutants [13].

3. Statistical methodologies to evaluate the risk assessment and air pollution correlated diseases

The first epidemiologic studies on the impact of air pollution on health were undertaken as a consequence of the extreme pollution episodes that took place in the decades from 1930 to 1960. The association between air pollution and certain health variables was made clear by simple graphic representations or by comparisons of mortality rates for these time periods [14, 15].
Since that time, air pollution levels have fallen substantially, such that, to evaluate their effects on health, longer time series are required. To this end, epidemiologists began to use dynamic regression models in the 1970s that consisted of models in which the relationship between the dependent and explanatory variables were distributed over time, rather than being expected to occur simultaneously. Moreover, investigators were able to control for residual autocorrelation, with the error being specified by means of autoregressive integrated moving-average models (ARIMA). The problem with these types of models is that they assume that the dependent variable is distributed normally, which, in fact, is extremely rare in the daily outcome count variables of morbidity and mortality events [16].
The early 1990s saw the appearance of linear models based on Poisson regression, in which a parametric approach was used to control for trend and seasonality because the event counts more typically have a Poisson distribution. These models use the variable “time” and its transforms, quadratic and sinusoidal functions (sine or cosine) of different frequency and amplitude, to control for the effect on the dependent variable (mortality or morbidity) of unmeasured variables that may vary seasonally, such as in pollen concentration, meteorological variables, and influenza outbreaks, or that may have a trend, such as changes in a city’s population distribution, in order to ascertain the effect of such variables on the dependent variable [16].

Insofar as changes in a city's population pyramid are concerned, Poisson regression is particularly useful only when cases, rather than the entire population, can be enumerated, because this form of regression analysis does not require knowledge of the denominator as long as population flux is in steady state.
Nevertheless, Poisson regression poses the problem that, if any of these unmeasured variables follows a cyclical component of varying frequency and width (as might be the case of pollen concentration or influenza), the parametric functions of time or of its sinusoidal transforms cannot be easily "adapted" to such changes. These limitations led to the development of nonparametric Poisson regression with the application of generalized additive models (GAMs) that use nonparametric functions of the variable "time" [17], which adapt flexibly to the irregular cyclic components of unmeasured variables and allow for flexible fits for important variables, such as temperature, barometric pressure, and relative humidity, thus reducing any potential confounding due to these factors.
One difficulty with this method is that the number of degrees of freedom of the smoothed nonparametric function must be specified by the researcher, with discrepancies arising as to the most appropriate way to calculate this. Because inappropriate determination of the number of degrees of freedom can lead to bias in the estimates of nonparametric Poisson designs, epidemiologists focused on the case-crossover (CCO) design that purported to control time trends. The CCO design was proposed to identify risk factors of acute events [18]; it is characterized by the fact that each subject serves as his or her own control by assessing referent exposure at a point in time prior to the event. By virtue of its design, this type of study controls for the influence of confounding variables such as sex, smoking history, occupational history, and genetics. This design was initially used to assess the effect of exposures measured at an individual level (telephone calls and traffic accidents, physical or sexual activity, and acute myocardial infarction) and was not applicable to exposures with a time trend, such as air pollution. Thus, if an investigator selected exposure control dates before the effect, and there was a trend, prior exposures would be systematically higher or lower than at the date of the effect. To circumvent this bias, [19] developed a variant of this design, bidirectional CCO, which is conceptually characterized by having control time periods before and after the event, something that made it possible to control for the effect of long-term trend and seasonality on the variable "exposure." This design was already appropriate for ecologic-type exposures, such as air pollution, because the existence of registries means that the values of such exposure can be ascertained even after the event. In addition, pollution values are not affected by the presence of prior morbidity and mortality events. In the CCO design, the referent time periods represent the counterfactual exposure experience of the individual, had he or she not become sick; because in air pollution pre- and post- event exposure values are independent of the hazard-period exposure, those that are post- event referent can be appropriate. One advantage of CCO design over Poisson regression is its ability to assess potential effect modification (i.e., statistical interaction) at the individual level rather than at the group level [20]. As an alternative analytic methodology to Poisson regression, the CCO approach allows for direct modeling of interaction terms, rather than depending on multiple subgroup analyses [20].
Besides the individual characteristics during the statistical analysis of epidemiological data it must be considered other variables, taken into account that the chemical characteristics of air pollutants mixture and particulate matter may change over time and depending on the geographical location, emission sources, atmospheric chemistry and weather conditions [21].
Interest in health effects of air pollution became more intense after two US cohort studies suggested that exposure to fine particulate matter in the air was associated with life shortening [22,23].
Exposure to pollutants such as airborne particulate matter and ozone has been associated with increases in mortality and hospital admissions mainly because of respiratory and cardiovascular disease, due to both acute and chronic exposure [24].
Health problems can include cancer, respiratory irritation, nervous system problems and birth defects.
According to the WHO, in the year 2012 ambient air pollution was responsible for 3.7 million deaths, representing 6.7% of the total deaths. Worldwide, ambient air pollution is estimated to cause about 16% of the lung cancer deaths, 11% of chronic obstructive pulmonary disease deaths, more than 20% of ischaemic heart disease and stroke, and about 13% of respiratory infection deaths. Furthermore, the International Agency for Research on Cancer (IARC), announced that it has classified outdoor air pollution as carcinogenic to humans (Group 1).
Typically exposure to toxic components of air pollutant causes the well-established correlated diseases, respiratory and pulmonary ones, such as decreased lung function, and increased incidence of chronic cough, bronchitis, chronic obstructive pulmonary disease, asthma and conjunctivitis [25,26,27].
Recent clinical and epidemiological data suggest also that cardiovascular disease may be related to pollution [28,29] especially those associate with fine particulate matter [30,31,32,33]. The effects of PM on the cardiovascular system seem to involve the activation of clotting factors, leading to the formation of thrombosis, but the destabilization of atherosclerotic plaques also cannot be excluded. In addition, there may be effects on the heart, mediated through effects on the nervous system or directly on the heart itself. The latter mechanism may include the release/leakage of stress mediators from the lung and/or the direct effect of soluble compounds or of ultrafine particles on the heart cells.
Health effects have been seen at very low levels of exposure, and it is unclear whether a threshold concentration exists for particulate matter and ozone below which no effects on health are likely.
It could be expected that the impact caused by a preventable risk factor would decline if the exposure to that risk factor could be reduced or removed. According to this approach, the proportional reduction in the number of health problems or deaths as a result of reducing the risk factor is known as the attributable fraction (AF) [34].
Public health agencies concerned with air quality perform risk assessments to determine the increased risk of illness from a specific human exposure to a toxic air pollutant.
The risk assessment approach outlined by the WHO in the Environmental Burden of Disease (EBD) series [35,36] includes the following steps:
1) determination of the ambient exposure of the population using data from model estimates or monitoring networks. A 'counterfactual' background or target concentration is also needed to determine the attributable disease or the potential gains of a reduction strategy;

2) number of people exposed to air pollutants;
3) baseline incidence of the adverse health outcomes associated with air pollutants (eg, the mortality rate in the population);
4) concentration-response functions (CRFs) that relate changes in air pollutants concentrations with changes in the incidence of adverse health effects.
The U.S. Environmental Protection Agency (US-EPA) divided the risk assessment process into the following four steps:

a. ***Hazard Identification***: it allows determining the potential human health effects from exposure to a chemical. This is based on information provided by the scientific literature.
b. ***Dose-Response Assessment***: it is the characterization of the relationship between a chemical exposure, or dose, and the incidence and severity of an adverse health effect. It takes into consideration factors that influence this relationship, including intensity and pattern of exposure, and age and lifestyle variables that may affect susceptibility. The dose-response relationship is evaluated differently for carcinogenic (cancer-causing) and non-carcinogenic substances. For carcinogens, it is assumed that there is a linear relationship between an increase in dose or exposure concentration and an increase in cancer risk, with no threshold. This is expressed as a potency slope or slope factor (SF). To evaluate risks from inhalation of carcinogenic substances, US-EPA and other regulatory agencies use potency slopes to develop unit risk factors (URFs). A URF can be defined as the upper-bound excess probability of contracting cancer as the result of a lifetime of exposure to a carcinogen at a concentration of 1 $\mu g/m^3$ in air. URF units are "per microgram (of chemical) per cubic meter (of air)" or (ug/m^3)-1. For inhalation effects from non-carcinogens, dose-response data are used to develop reference concentrations (RfCs), for both long-term (chronic) and short-term exposures. Unlike carcinogens, non-carcinogens are assumed to have thresholds for adverse effects, meaning that injury does not occur until exposure has reached or exceeded some concentration (a threshold). An RfC is derived from a no-observed adverse effect level (NOAEL) or lowest-observed adverse effect level (LOAEL) determined through human or animal exposure studies.
c. **Exposure Assessment**: it determines the extent (intensity, frequency, and duration, or dose) of human exposure to a chemical in the environment.
d. There are three components to exposure assessment:
    i. Estimation of the maximum quantity of each pollutant emitted from the source of concern (based on data from previously existing sources or engineering estimates).
    ii. For each contaminant emitted from a source, estimation of the resulting maximum annual average and (where applicable) maximum short-term average ambient air concentrations, using dispersion models, or air impact values based on dispersion models.
    iii. Estimation of the amount of contaminant taken in by a human receptor.
e. **Risk Characterization**: which is the final step in risk assessment, in which human health risk is calculated and described, based on the information gathered in the first three steps. It should also include some consideration of uncertainty, scientific judgment, and the major assumptions that were made, especially regarding exposure.

- ***Carcinogens***

Human health risk estimates for inhalation of carcinogens are based on the following calculation:

Cancer Risk = C x URF

where:
C = maximum annual average ambient air concentration of a pollutant, µg/m3
URF = pollutant-specific inhalation unit risk factor, $(\mu g/m^3)$-1
For routes of exposure other than inhalation, risk is calculated by multiplying the estimated chemical dose (in mg/kg/day) by the chemical-specific oral slope factor (in (mg/kg/day)-1).

- ***No carcinogens***

Human health risk estimates for inhalation of non carcinogens are based on the following calculation:

Hazard Quotient = C/RfC

where:
C = maximum ambient air concentration, $\mu g/m^3$
RfC = pollutant-specific reference concentration, $\mu g/m^3$
The averaging time for non-carcinogen concentrations can be either annual, or a specific number of hours, depending on the basis of the reference dose [37]. For routes of exposure other than inhalation, the hazard quotient is calculated by dividing the estimated chemical dose (in mg/kg/day) by the chemical-specific reference dose (in mg/kg/day).
Hazard quotients can be summed (separately for inhalation and oral exposures, and for different averaging times) to give a hazard index.

4. Evaluation of indoor air pollution and comparison with the urban and high risk sites.

Clean air is a basic requirement for a healthy life maintaining. The quality of air inside homes, offices, schools, day care centers, public buildings, health care facilities or other private and public buildings where people spend a large part of their life is an essential determinant of health. Hazardous substances emitted from buildings, construction materials and indoor equipment or due to all human activities indoors lead to a broad range of health problems and may even be fatal for infants and children. Indoor environmental issues are still a open topic of public health, including health risks and the means by which human exposures can be reduced [38].

Mistakes of evaluation or unacknowledged by public about health risks associated with a variety of indoor environmental pollutants and sources of pollution (eg: radon, mold and moisture, secondhand smoke and indoor wood smoke) cause a minor efficacy of prevention and/or risk's low perception. In poorly ventilated dwellings, smoke in and around the house can exceed acceptable levels for fine particles 100-fold [39] respect to outdoor levels already known. In fact, an inadequate ventilation can increase indoor pollutant levels for not complete dilution of these. High temperature and humidity levels can also increase concentrations of certain pollutants [40]. Outdoor air enters and leaves a house by: infiltration, natural ventilation, and mechanical ventilation. Air flow associated with infiltration and natural ventilation is caused by air temperature differences between indoors and outdoors or by wind. The rate at which outdoor air replaces indoor air is described as the air exchange rate. When there is little infiltration, natural ventilation, or mechanical ventilation, the air exchange rate is low and pollutant levels can increase rapidly [41].

There are many sources known of indoor air pollution in any home. These include combustion sources such as oil, gas, kerosene, coal, wood, and tobacco products; building materials and furnishings as diverse as deteriorated, asbestos-containing insulation, wet or damp carpet, cabinetry and objects made with certain pressed wood products (eg formaldehyde, pesticides, etc.); products for household cleaning and their maintenance (phtalates, bisphenol A, fragrances, pesticides, detergents, chlorine bleach, lye, ammonia, etc.), cosmetics for personal care (solvents, phtalates, bisphenol A, fragrances, mineral oil, ethoxylated surfactants and 1,4-dioxane, formaldehyde, lead, oxybenzone, parabens, toluene, triclosan, etc.), chemicals used for hobbies(solvents, lead, pesticides, mineral oil, cadmium, manganese dioxide, cobalt, formaldehyde, aromatic and chlorinated hydrocarbons, ethylene glycol monomethyl ether, ethylene glycol monobutyl ether, etc); central heating and cooling systems and humidification devices (mold, viruses, fungi, bacteria, mycotoxins, etc.); and outdoor sources such as radon, pesticides, and outdoor air pollution likely to come into the house where can concentrate. Some of these sources (building materials, outdoor sources, wood furnishings, etc) release pollutants more or less continuously. Other sources, related to activities carried out in the home, release pollutants intermittently and their concentrations can remain in the domestic air for long periods after these activities. The relative importance of any single source depends on how much of a given pollutant it emits and by proved hazard of those emissions. In some cases, factors such as, how old the source is and whether it is properly maintained are very significant (eg, an improperly functional gas stove can emit more carbon monoxide than one that is properly adjusted).

Exposure to indoor air pollution is particularly high among women and young children, who spend the most time in the domestic environment and health effects may be shown soon after exposure or, years later.

According to WHO, 4.3 million people a year die from the exposure to household air pollution [39]. In fact, especially cooking and heating with solid fuels (wood, charcoal, etc..) produces high levels of smoke both in and around the home and this contains a large variety of health-damaging pollutants [42].

Immediate effects as irritation of the eyes, nose, and throat, headaches, dizziness, and fatigue, may show up after a single acute exposure or repeated sub acute exposures. These are usually treatable and short-term effects. Oftentimes the simply elimination of person's exposure to the identified source of pollution is sufficient for health restore.

Additional problem is the recurrent multiple indoor pollution exposure of residents complicating and amplifies the health effects [43].

There is strong evidence that exposure to indoor air pollution can lead to a wide range of child and adult disease outcomes, both acute and chronic respiratory conditions (e.g. pneumonia, chronic obstructive pulmonary disease) [39, 44], lung cancer [45; 46], ischemic heart disease [46], stroke [46] and cataract [46].

There is emerging evidence, although based on fewer studies, that suggests that household air pollution, especially in developing countries, may also increase the risk of other important child and adult illness such as:

- low birth weight and perinatal mortality (still births and deaths in the first week of life) [45,46];
- asthma [39, 45];
- otitis media (middle ear infection) and other acute upper respiratory infections [39];
- tuberculosis [45];
- nasopharyngeal cancer [39];
- laryngeal cancer [39];
- cervical cancer [39].

Also exposure to unhealthy concentrations of fine PM has been connected to increased respiratory/cardiovascular illnesses [39, 47]. In fact, the smaller air particles can penetrate into the deeper lung. PM is being linked to adverse birth outcomes [46], neurodevelopment, cognitive function [48] and diabetes [39].

Semple et al. [49] said that median $PM_{2.5}$ concentrations from 93 smoking homes were 31 $\mu g/m^3$ (ranged between 10 to 111 $\mu g/m^3$) and 3 $\mu g/m^3$ (ranged between 2 to 6.5) $\mu g/m^3$ for the 17 non-smoking homes and still showed that non-smokers living with smokers typically have average $PM_{2.5}$ exposure levels more than three times higher than the WHO guidance for annual exposure to PM2.5 (10 $\mu g/m^3$). So, fine particulate pollution in homes where smokers live is approximately 10 times higher than in non-smoking homes. Taken over a lifetime the non-smokers living with a smoker inhale a similar mass of $PM_{2.5}$ as a non-smoker living in a heavily polluted city such as Beijing. This condition is likely to be greatest and dangerous for the very young and for older members of the population because they typically spend more time at home. Zhou and colleagues [50] have demonstrated that in New York city hookah bars, despite the tobacco smoking ban some hookah bars serving tobacco-based hookahs and, in these particular indoor environments, the authors have found elevated concentrations of pollutants that may present a real health threat to visitors and employees. The mean real time $PM_{2.5}$ level was 1179.9 $\mu g/m^3$, whereas the filter-based total PM mean was 691.3 $\mu g/m^3$. The mean real time black carbon level was 4.1 $\mu g/m^3$, organic carbon was 237.9 $\mu g/m^3$, and carbon monoxide was 32 ppm. Airborne nicotine was present in all studied hookah bars (4.2 $\mu g/m^3$).

Dorizas et al. [51] with their study showed that in nine naturally ventilated primary schools of Athens (Greece) during spring, PM concentrations were significantly affected by the ventilation rates and presence of students. Both PM_{10} and $PM_{2.5}$ were greater during teaching than the non-teaching hours and, in many cases, the $PM_{2.5}$ concentrations exceeded their limit values. For most of the cases the indoor to outdoor concentrations ratios of PM_{10} and $PM_{2.5}$ were much greater

than one, indicating that the indoor environment was being mostly affected by indoor sources instead of the outdoor air. Furthermore it was found that chalk and marker boards' usage significantly affect indoor pollutant concentrations.
No similar characteristics between indoor pollution and urban and high-risk sites outdoor pollution, because the poorly ventilation of houses and buildings in general, allows the concentration of chemical and biological pollutants that not found in similar outdoor concentrations also in severe pollution event. Urban outdoor air pollution refers to the air pollution, which the populations are exposed living in and around urban area. Indoor air pollution refers to the pollutants found in indoors. A important difference is in the heavy metals concentration, generally most abundant and with major variability of species in urban and industrial air outdoor pollution respect to indoor pollution.
At the moment, in Italy, a reference rule has not been set. For this reason, until today main information concerning some guidelines or reference values in indoor air are obtained by the international scientific literature or by the few guidelines issued by other European countries or, for analogy, by other guidelines values regarding outdoor air. However public health awareness on indoor air quality is still lags significantly behind that of outdoor air quality.
The main areas at high risk of environmental crisis in Italy are described below.

5. Case reports: ILVA-Taranto, Melilli-Priolo-Augusta sites, Gela and Milazzo emerging situation, "Terra dei Fuochi" and Seveso.

In order to cope the huge problem of pollution experts were mobilized at national and regional level in the drafting of numerous scientific papers in order to initiate actions to protect health in the areas most affected by the emission of high quantities of contaminants. In many cases the results of these studies support arguments about correlation between the exposition to pollutants and outbreak of neoplastic diseases, however for some areas it has been highlighted a higher incidence in urban areas rather than in sites of national interest, bringing to speculate about the etiologic implication of non-industrial contaminants.
At the moment in Italy the most interesting areas for their extension and extent of involved population are represented by the industrial pole of Taranto, Melilli-Priolo-Augusta, Gela e Milazzo sites, "Terra dei fuochi" as well as the outcome of the tragedy that occurred in 1976 in Seveso. An overview of current developments of studies and the status of remediation undertaken in these areas will be given below.

5.1 ILVA-Taranto

Founded in 1961, ILVA of Taranto is a steel plant at full cycle, where occur all the steps that lead from iron ore to steel [52-54]. The plant, which is partially impounded by order of the judiciary, is the largest steel maker in Europe. The area of Taranto is identified at high risk of environmental crisis because of an extensive industrial area developed close to the urban settlement. Industrial activities are responsible for environmental pollution, mostly due to polycyclic aromatic hydrocarbons (PAHs), heavy metals, organic solvents, polychlorinated biphenyls (PCBs), particulate matter (PM) and dioxin.
The table 1 shows the main pollutants found in soil, groundwaters and sediments of the area of Taranto.

Table 1. Main pollutants found in soil, groundwaters and sediments of the area of Taranto

Soil	antimony, arsenic, beryllium, cadmium, cobalt, chromium total, chromium VI, mercury, lead, nickel, zinc, copper, vanadium, cyanide, hydrocarbons C <12 and C> 12, PAHs, benzene, xylene, dioxins
Subsurface	antimony, arsenic, beryllium, cadmium, cobalt, chromium total, chromium VI, mercury, lead, nickel, zinc, copper, vanadium, cyanide, hydrocarbons C <12 and C> 12, PAHs, benzene, xylene, dioxins
Groundwater	arsenic, selenium, aluminium, iron, manganese, nickel, lead, cobalt, total chromium, chromium VI, cyanides, sulfates, nitrates, BTEXS, PAHs, hydrocarbons and MTBE
Sediments	arsenic, nickel, lead, total chromium, copper, mercury, zinc, total PAHs, PCBs

To define the extent of the health risk, rigorous epidemiological studies have been conducted to assess both the short-term effects that occur in acute as a result of rapid changes in the concentrations of pollutants, and the long-term effects, caused by prolonged exposures and which occur 10-15 years after the start of exposure.
In 2006, the Ministry of Health has funded a project called "S.E.N.T.I.E.R.I." (Studio Epidemiologico Nazionale dei Territori e degli Insediamenti Esposti a Rischio da Inquinamento - National Epidemiologic Study of the Territories and

Settlements Exposed to Risk from Pollution) with the purpose to analyse the mortality of populations residing in proximity of a number of industrial agglomerates which by their nature potentially have a high factor of hazardous health and/or environmental contamination such as to be classified as SIN (Sites of National Interest for the remediation).
The population of Taranto has been the subject of several multi-centre epidemiological studies that have documented the role of air pollution on the increase in short-term and long-term effects [52,53].
Epidemiological analysis of the residents of the city revealed death rates from all causes, for lung, pleura and bladder cancer and for non-Hodgkin lymphoma. A case-control study on incident cases of these diseases in Taranto suggested a possible link between risks and residence close to the sources of emissions.
A recent study called EpiAir in which subjects were recruited rigorously and it was taken into account the exact georeferencing of areas of residence and employment, analyzed the spatial variability of air pollutants in Taranto and showed that atmospheric pollution in this city is not distributed homogeneously, but it is mainly widespread in the areas adjacent to industrial pole. In the results of this study have been taken into account the socio-economic status and calculated indices of deprivation; these aspects have a great importance as many individual habits, such as cigarette smoking, alcohol consumption, physical activity and obesity, are often associated with social status so that the adjustment made for the socio-economic factor has also adjusted the individual variables not directly measured, providing very reliable data. Moreover in this study mortality rate and hospitalization rate were measured to evaluate both long and short terms effects. Data about mortality are reliable as 98% of the causes of death was recovered thanks to the linkage of personal data with the database of the ASL and show an excess of mortality for cancer, cardiovascular and respiratory diseases. As far as hospital admissions, evaluated from hospital discharge schedule, it was difficult to get accurate data because the comparison was made only on the hospital area of Taranto, without taking into account the extra-regional mobility and the secondary diagnosis; although these limits, data show an increase of hospitalization for the above-mentioned causes. The results of this study have strengthened the argument that there is a correlation between exposure to emissions from the steel plant of Taranto and an increase of cancer and cardiovascular and respiratory diseases [55].
The European Environment Agency, in the list that shows the 622 most polluting industrial plants in Europe, included more than 60 Italian companies; Ilva of Taranto is placed second. As a result, the situation with the city of Taranto and Ilva is currently the subject of discussion and great concern [53,54,56]. To control the situation in the area, were enacted several regional laws aiming to carry out the assessment of environmental impact and damage health in order to take targeted action to protect the environment and public health. Moreover in the Italian Act 6 of February 2014, strategies are defined to make the remediation of contaminated areas from emissions of ILVA.

5.2 Sicily (Italy) quality air situation

In Sicily four Sites of National Interest have been individuated and the industrial areas of Melili-Priolo-Augusta (Siracusa), Gela (Caltanissetta) and Milazzo (Messina) have been declared by national and regional legislation "areas high risk of environmental crisis". It is likely that the excesses of mortality and morbidity observed in areas Melili-Priolo-Augusta, Gela and Milazzo is attributable to occupational exposures and environmental concerns related to the number of plants and the consequent contamination of environmental matrices [57], although the last reports show how these rates do not exhibit a significant increase.

5.2.1 Melilli-Priolo-Augusta sites

The large industrialized coastal area of eastern Sicily within the territory of the municipalities of Augusta, Priolo Gargallo and Melilli is defined “petrochemical pole of Siracusa”. These territories started to be subject to industrialization in 1948 with the construction of a refinery (the RA.SI.O.M) and in the following years other industrial facilities were born; currently the petrochemical pole host five refineries of petroleum products, two centrals of ENEL, a gas plant and cogeneration, a factory of magnesite, a cement plant, a purifier of industrial and urban waste and a shipyard.
In these areas, the increase in the number of illness might be linked with particulate matter, which are released into the atmosphere from industrial chimneys and have the ability to convey inside the body, through the lung, every kind of pollutants from the atmosphere. This potential association has also been noted by the residents, who have expressed their concerns to environment organizations and public heath institutions.
Official data on emissions point out a long list of definitely carcinogenic and teratogenic chemicals (acrylonitrile, benzene, cadmium, hexavalent chromium, nickel, silicon, vanadium, dioxins and furans), and many other potentially hazardous, according to the IARC (Agency International Agency for Research on Cancer).
About particulate matter, the main substances contained in it are represented by heavy metals how showed by the results of a study conducted by the Faculty of Agriculture of the University of Palermo, which used lichen for biomonitoring as their action of bio-accumulators for heavy metals, highlighting a significant presence of these hazardous metals in the environment concerned [57, 58].
These evidences induced the Ministry of the Environment to recognize the Priolo-Augusta-Melilli site as "an area in environmental crisis for which it has become necessary a legislative and Financial able to address in a timely manner the dramatic emergency". The large amount of epidemiologic studies conducted in these areas highlight the role of atmospheric pollution in the development of some cancers although recent data published by AIRTUM (Associazione Italiana dei Registri Tumori – Italian Association of cancer registries) [59] show that the higher incidence of cancer in Sicily is found in the city of Catania and in other metropolitan areas, such as Palermo and Messina, as well as in big countries like Acireale and Gravina, leading to hypothesize the role of other risk factors, probably linked to road traffic and unhealthy lifestyle, contributing in the outbreak of above mentioned diseases. According to the last published report,

the industrial sites are not among the areas with the highest incidence of cancer, as supposed, and surprisingly the SIN of San Filippo del Mela does not present excess in the incidence of tumors.

5.2.2 Gela and Milazzo emerging situation

In the area of Gela and the surrounding area rises one of the main industrial centres of the island. The area, declared "area at high risk of environmental crisis ", includes the municipalities of Gela, Niscemi and Butera. Within the bounded area subjected to remediation there is a large industrial centre, consisting of plants for refining and extraction of crude oil and petrochemical plants. In particular productions regard: polyethylene, molten sulphur, sulphuric acid and phosphoric acid, ammonia and fertilizers complexes [57].
The environmental impact of the refinery of Gela comes mainly from emissions into the atmosphere and the consequent presence of pollutants such as SO_2, NO_x, dust, H_2S, CO. Conveyed emissions are mainly generated in the combustion process and are coming out of the chimneys.
Data provided by ARPA (Regional Agency for Environmental Protection) reveal exceedances in ambient town, some parameters such as benzene, methane, hydrocarbons and PM10 containing heavy metals such as nickel.
A scientific study has shown that the entire area of Gela is heavily influenced by emissions of metals and non-metals from both car traffic both vehicular pollution industrial. In particular, the study highlights pollution of the particulate present in the aerosol analysing the deposition of the particulates on pine needles. The analysis of pine needles is a fast method for monitoring of the pollutants present in the air: the pine needles provide information for the long-term impact of even low levels of pollutants. As far as neoplastic diseases, it has not been showed an excess of incidence in this area, although some Sicilian studies highlight an increase of Relative Risk for these diseases compared to other areas of the Region, not characterized by the presence of industrial agglomerates. Moreover in this area an important role is played by current wind, responsible of the transport of substances emitted by plants of Gela for long distances, interesting in particular Niscemi where was found contamination of soils by the above mentioned pollutants.
The industrial area of Milazzo is characterized by the presence of a large industrial centre, including a oil refinery, a thermoelectric central, a co-generator, a steel mill, a plant for the recovery of lead from spent batteries and different other smaller factories. In the vicinity of industrial installations, there are several common, among which are those belonging to "area at high risk of crisis environment".
One study of Milazzo area reveals the exposure assessment, by ambient monitoring and personal monitoring, documented children's exposure to elevated concentrations of sulphur dioxide, nitric oxide, and PM 2.5. During some weeks, the average concentration value for sulphur dioxide was more than 20 $\mu g/m^3$, and the PM 2.5 average in the study period was about 23 $\mu g/m^3$, twice that of the WHO air quality guideline limit. Also, epigenetic markers were associated with air pollutant concentrations – particularly, with regard to the nitric oxide pathway [57, 58].

5.3 Terra dei fuochi

One of the greatest environmental and health criticality that covered Italy in the last two decades is linked to the illegal waste disposal, triggering serious repercussions both in the territories concerned and the health of the residents in these areas and leading the Institutions to take actions that stiffen confidence in themselves and protect the health of the population. Studies carried out in the areas affected by this phenomenon, although not definitive, confirmed an increase in health risks resulting from waste disposal, highlighting in particular an increase in mortality from all causes, the excesses of mortality from specific cancers (liver, lung, stomach, kidney, and bladder) as well as an increase in non-neoplastic diseases of the respiratory system. The limits of ecological studies mainly reside in the fact that it is not possible to assess the individual characteristics of involved subjects, data on the amount and types of substance emitted are not exact and, therefore, extent of population exposure is not certain, and estimates arising from these studies not provide reliable data on the correlation. Despite the necessity of deepening the studies above, on February 2014 the Italian Parliament approved a law for the protection of these specific areas, which has as main innovations the request of a mapping of polluted areas and crops of these territories, the allocation of funds to carry out a health screening and the introduction of the crime of burning waste.
This low, if one side has paid attention on the problem, on the other hand has created problems for the application of screening, excellent in itself as a means of prevention, but totally inappropriate to the case in question. It should be noted that on such land occurred the burning of hazardous waste, even radioactive in nature, and that substances emanating from these processes have not been proven to be in correlation with cancers for which screening is scheduled (colorectal, breast, cervix). Moreover alarmism generated by media has also created skepticism in consumers, even internationally, with a substantial drop in sales of the excellent products from Campania.
However, contrasting the illegality and protect public health is a duty of the institutions, as well as civic, and to implement the cited actions the Institutions with the collaboration of experts, gathered in the Technical Committee for the Contaminated Territories (CTTC) that provide information on correct methodology to implement the definition of the criteria for the mapping of sites, for the identification of specific diseases to perform a targeted screening and for implementing the operations of monitoring and remediation.

5.4 Seveso

On July 1976 in Meda (Italy) at the chemical plant ICMESA (Industrie Chimiche Meda Società Azionaria) occurred the Seveso disaster [60]. During the usual production of trichlorophenol, a fungicide, an uncontrolled reaction that sparked the safety valves of the tank reactor took place, releasing the deadly chemical vapour into the atmosphere. About 3000 Kg of toxic cloud compound containing dioxin TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) was released into the air. The

wind immediately dispersed the toxic cloud eastwards: the dioxin could begin to generate its catastrophic effects, affecting the inhabitants of the area, but also making uninhabitable the territory on which it was deposited.
The chemicals released into the air from the ICMESA were carried by the wind and caused the contamination of, mainly, four municipalities: Seveso, Meda, Desio and Cesano Maderno.
Since no one was at the plant when it happened, the seriousness of the disaster was not immediately observed.
Dioxin has been considered to be the most toxic human-made substance; the Seveso disaster represents the highest known TCDD exposure to residential populations and, probably, the most studied dioxin contamination incident in history [60, 61].
The most common sign of human health problems was skin disorder. The immediate effects on the population were evident especially from a dermatological point of view: after two days already appeared the first cases of chloracne, a disease that is documented to be associated with dioxin.
In order to estimate health problems of population, a great number of laboratory tests were carried out on blood samples. In 1987 it became possible to measure low levels of dioxin in blood samples. Another important effect of the dioxin exposure concerned the reproduction, in particular affecting the sex ratio (an higher proportion of females were born in the first 7 years after the accident). In addition, a large number of pregnancies ended as spontaneous abortions was reported.
The affected places still show signs of contamination. The new EU legislation on industrial equipment of chemical and their coordinated management was started in June of 1982, when the Council of Ministers approved the European Union's Council Directive 82/501/EEC, the Seveso Directive.
A central part of the directive was made by reference to the obligation of transparent public information about industrial accidents, as well as new security measures to be taken in case of an accident [60, 61].
The new concept was approved, for industrial workers and the public, the right to know the substance and the form of the problems that could threaten them and the exact operation of the safety procedures.

6. Air quality guidelines and comparison between emerging and underdeveloped countries.

Generally, the effect of environmental factors on health and policy-making can be explained today through the Driving Force-Pressure-State-Exposure-Effect-Action (DPSEEA) model [62]. Ideal policy-making, in terms of environmental health, involves a reduction of environmental risk exposure, as well as the risks themselves, in every stage of the process. However the accurate policy-based intervention is not simple, as the time lag between the reduction of exposure to environmental risk factors and its effect on disease prevalence, as well as other variables that affect biological health, make the intervention very difficult to implement [63]. With regard to the DPSSEA model, the national policy-based intervention for air pollution is closely related to the establishment of air quality standards, as the setting-up of those standards can lead to management and reduction of sources of pollution so decreasing pollutant concentrations and subsequent relevant health risk factors to ensure healthy residents [62]. Moreover, air quality standards setting may be considered to be a reliable method for reducing exposure to air pollutants.
Air quality guidelines have been published by WHO in 1987 and they were revised in 1997 [64]. U.S.EPA has set National Ambient Air Quality Standards (NAAQS) for six principal pollutants, which are called "criteria" pollutants [65]. The Ambient Air Quality and Cleaner Air for Europe (CAFE) Directive (2008/50/EC) [66] was published in May 2008. It replaced the Framework Directive and the first, second and third Daughter Directives.
Ambient air quality has been regulated in China since 1982 with setting of initial limits for TSP (Total Suspended Particulates), SO_2, NO_2, Pb, and BaP. In 1996, the standard was both strengthened and expanded from 1982 levels under National Standard GB 3095-1996 but in MEP Announcement [2000] No. 1, the standard was updated with less stringent limits for certain pollutants [67].
Conselho Nacional do Meio Ambiente or CONAMA, the core agency of Brazil's National Environment System (SISNAMA) have setted the brazilian Air quality guidelines but, the national air quality limits are only to be used in absence of local ambient air quality standards [68].
The most recent environmental laws are based on the Kyoto protocol the most important international agreement concerning global environment and signed in the Japanese city of Kyoto on 11 December 1997, by more than 180 countries at the Conference of the COP3 United Nations Framework Convention on Changes Climate (UNFCCC). The treaty entered into force on 16 in February 2005. The Kyoto Protocol represented the first major bank test for negotiation on climate. According to this treaty, all member countries must struggle to reduce by at least 5% below 1990 levels emissions of polluting gases, and therefore harmful to the atmosphere by 2012; in particular, it is necessary to reduce carbon dioxide to avoid the 'greenhouse effect' and the enlargement of the ozone hole [69].

Table 2

POLLUTANT	WHO	NAAQS	CAFE	CHINA	Brazil
PM 2.5	10 µg/m^3 annual mean 25 µg/m^3 24 hour mean	12 µg/m^3 annual mean 35 µg/m^3 24 hour mean	20 µg/m^3 annual mean	15 µg/m^3 annual mean 35 µg/m^3 24 hour mean	–
PM 10	20 µg/m^3 annual mean 50 µg/m^3 24 hour mean	150 µg/m^3	40 µg/m^3 annual mean 50 µg/m^3 24 hour mean	40 µg/m^3 annual mean 50 µg/m^3 24 hour mean	–
O3	100 µg/m^3 8 hour mean	0.075 ppm	120 µg/m^3 8 hour mean	100 µg/m^3 8 hour mean 160 µg/m^3 1 hour mean	160 µg/m^3 1 hour mean
NO2	40 µg/m^3 annual mean 200 µg/m^3 1 hour mean	53 ppb 100 ppb	40 µg/m^3 annual mean 200 µg/m^3 1 hour mean	40 µg/m^3 annual mean 200 µg/m^3 1 hour mean	100 µg/m^3 annual mean 320 µg/m^3 1 hour mean
SO2	20 µg/m^3 24 hour mean 500 µg/m^3 10 minute mean	75 ppb 1 hour mean 0.5 ppm 3 hours mean	350 µg/m^3 1 hour mean 125 µg/m^3 24 hour mean	50 µg/m^3 24 hour mean 150 µg/m^3 1 hour mean	80 µg/m^3 annual mean 365 µg/m^3 24 hour mean
CO	100 µg/m^3 15 minute mean 30 µg/m^3 1 hour mean	–	10000 µg/m^3 (Not to be exceeded)	4000 µg/m^3 24 hour mean 10000 µg/m^3 1 hour mean	40000 µg/m^3 1 hour mean 10000 µg/m^3 8 hour mean
COV	–	–	–	–	–
Nafthalene	10 µg/m^3 annual mean	–	–	–	–
B(a)P	8.7x10^{-5} (UR/lifetime)	No safe level can be recommended.	0.001 µg/m^3 annual mean	0.001 µg/m3 annual mean 0.0025 µg/m3 24 hour mean	–
Tetrachloroethylene	250 µg/m^3 annual mean	–	–	–	–
Formaldehyde	100 µg/m^3 30 minute	–	–	–	–
Benzene	No safe level of exposure can be recommended.	No safe level can be recommended.	5 µg/m^3 annual mean	No safe level can be recommended.	No safe level can be recommended.
Toluene	260 µg/m^3 7 days 1000 µg/m^3 30 minute	–	–	–	–

The Kyoto Protocol is about the emissions of six greenhouse gases:

- carbon dioxide (CO_2);
- methane (CH_4);
- nitrous oxide (N_2O);
- hydrofluorocarbons (HFCs);
- perfluorocarbons (PFCs);
- sulphur hexafluoride (SF_6).

The industrialized countries of Annex I of the Kyoto Protocol, responsible in 1990 for over the half of global emissions of greenhouse gases and subjected to reduction obligations, between 1990 and 2010 have reduced their emissions by almost 9%: 19 billion tonnes of dioxide carbon dioxide equivalent ($GTCO_2eq$) to 17.3 billion. It is very likely that the final figures for the last two years will confirm compliance with the final objective of the Protocol, equivalent to a reduction in emissions by Annex I with, respect to 1990, of at least 5.2% average for the period 2008-2012. However, due to the unexpected and tumultuous growth emerging countries, particularly China, the model of Kyoto Protocol was inappropriate to the objective main of the Framework Convention on Climate Change UN: stabilization of atmospheric concentrations of greenhouse gases at levels not dangerous. In fact, from 1990 to 2010 global emissions have increased from 37 to almost 50 $GTCO_2eq$. If this trend is confirmed, by 2050 it would exceed 80 $GTCO_2eq$, with a consequent increase in the average temperature of the Earth of 4° C, well beyond the 2° C indicated as threshold security from the international scientific community.
During the seventeenth Conference of the Parties Convention, held in Durban in November 2011, it was reached an agreement to draw up by 2015 a new global treaty on climate change that will set new commitments reduction from 2020. In this instrument, which is currently being finalized and is expected to exceed the limits shown by the Kyoto Protocol, are anchored hopes to avoid a climate crisis from the potentially disastrous consequences [70].
Among the countries not members include the US, responsible for 36.2% of the total emissions of carbon dioxide. India and China, which have ratified the protocol, are not required to reduce carbon emissions under the present agreement despite their relatively large population. China, India and other developing countries were therefore exempt from the requirements of the Kyoto Protocol because they were not a major contributor of greenhouse gas emissions during the period of industrialization.
Ban Ki-moon, current Secretary-General of the United Nations, in a recent UN report of November 2014, has issued a dire warning in the latest scientific assessment on Climate Change. The major concerning regards, in fact, the concentration of carbon dioxide which has increased to a level unprecedented in at least the last 800.000 years It warns that, if left unchecked, climate change will increase the likelihood of severe, pervasive and irreversible impacts [69,70].

7. Conclusions

Although Institutions have implemented several containment measures, environmental pollution has nor ceased to be a problem of Public Health. Currently, in Italy, there are about 15.000 sites to characterize, reclaim and monitor that represent more than 2% of the entire territory and require the allocation of 25-30 billion euro.
To solve this situation, firstly rigorous epidemiologic studies must be previewed and conducted, taking into account a careful evaluation phase to confirm the association between environmental exposure and health effects and considering the wide range of contaminants deriving from all industries. Performing a thorough epidemiological investigation is essential to proceed to Risk assessment and Risk management. In the management of this route, greater emphasis must be attributed to activities of Prevention Departments and ARPA and a central role must be performed by technical Committees consisting of experts, that can give useful indications to Legislators to improve and promulgate laws to protect collective health. The aim of this cooperation is achieving a “sustainable risk”, that is the risk that remains after the interventions of control and prevention and that can be more easily managed by the competent bodies.
Not least it is necessary to consider that the bases to make the most of these actions are the training of the operators and the information, so that in this view activities of continuous updating for Public Health professionals must be promoted.

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