Title:

Analysis of airborne contamination distribution in mixed flow cleanroom and consequences in the control techniques

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Introduction

The present analysis can be applied to all vertical mixed flow cleanrooms, that are those where the air introduction is done by terminal HEPA filters installed in the ceiling. It is well known that this kind of typology is largely used as valid technical and economical compromise in order to have the critical working areas protected by unidirectional flows without using a total unidirectional flow cleanrooms. This solution is possible because from many years there are on the market HEPA or ULPA filters able to generate an outgoing air stream with a velocity profile able to fulfil the requirements required for the unidirectional flows. The utilization of these filters gives the possibility of having air just filtered distributed in a unidirectional way directly close to the areas which are the most sensitive to the airborne contamination. Gathering together many of these filters it is possible to achieve the necessary air flow dimensions as they become necessary. These cleanrooms have a large scale application in many sectors as pharmaceutical, food, electronics industries and hospitals. This kind of ventilation system requires an accurate design because the quantity of air to put in to the cleanroom should:

- Be sufficient to protect all the critical areas with the unidirectional air flow,
- Assure the expected contamination class outside of them,
- Assure the inside thermal and humidity conditions,
- Assure the removal of airborne contaminants (gases, particles) from the cleanroom without the creation of zones where the air is stagnant,
- Assure the ambient overpressure
- Assure the comfort conditions for the operators taking into consideration that they can operate in an environment where it's easy to pass through areas with relatively still air and areas where air moves with a velocity of almost 0,5 m/s.

The designer is therefore obliged to carry out an optimization in function of various parameters, sometimes in contrast among them, and moreover, with the necessity to contain the building and maintenance costs. By the usage of models will be shown that knowledge of the transport and removal mechanism of the airborne contamination is a remarkable helpful both to perfect a useful methodology for the evaluation of the ventilation system performance and for system management, certification and design. It will be shown that one useful parameter to assess such transport and removal characteristics is the recovery time measured according to the ISO 14644/3 standard.

1) - Descriptive models of the transport and removal phenomenology of the airborne contamination

1.1) – Models for the evaluation of average concentration

The first models developed were based on the hypotheses of the immediate particles diffusion within the entire volume of the cleanroom neglecting the gravitational deposition (settling) . This ultimate hypothesis is surely valid for particles whose diameter is less than 1 micron due to the fact that their final velocities are certainly lower than the velocities which characterize the motion field in a mixed cleanroom. They give trustworthy results for the evaluation of particles average concentrations, but, as it will be seen, these results are not generally valid for the evaluation of the maximum concentration and for the removal dynamics. This makes unsuitable their utilization for the system management as well as for cleanliness class evaluation in plant design phase, inasmuch the latest one depend on the maximum concentrations of particles in the environment.

We suppose to have a mixed cleanroom, as shown in Fig. 1.1, with the ventilation system off. Inside the chamber, the concentration C_o will almost be constant inside the entire volume. If at the time t = 0 the ventilation system is switched on, the average concentration in function of time, simplifying the general theory, can be expressed with Equation (1) : /2/ ; /3/
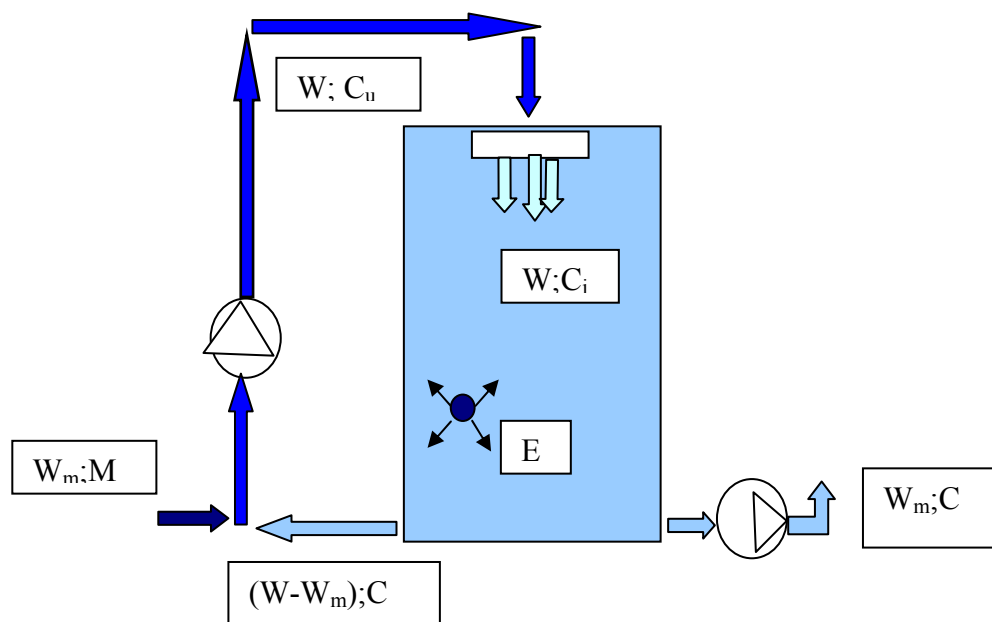

Fig. 1.1: Simplified model of the cleanroom test chamber

$$C = C_o e^{-RAt} + \frac{RMS\ (1-h)+G}{RA}(1-e^{-RAt})$$ (1)

Where :

A   = $[1 - (1 - S)(1 - h)]$
C_0 =   Internal cleanroom particle concentration at t=0, hence when system starting.
R   =   Circulation ratio, W/v
W   =   Total air flow rate
W_m =   Make- up air flow rate
W_r =   Recycled air flow rate
v   =   Clean room volume
M   =   Particle concentration in the make-up air
h   =   Total collection efficiency of the filtration systems
S   =   Ratio between the make-up and total air flow rate = W_m/W
G   =   Total internal particle source per unit of time and volume
C_∞ =   Particle concentration for "t " tending to infinity
E   =   total internal particle source per unit of time, G·v

The first part of Equation (1) is called "Decontamination curve" and it is representative of the internal contamination during transient periods. The second part, instead, is called "Contamination curve". For "t" long enough the value of the concentration can approximately be calculated as shown in Equation (2):

$$ C = \frac{R M S (1 - h) + G}{R [1 - (1 - S)(1 - h)]} = C_\infty \qquad (2) $$

If G = 0

$$ C_\infty = \frac{RMS (1 - h)}{R[1 - (1 - S)(1 - h)]} \qquad (2') $$

The previous equation can also be represented in a useful graphical way for better highlighting the trend, see Figure 1.2.
The term C_∞, for constant values of G, becomes indicative of the average concentration at stationary conditions.

Once the particle diameter to which applying Equation (1) is established, we can define the cleansing coefficient $t_{(100)}$, /1/, as the necessary time to reduce the particle concentration of fixed diameter by a 100 factor, in absence of internal source, namely :

$$ t_{(100)} = -\frac{1}{RA} \ln\left[\left(\frac{C_o}{100} - \frac{RMS (1 - h)}{RA} \right) \left(\frac{RA}{C_o RA - RMS (1 - h)} \right) \right] \qquad (3) $$

for h sufficiently big, as it usually is in HEPA filters, and S sufficient small, as it usually in the cleanrooms, the contamination due to make-up air is negligible and the formula can be simplified as shown in Equation (4):

$$ t_{100} = -\frac{1}{R} \ln\left[\left(\frac{1}{100} \right) \right] = \frac{4,6}{R} \qquad (4) $$

In a real installation the internal source G is never equal to zero. Depending on the carefulness of the installation, on the suitability of construction materials (low surface shedding and easy to clean) and on the cleaning procedures and materials, the internal source can be reduced to values

sufficiently low in "At Rest" conditions, so that it is not influent in the practical determination of the measurements of $t_{(100)}$.

More in general, the Equation (3) can only be used if the value of C_0 is sufficiently higher than C_∞, so that between C and C/100 the decontamination curve approximates Equation 1. In the diagram of Figure 1.2, drawn up in theoretical way from real parameters, it is possible to note how is simple to comply with this hypothesis.

In practice, the theoretical values of $t_{(100)}$ expected with Equation (3) are verified, but only at first approximation, in all the cleanrooms where the hypotheses of immediate diffusion of particles is plausible, or rather only in the case where the distribution is quite turbulent (conventional cleanrooms). In this kind of cleanrooms the introduction of air takes place by means of devices with high induction effect in order to facilitate the mixing between the ambient and the introduced air. In this case the value of C_∞ given by Equation (2) can be taken as the value which approximates the cleanliness class. In the specific case of mixed flow cleanroom, this value will not represent anymore the cleanliness class because within the cleanroom there will be areas much more clean than others, i.e. under the HEPA filters, and areas quite dirtier outside these. Is the contamination of dirty areas that will be determine the cleanliness class. Likewise, the $t_{(100)}$ coefficient will depend on the aerodynamic of these zones and therefore it will be different from the theoretical value given by Equation (3), normally greater.
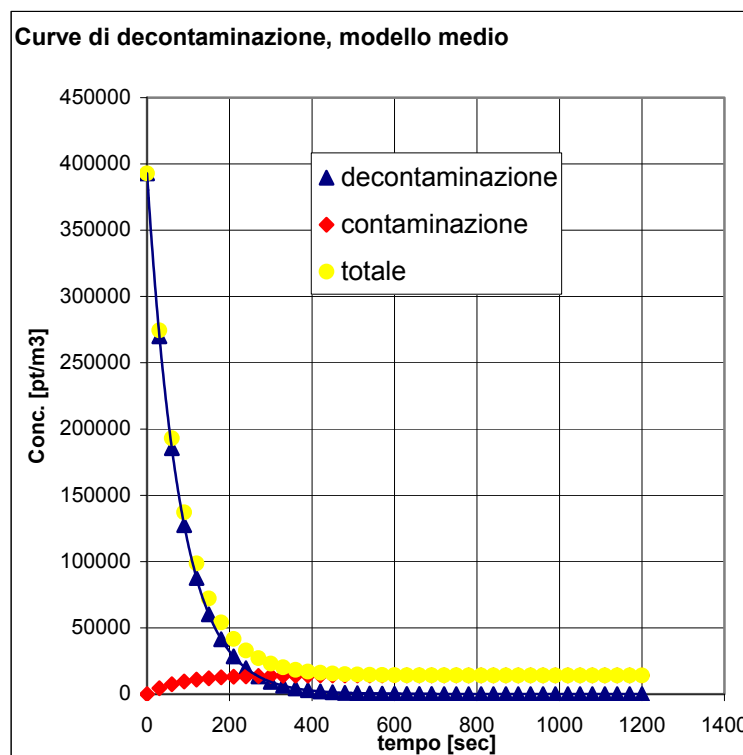

Figure 1.2: Trend of Equation (3) with real parameters

Historically the cleansing coefficient in the form shown in formula 4 was introduced for the first time by Dennis Mc Quillen [1].

1.2) – Two flux models for the evaluation of the maximum concentration

1.2.1) – Particles case

In order to take into account of the real decontamination times, many years ago a two flux model was proposed in which was taken in consideration the not immediate diffusion of the particles. /2/
In this model the particles move inside the clean room carried by means the air flow induced from the main one that come from the terminal Hepa filters. With this hypothesis we have two air flows, one, the main W, that transport the particle outside the cleanroom and the induced flow, W_a, which is responsible for the particles transport within the cleanroom itself. In Figure 1.3/1 the ground plan of the supposed phenomenology is shown .
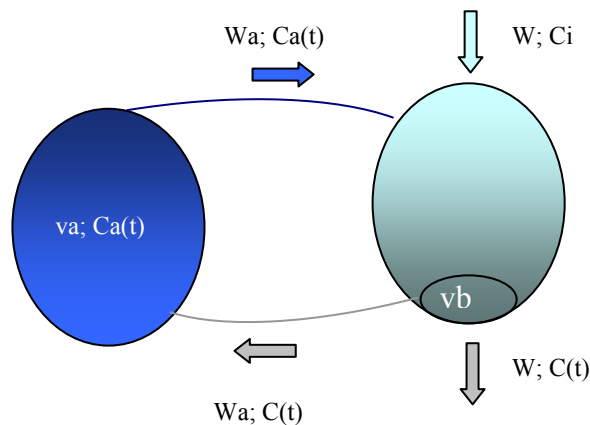

Figure 1.3/1 : Schematization of Two flux ... or particles

In practice, this consists in dividing, functionally, the cleanroom in two parts, one with volume v_a and another one with volume $(v-v_a)$. The volume v_a is the volume that isn't directly interested by the main air flow W, but, by means of the self-induced air flow W_a, contaminates the volume $(v-v_a)$. This volume represents the clean zone under the filters and includes the mixing volume from which the total flow $(W+W_a)$ come out with a concentration C(t). The concentration C(t) represents the air concentration at the cleanroom exit, for example at the exhaust air vent.
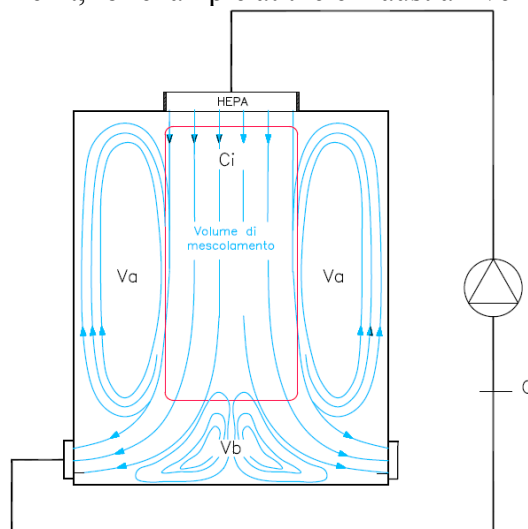

Figure 1.3/2: supposed aerodynamical fluxes as forecasted by the model.

In Figure1.3/2 are shown the supposed aerodynamic fluxes as the model foresees. The volume v_b represents the stagnation volume located close to the floor. This volume is not part of the dirty volume v_a, but is the latest part of the mixing volume. In it the particles concentration should be equal to the average concentration at the exit of the chamber.

Considering G uniformly diffused in all the room volume V and the contamination in the only just filtered air negligible (C_i=0), the mass balance between the entry and exit of the mixing volume gives:

$$C_a(t) = (1+b)C(t) - G(v - v_a)/W_a \qquad (5)$$

with: $b = W/Wa$ as Self-Induced ratio.

For $G = 0$

$$C_a(t) = (1+b)C(t)$$

Taking :

$C_a = C_{ao}$ for $t = 0$.

The concentration in volume v_a become:

$$C_a = C_{ao}\, e^{-\frac{Wt}{(1+b)v_a}} + \frac{G}{W}(v_a b + v)\left(1 - e^{-\frac{Wt}{(1+b)v_a}}\right) \qquad (6)$$

The representative equation of the phenomenology is, also with this model, represented as the sum of two functions, one representing the decontamination and the other one the contamination.
Focusing on the decontamination curve only, relatively to the volume v_a, the cleansing coefficient, that we call "internal", becomes:

$$t'_{(100)i} = \frac{v_a}{W}(1+b)4,6 \qquad (7)$$

from which:

$$C_a = C_{ao}\, e^{-\frac{4,6t}{t'_{(100)i}}} + G\left(\frac{t'_{(100)i}\, b}{4,6(1+b)} + \frac{1}{R}\right)\left(1 - e^{-\frac{4,6t}{t'_{(100)i}}}\right) \qquad (8)$$

For t long enough, the internal concentration at stationary condition becomes:

$$C_{a\infty} = G\left(\frac{t'_{(100)i}\, b}{4,6(1+b)} + \frac{1}{R}\right) = G\left(\frac{v_a}{W}b + \frac{1}{R}\right) = G\left(\frac{1}{R_a} + \frac{1}{R}\right) \qquad (9)$$

In the case that the source G is diffused only within the volume $(v-v_a)$, we obtain :

$$t'_{(100)i} = \frac{v_a}{W}(1+b)4,6$$

$$C_{a\infty} = G\left(\frac{1}{R} - \frac{t'_{(100)i}}{4,6(1+b)}\right) \quad (9')$$

While, if G is diffused only within the volume v_a, we have:

$$t'_{(100)i} = \frac{v_a}{W}(1+b)4,6$$

$$C_{a\infty} = G\frac{t'_{(100)i}}{4,6} \quad (9'')$$

Three important considerations can immediately be inferred :

- The internal cleansing coefficient is independent from the contamination procedure
- The contaminants concentration, at stationary conditions and with constant source, depends on the source position.
- The knowledge of the cleansing coefficient and of the self-induced ratio let us estimate the expected cleanliness class.

The Equation (8) can be written in a more general form which is valid for every kind of contamination procedures, just introducing the term $C_{a\infty}$ in it:

$$C_a = C_{ao}e^{-\frac{4,6t}{t'_{(100)i}}} + C_{a\infty}\left(1 - e^{-\frac{4,6t}{t'_{(100)i}}}\right) \quad (10)$$

If the contamination generation is limited to the volume v_a only, there is a huge simplification. In this case it isn't anymore necessary the knowledge of the "b" value for characterizing the concentration: in fact, now it is sufficient to have only the cleansing coefficient and the source intensity (see equation 9").

The decontamination curve can also be represented in semi-logarithmic scale diagram. If we put in the abscissa axis the time and in the ordinate axis the logarithm of concentrations, the slope of the obtained lines, without the factor 4,6, is equal to the cleansing coefficient. (see Figure 1.4)
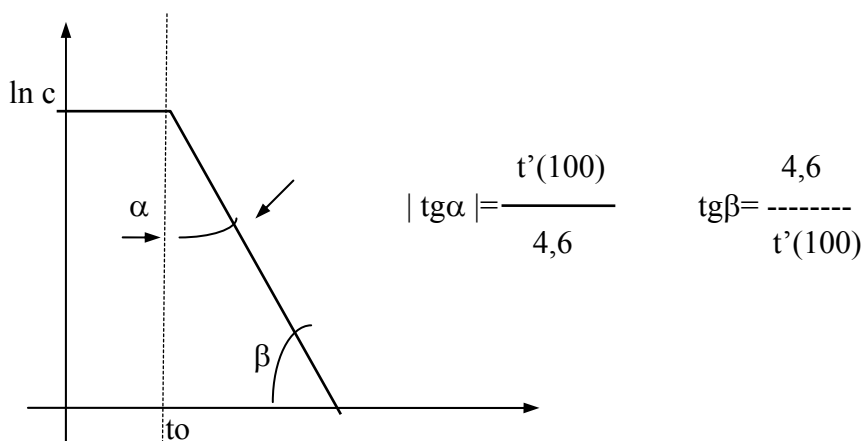

$$|tg\alpha| = \frac{t'(100)}{4,6} \qquad tg\beta = \frac{4,6}{t'(100)}$$

Figure 1.4: method for obtaining "$t_{(100)}$" from experimental measurements

When the measurement of the cleansing coefficient is difficult to perform, it is possible to do an estimation using the formulas quoted in Figure 1.4. This can be useful in those cases where it is not practically possible to contaminate the cleanroom sufficiently or when, due to the low air flow rates, the decontamination curve becomes quickly unstable with the decrease of concentrations. In all of these cases the contamination curve has a sensible influence.

Referring to Figure 1.4 and considering C1 and C2 as two points located in the upper part of the curve, we obtain:

$$tg\beta = log(C1/C2)/(t2-t1)/log(e) = 4,6/t'_{(100)i} \qquad (11)$$

Example:

C1= 9500 pt/ft3; C2=1500 pt/ft3; t1 = 12 s; t2= 320 s.

$tg\beta = 5,993exp(-3)$ from which : $t'_{(100)i} = 767$ s

An remarkable thing that should be highlighted at this point is the identity of the cleansing coefficient whether if it is measured with regard to $C_a(t)$ or $C(t)$ ("external" cleansing coefficient). Indeed, taking into consideration the hypothesis that for particular values of particles concentration is possible to substitute the total contamination trend with the decontamination curve, put G= 0 and dividing Equation (8) by (1+b), it becomes:

$$C = C_o e^{-\frac{4,6t}{t'_{(100)i}}}$$

from which we derive : $t'_{(100)e} = t'_{(100)i}$.

Than the decontamination curves for the volume v_a and for the mixing volume, represented in semi-logarithmic scale diagram, are two parallel straight lines. Furthermore the starting concentrations, C_o and C_{a0} , are different then the lines aren't coincident.

This equality gives, also, the opportunity to obtain a simple method for the determination of "b". If Equation (5) , with G = 0, is solved for b, it gives:

$$b = \frac{C_a(t_n)}{C(t_n)} - 1 \qquad (12)$$

Therefore, if the internal and external cleansing coefficient are experimentally measured simultaneously, it is just enough to introduce into Equation (12) the internal and external concentrations measured at the same instant in order to calculate "b". In this way, the values of "b" for different geometries can be obtained experimentally.

The estimation of the efficiency of a mixed flow system in comparison with a quite turbulent system can be carry out by means the ratio between the two theoretical cleansing coefficient:

$$E_s = t_{(100)} / t'_{(100)i} = \frac{v}{v_a(1+b)} = \frac{4,6}{Rt'_{(100)i}} \qquad 13)$$

The term E_s is always less than 1 and can be considered as an index of quality for cleanrooms. Equation (10), can now be rewritten as:

$$C_a = C_{ao}e^{-E_sRt} + C_{a\infty}\left(1 - e^{-E_sRt}\right)$$

The formulas showed till this moment are suitable for the calculation of the maximum concentration occurring inside a mixed flow cleanroom once the parameters $t'_{(100)i}$ and b are known. Therefore the expected cleanliness class, which is a problem in the design of a system, can be estimated by these formulas. Moreover, they can be utilized for the estimation of the performance with regard to operative procedures variations or clean room restructurings. They also can be a worthwhile tool for the assessment of the environmental deviations impact according to the risk analysis methodologies.

1.2.2) – Gas case

In the nineties years it was supposed an extension towards the study of the distribution of gas contaminants inside mixed flow clean room. This enlargement was based on the observation that the gas diffusion velocities, especially for gases with three or more atoms in the structure, were certainly much lower than the typical clean room inlet air velocities from HEPA filters and that the stratification problem, caused by the motion field, was negligible. In Figure 1.5 is shown the schematization of the supposed phenomenology.
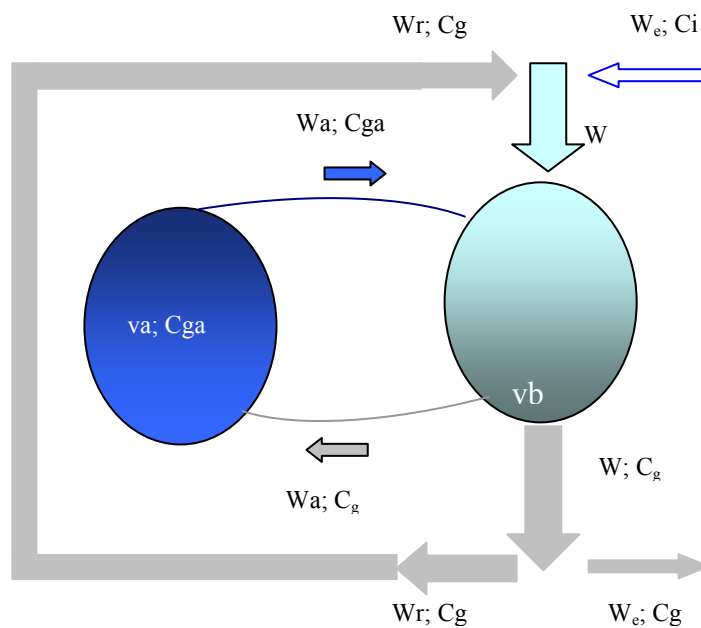

Figure 1.5 : Schematization of the supposed phenomenology for gas

In this case the use of HEPA filter have not impact in gas concentration. In analogy with the particles model, considering G_g uniformly diffused in all the volume v and the gas contamination in make-up air negligible, the mass balance between the entry and exit of the mixing volume gives:

$$W_aC_{ga} + W_eC_i + W_rC_g + G_g(V - V_a)+ = WC_g + W_aC_g$$

$$C_g = \frac{C_{ga}}{1+bS} + \frac{G_g}{W}\frac{b}{1+bS}(V - V_a)$$

The mass balance in the volume v_a, gives:

$$V_a[C_{ga}(t+dt) - C_{ga}(t)] = [W_a C_g - W_a C_{ga} + G_g V_a]dt$$

$$C_{ga} = C_{ga0} e^{-\frac{W}{V_a}\left(\frac{S}{1+bS}\right)t} + \frac{G_g}{WS}(V + V_a bS)\left(1 - e^{-\frac{W}{V_a}\left(\frac{S}{1+bS}\right)t}\right) \qquad (6')$$

The internal cleansing coefficient for gas become:

$$t_{(100)gi} = 4{,}6\frac{V_a}{W_m}(1+bS) \qquad (7')$$

And the equation of self-induced ratio, expressed with gas concentration, is:

$$b = \left(\frac{C_{ga}}{C_g} - 1\right)\frac{1}{S} = \frac{W}{W_a} \qquad (12')$$

It's possible to demonstrate that all the considerations give at point 1.2.1 for particles are valid for gas too, particularly:

- The internal cleansing coefficient is independent from the contamination procedure.
- The contaminants concentration, at stationary conditions and with constant source, depends on the source position.
- The knowledge of the cleansing coefficient and of the self-induced ratio let us estimate the maximum gas concentration.
- The external and internal cleansing coefficient are equal.

Furthermore it's possible to calculate the gas cleansing coefficient from particles related data :

$$t_{(100)gi} = t_{(100)i}\frac{(1+bS)}{S(1+b)}$$

In other words it's possible to calculate the gas distribution when the particles distribution is know.

1.3) – Experimental tests of the two flux model

1.3.1) – Validity and limits of the model for particles

The overall validity of the model has been largely illustrated during the nineties in many applications /2/,/5/,/4/. A better verification have been done by using both tracer gases and particles. This verification was conducted in the cleanroom test chamber at the laboratories of the Lesatec society in Opera , Italy, shown in Figure 1.6. This verification, executed utilising SF_6 like tracer gas and airborne particles generate through Drager vials, was the argument of an experimental master degree thesis /6/ and a summary of this work was presented at the ICCCS Symposium in 2004 /7/.

The results of this experimentation demonstrated in an unequivocal way the descriptive validity of the transport phenomenology of contaminants in the two flux model together with some limits. In particular, after the definition of the system geometry, it was tested:

- The existence of cleanroom zones (v_a) with contaminants concentration practically constant and higher than the average.
- Equality of internal and external cleansing coefficient for both gases and particles.

- The validity of mathematical link between the particles and gases cleansing coefficient.
- The validity of mathematical link between the parameter "b" and both cleansing coefficient and inlet velocity.

The highlighted limits were:

- The strong dependency of the cleansing coefficient, or of the self-induced ratio "b", from the temperature difference between the intake and ambient air in cleanroom (the so called grade of sub-cooling: T_{inlet}-$T_{ambient}$).
- less descriptive correspondence for the internal cleansing coefficient in the case of strong concentrated introduction of contaminants because the self-induced turbulences are not able to make homogeneous, sufficiently rapid, the concentrations inside the volumes v_a. In these situations the parameter that still is descriptively correct is the external cleansing coefficient.
- the possibility of "by–pass" phenomena for high number of circulations ratio in function of particular geometries. The by-pass phenomena introduce a very great error in the external cleansing coefficient measurement.

From the experimental point of view the particles concentration in a characteristic point of the volume v_a (A) and on the exhaust air vent are alternatively measured after contamination during the same cleaning transient period. For this purpose the test chamber was provided with a multipoint iso-kinetics sampling system on the exhaust air vent and with a fixed probe on the point A.

Figure 1.6: Cleanroom test chamber

The particles measurements were alternatively performed with a DPC, during the same test, in order to use the same measuring instrument to minimize the eventual calibration errors. For gas the measure instruments was a photo acoustic multi channel monitoring system.

In Table I are reported some interesting results of this first systematic experimental verification. It's interesting to note the influence of the degree of sub-cooling (ΔT). For example, in correspondence of some values of velocities and sub-cooling degree the values of "b" become negative. In Figures 1.7 are shown the experimental diagrams which help to pick out the phenomenon for both gases and particles. These measurements have been performed contemporaneously for both the gaseous and particles tracers with a constant velocity of air introduction, obtained utilizing an HEPA filter of dimension 610*305 mm.

ΔT[°C]	velocity[m/s]	"b"part	"b"gas	Exp ratio	S
0,6	0,35	-0,39	-0,31	0,51	0,47
0,9	0,44	0,31	0,27	0,47	0,46
0,7	0,55	0,77	0,70	0,49	0,45
0,9	0,36	-0,63	-0,5	0,61	0,58
0,7	0,46	0,28	0,24	0,59	0,60
0,1	0,55	0,52	0,48	0,59	0,57

Table I: Data obtained with an HEPA filter 610*310 mm and the simultaneous measure of cleanliness coefficient for both particles and gases in function of the subcooling degree and the intake air velocity.

In these two diagrams the measurements performed at the point A (fig. 1.9) are indicated with the blue colour, while the ones performed into the exhaust air-vent are in red colour. The degree of sub-cooling, is represented in black colour. The inversion point is the point in which the blue line passes underneath the red line.
As it can be noticed from diagrams this passage takes place at a certain value of the introduction temperature. The overheating of the introduced air is represented by the black line.
From a physical point of view, the "b" value is calculated by Equation 11, this means that after the inversion the concentration in the volume v_a is less than the concentration in the mixing volume, and so, less than the value measured in to the exhaust air vent. Researches conducted with smoke tracers clearly explained the sign change of the parameter "b". Figure 1.8 can help on clarifying the concept.
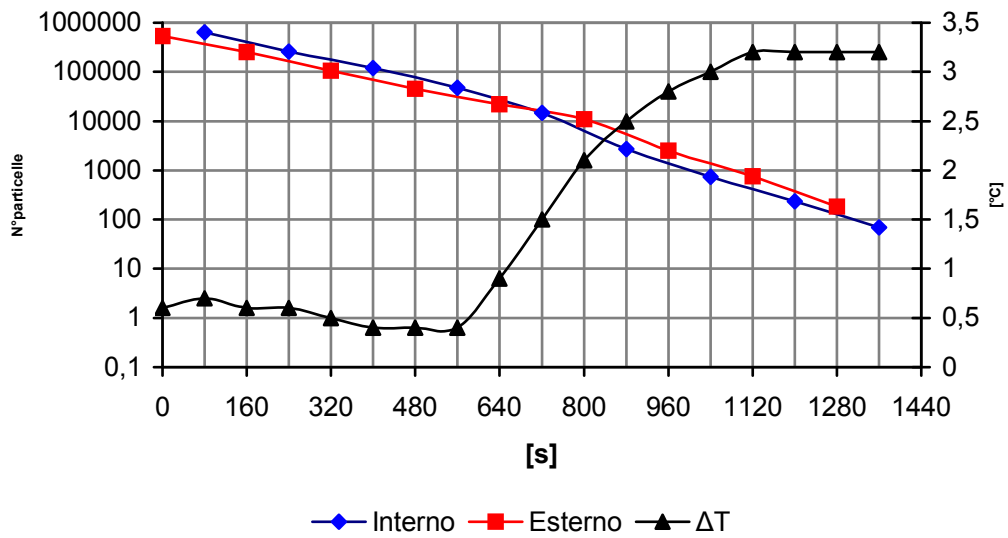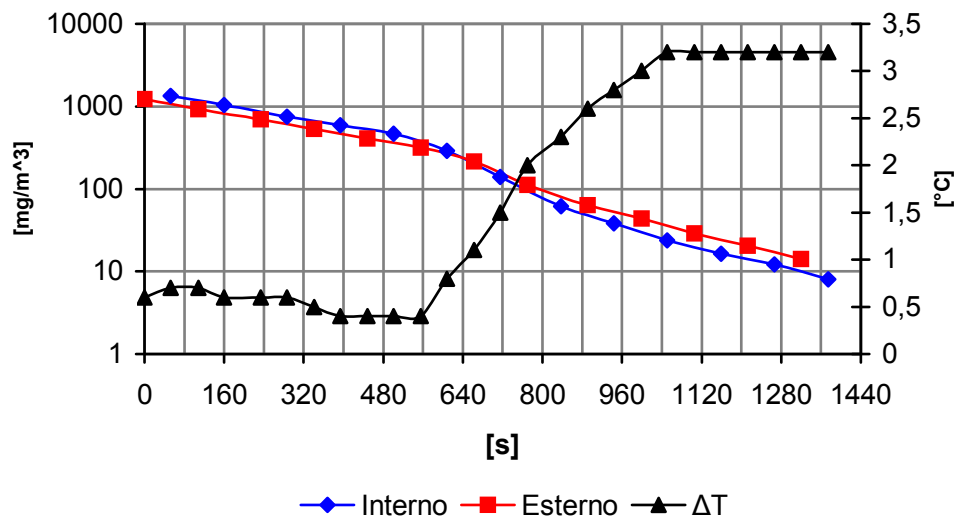
Figure 1.7/a: Inversion test for particles
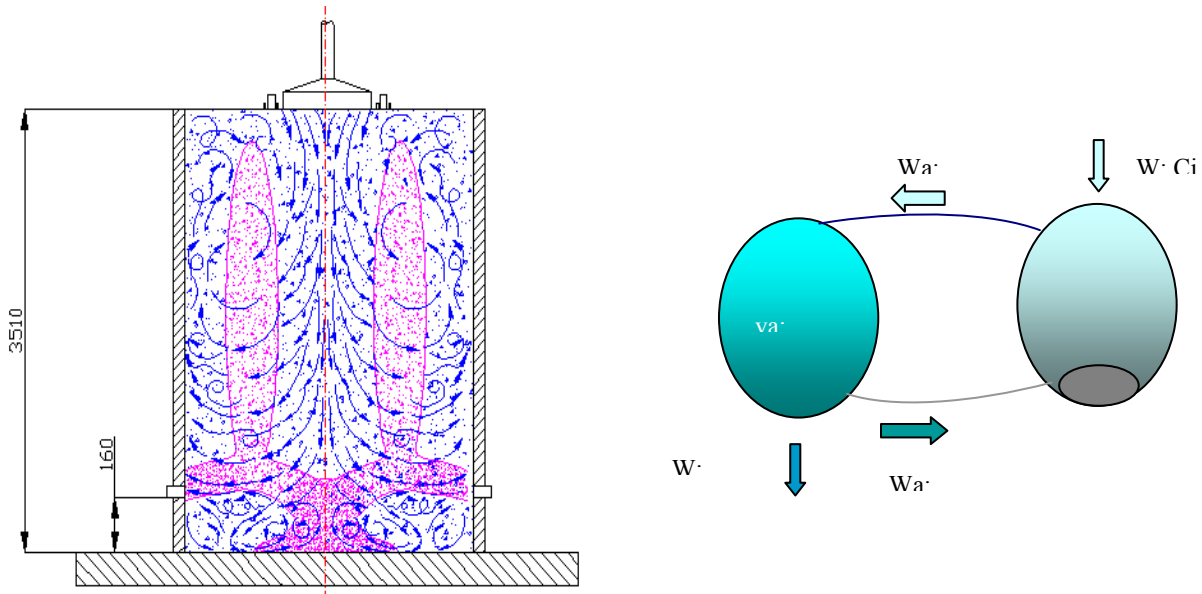

Figure1.7/b: Inversion test for gases

Figure 1.8 : a) Inverted flux model   b) Schematization of the supposed phenomenology

In normal condition of subcooling (-2; -3…°C) the volume with the higher presence of contaminants is the volume v_a while the volume v_b (an apparently stagnation zone located next to the floor directly under the filter) has a lower average concentration, almost similar to that of the air at the exhaust air–vent. As the subcooling decreases, this volume (v_b) becomes the dirtiest volume assuming the characteristics of the volume v_a. Tests conducted with smokes have point out that at the borders of the primary flux micro vortex of mixing were created. These micro vortex, transported by the primary flux, did not affect anymore the volume v_b, but only and immediately the volume v_a. In simple words, it looks like if the primary flux would enlarge itself towards the top of the chamber more than in normal conditions, permitting , in this way, the direct wash of the volume v_a. The scheme in Figure 1.3 is not valid anymore because the flow rate Wa, now, does not entry with a concentration C(t) but rather with a concentration close to Ci. From this volume will still flow out a flow rate W_a with concentration C_a which will go to wash the volume v_b. This inversion of functioning was first demonstrated by means of smoke tracers and than by means of direct measurements of the cleansing coefficient of the volume v_b. Due to the importance of this phenomenology a second field of survey and research were planned as topic of a new experimental master thesis /8/ where the conditions at which the inversion takes place where carefully analyzed using the same instruments properly set for the first experimentation. For the analogy demonstrated between gas and particles, the second study was limited, like contaminant, to the airborne particles.

1.3.2) – Analysis of the inversion conditions

The test were performed in two points inside the room, one located in the volume v_a and another one in the volume v_b, and on the exhaust air vent in function of a prefixed degree of subcooling and for three different values of introduction air velocities.

The test procedure were the same as the first experimentation, hence for every test the internal and external cleansing coefficient were contemporaneously determined. The measured data were utilized for obtaining a descriptive equation of the inversion condition by means of the dimensional analysis. The measurement points, utilized for this purpose, are shown in Figure 1.9.
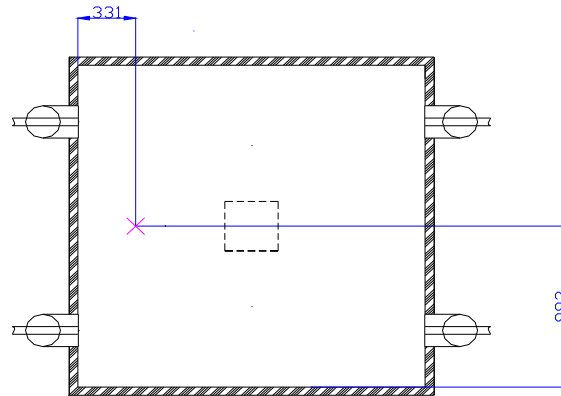
Figure1.9: positions of the sampling points (locations). Point A is indicated with X ,while point B with the square located in the centre. The height of point A is of 1500 mm from the pavement, while for point B is 300 mm.

i) Experimental data

Some of the tests performed relatively to the point A and B are shown in the diagrams of Figures 1.10 and subsequent. The same as before, the blue points represent the measures in the point A and the red ones in the exhaust air-vent. The green point are representative of the concentration in the point B. In order to facilitate the comprehension in the various diagrams are also shown the test conditions, the representative equations of the decontamination curves, obtained by interpolation, the relative cleansing coefficients and the value of "b".
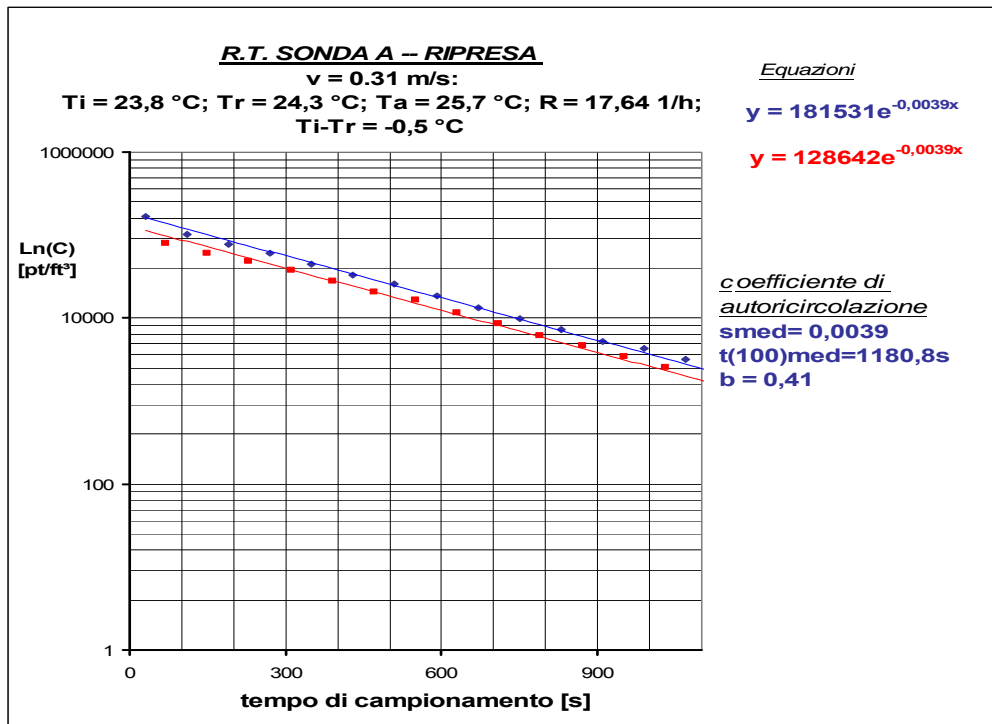
Figure 1.10: Decontamination curves

R.T. SONDA A – RIPRESA
v = 0.31 m/s:
Ti = 23,6 °C; Tr = 23,5 °C; Ta = 22,5 °C; R = 16,97 1/h;
Ti-Tr = +1,1 °C

equazioni:

$y = 194385e^{-0,0053x}$

$y = 573635e^{-0,0053x}$

coefficiente di autoricircolazione
smed= 0,0053
t(100)med=868,9s
b =- 0,66

Ln(C) [pt/ft³]

tempo di campionamento [s]

Figure 1.11: Decontamination curves

R.T. SONDA A -- RIPRESA
v = 0.31 m/s:
Ti = 24 °C; Tr = 24,5 °C; Ta = 26 °C; R =16,97 1/h;
Ti-Tr = -0,5 °C

equazioni:

$y = 33991e^{-0,004x}$

$y = 132858e^{-0,0041x}$

coefficiente di autoricircolazione
s= 0,0041
t(100)med= 1137 s
b=-0,74

Ln(C) [pt/ft³]

tempo di campionamento [s]

♦ Serie1
■ Serie2
— Espo. (Serie2)
— Espo. (Serie1)
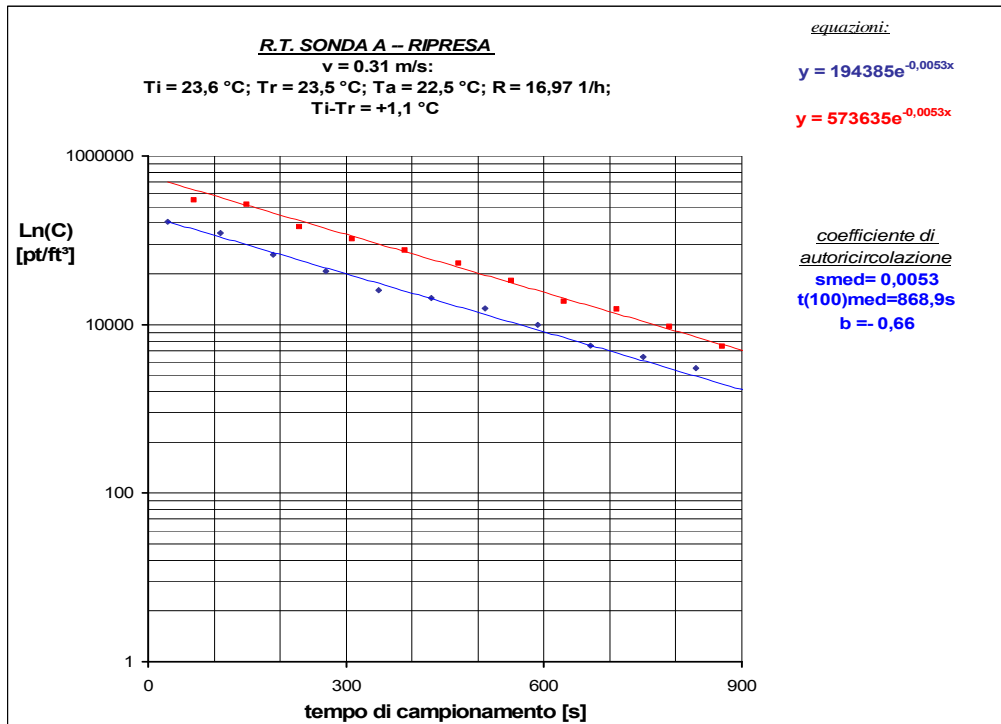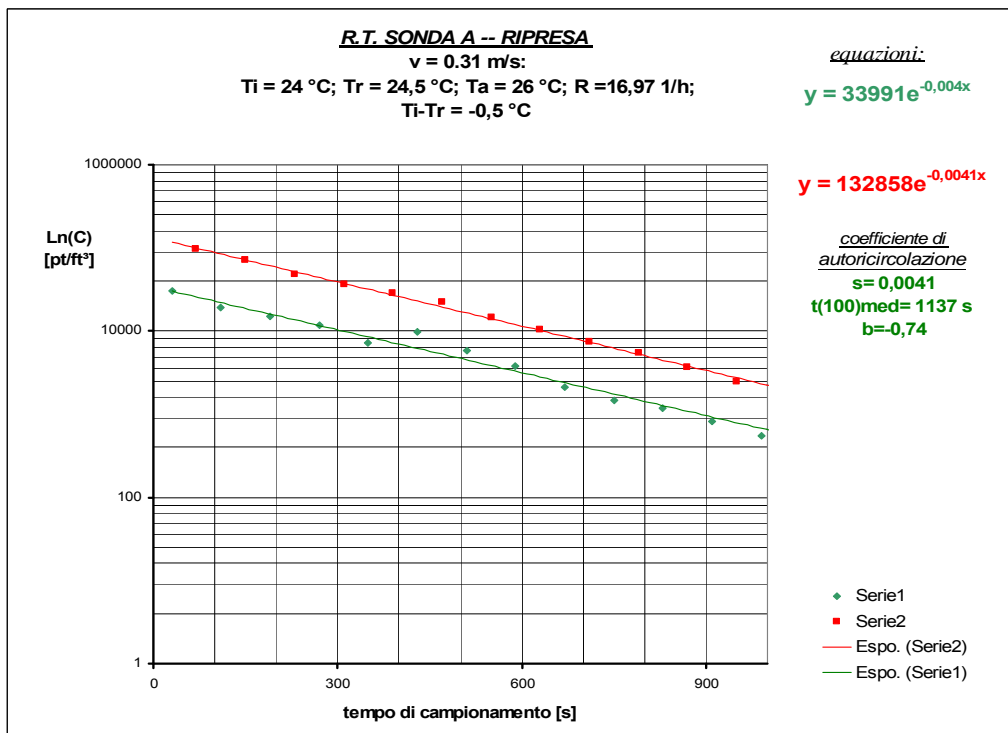
Figure 1.12: Decontamination curves
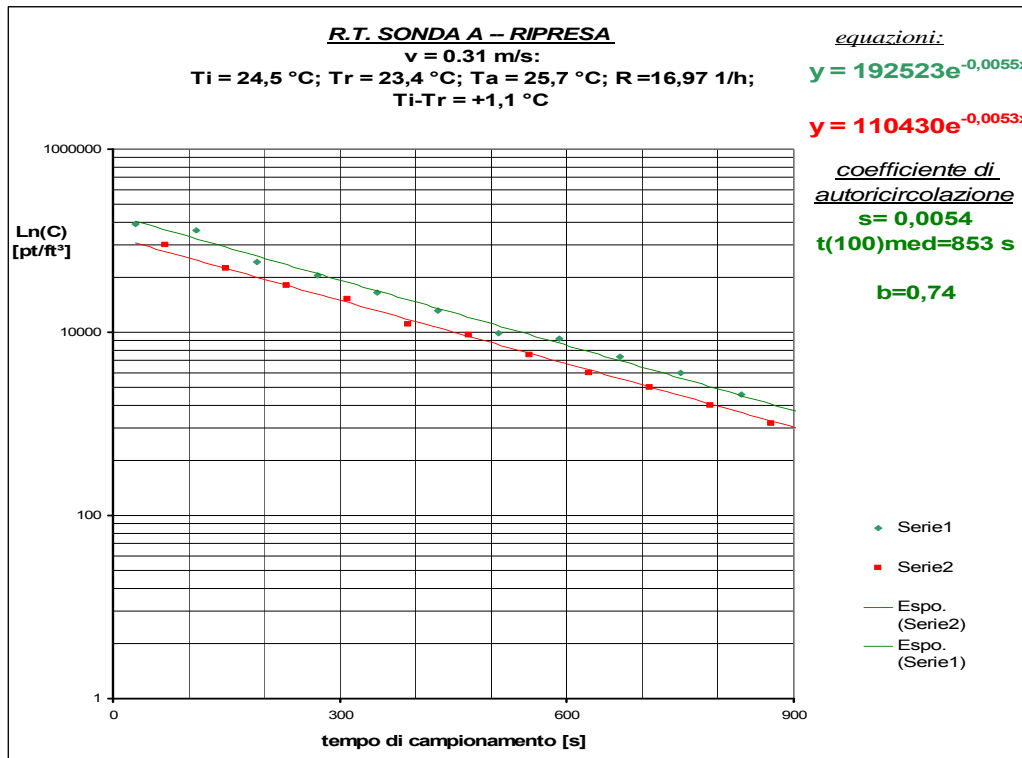
Figure 1.13: Decontamination curves

The global results are shown in synthetic form in Table II and charted in Figure 1.14 using the usual convention for the colour of points.

Ti - Tr [°C]	v = 0,31 m/s		v = 0,41 m/s		v = 0,51 m/s	
	b(A)	b(B)	b(A)	b(B)	b(A)	b(B)
-0,5	0,41	-0,74	0,68	-0,47	1,42	
-0,3	0,33	-0,5	0,35	-0,77	0,65	
-0,1	0,14	-0,43	0,28	-0,68	0,58	-0,91
0,1	0,03	-0,25	0,16	-0,55	0,46	-0,81
0,3	-0,25	-0,24	0,11	-0,34	0,44	-0,51
0,5	-0,3	-0,48	-0,02	-0,05	0,28	-0,43
0,7	-0,53	0,34	-0,22	0,23	0,15	-0,38
0,9	-0,59	0,43	-0,12	0,32	-0,01	-0,10
1,1	-0,66	0,74	-0,46	0,44	-0,35	0,05

Table II: Data recapitulation for the values of "b" calculated for the volumes v_a and v_b

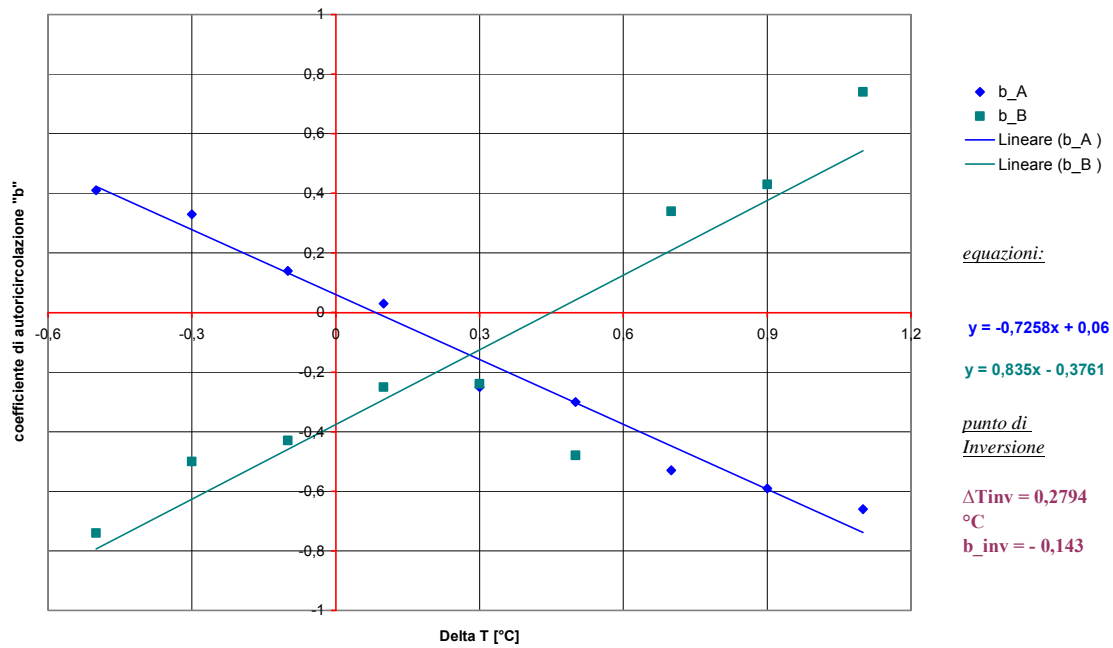Figure 1.14a: Trend charts of b in function of (Ti-Ta) for V= 0,31 m/s
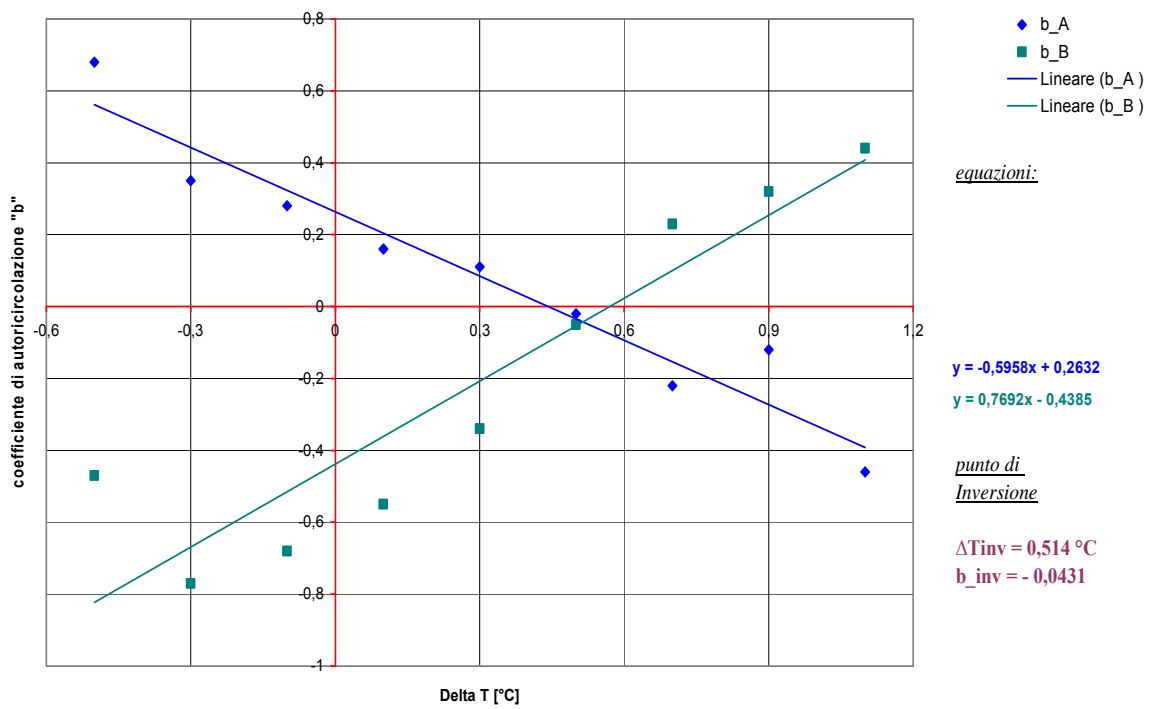

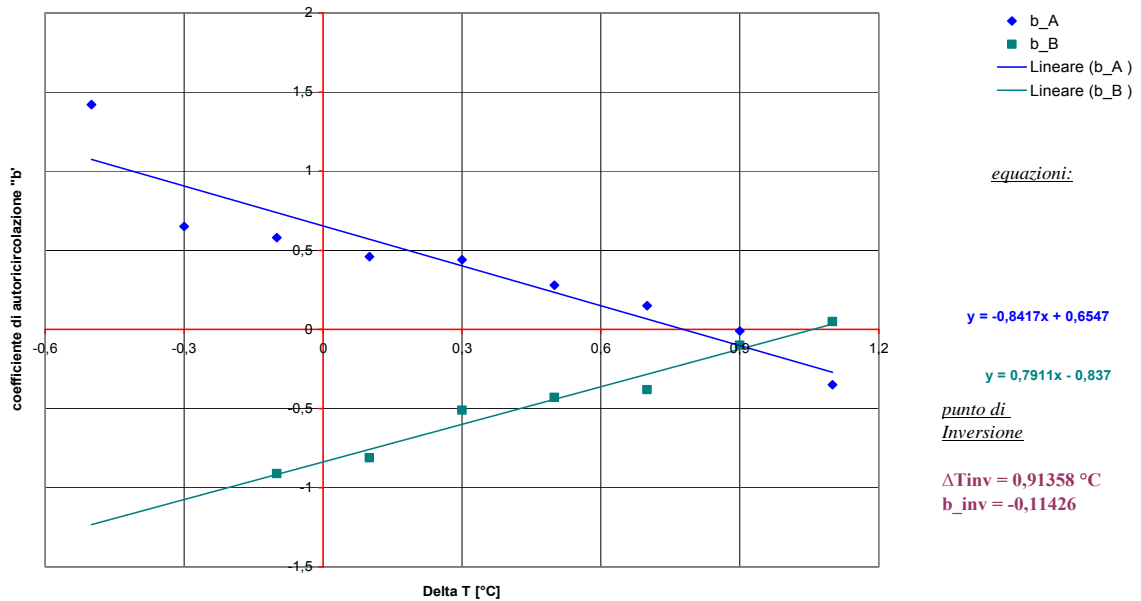Figure 1.14b: Trend charts of b in function of (Ti-Ta) for V= 0,41 m/s

Figure 1.14c: Trend charts of b in function of (Ti-Ta) for V= 0,51 m/s

From the data shown in the table one can infer the considerable dependence of the cleansing coefficient from the degree of sub-cooling in particular for introduction velocities quite low.

One can, moreover, pinpoint an important detail, in reality it is better to consider an inversion zone rather than an inversion point. Indeed, in all the three charts the points in common with the interpolation lines are characterized by negative coordinates, sign that exists a zone of instability in which there is an intermediate functioning, hence in between the two forecasted functionings. On the other hand, in the zones where the coordinates are positive, the functioning results stable.

ii) Data generalization

The generalization of data has been done by means of the dimensional analysis performed with the BUCKINGHAM method. In particular, taking the reference system with M (mass), L (length), T (time) and Θ (temperature), it was chosen to consider as primary quantities relevant to the inversion problem the following :

- temperature difference between the introduced air and the one recirculated**,** ΔT expressed in $[\Theta]$

- density of the introduced air**,** ρ expressed in $\left[\dfrac{M}{L^3}\right]$

- velocity of the introduced air evaluated under the filter, v_i expressed in $\left[\dfrac{L}{T}\right]$

- self induced air flow rate, W_a expressed in $\left[\dfrac{L^3}{T}\right]$

- filter section, A_f expressed in $\left[L^2\right]$

- dynamic viscosity or air, μ expressed in $\left[\dfrac{M}{LT}\right]$

- specific heat of air, c_p expressed in $\left[\dfrac{L^2}{T^2\Theta}\right]$

- height of chamber, h expressed in $\left[L\right]$

- gravitational acceleration, g expressed in $\left[\dfrac{L}{T^2}\right]$

Finally, the experimentation has noticed that variations of the temperature of the introduced air cause variations in the interaction between the unidirectional flow and the air present in the environment, this is caused most probably due to slight differences in the air density.

Supposing that the air undergoes, in the mixing volume, a transformation which can be approximated with a polytrophic, the local variation of pressure can be linked to the density variation of air through the following relation:

$$\frac{p}{\rho^n} = \cos t$$

Deriving this expression with respect to the specific volume one can obtain the last relevant quantity :

- $$\varepsilon = \frac{n \cdot p}{\rho} \text{ expressed in } \left[\frac{L^2}{T^2}\right]$$

Being 10 the primary quantities hypothesized and 4 the measuring units used, the ultimate relation will be represented by an equation like that:

$$\phi(\Pi_1;\Pi_2;\Pi_3;......\Pi_6) = 0$$

Finally, the relation obtained is:

$$b = \Psi\left(\frac{c_p \cdot \Delta T}{g \cdot h};\frac{\rho \cdot v_i \cdot h}{\mu};\frac{n \cdot p}{\rho \cdot v_i^2}\right)$$

which, by analogy with the experimental data obtained and shown in the charts of Figure 1.14 can be rearranged in a different form, as shown:

$$b = \xi \cdot \frac{c_p}{g \cdot h} \cdot \Delta T + \sigma \cdot \frac{\rho^2 \cdot v_i^3 \cdot h}{\mu \cdot n \cdot p}$$

where the values of ξ and σ can be extracted from the experimental data. Making a short resume, one can have:

- for the series "A –R"

$$b_{AR} = -0.018 \cdot \frac{c_p}{h \cdot g} \cdot \Delta T + 1.524 \cdot \frac{\rho^2 \cdot v_i^3 \cdot h}{\mu \cdot p}$$

- for the series "B –R"

$$b_{BR} = 0.0225 \cdot \frac{c_p}{h \cdot g} \cdot \Delta T - 3.593 \cdot \frac{\rho^2 \cdot v_i^3 \cdot h}{\mu \cdot p}$$

Taking $b_{AR} = b_{BR}$, one can obtain the relation that links the ΔT of inversion velocity for a defined geometry.

It's interesting to note that is possible to use these particle transport model to determine the b value in function of internal temperature distribution and, of course, internal heat generation. In other word it's possible to use the two flux model to investigate the distribution of gas, particles and temperature too inside a cleanroom. From this point of view the cleansing coefficient is a good parameter for the description of internal aerodynamic efficiency.

iii) Consideration about the by-pass factor

Due to the difficulty of evaluation of the internal cleanliness coefficient one could think to measure the external cleanliness coefficient, or rather to perform the measurements on the ducts or exhaust air-vent.
The possibility of evaluating the cleansing coefficient in this way exists in reality and it was also demonstrated the equality of the internal and external parameters. Moreover, the decontamination curves are performed at "at rest" conditions and with a level of concentration almost stable within the cleanroom, therefore they do not depend, taking into account all the hypotheses done, that G has a diffuse or concentrated behaviour. However there is a phenomenon that makes these two parameters totally different in the case of mixed flow cleanrooms with an high number of recirculations. This phenomenon is due to the fact that part of the clean introduced air doesn't completely mix with the air in the environment before it reaches the exhaust air-vent. So, for high recirculation, part of the air can by-pass the mixing volume and consequently can not contribute to the removal of the airborne contaminants present in the environment (see Figure1.15). In this case there is not anymore the correspondence between the internal and external coefficient, in particular the external coefficient tends to become much smaller than the internal one. Extensive measurements performed in real cleanroom with high number of air change, have confirmed this behaviour.

It is clear that at this conditions this parameter looses many of its descriptive prerogatives of the cleanroom functioning. To solve the ambiguity between recirculations and cleansing coefficient is

necessary to introduce another important parameter, the by-pass factor (y) which is variable in function of the flow rate within the chamber. The by-pass factor is defined as the ratio between the quantity of air that is introduced and the quantity of air that by-passes the chamber. Therefore it is advisable, if one wants to utilize the cleansing coefficient as an index of functioning of the cleanroom, to refer to the internal one, especially in presence of high recirculation number.
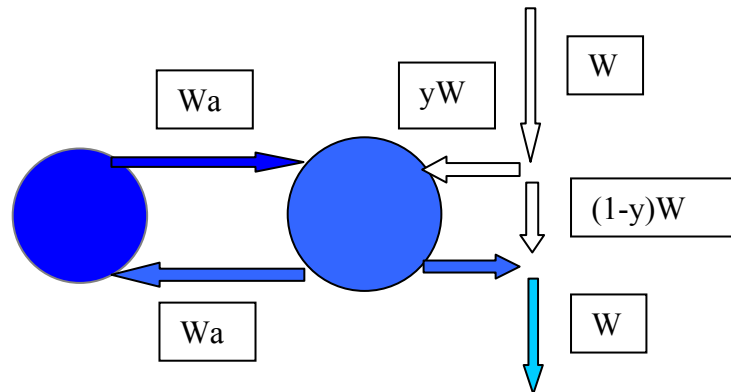
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Fig 1.15: Schematization of the supposed phenomenology in presence of by-pass

1.3.3)- Cleansing coefficient and Recovery Time according to ISO 14644-3

In the standard is described a methodology for the measurements of the recovery time almost similar to that previous described for the calculation of the cleansing coefficient. From the theoretical point of view the two parameter are similar. Some differences in the procedure can, on the other side, lead to different results and make the measured data non useful for the design of systems.

A detailed overview of the standards is here done .

The test is performed for determining the ability of the installation to eliminate the airborne particulate and it cannot be used in unidirectional flow system. The condition for performing the test can be *as built* and *at rest*.

Some definitions are introduced:

-Recovery rate
This parameter measures the speed of variation of the particles concentration

- 100:1-recovery time
It is defined at the necessary time to decrease of 100 times the initial concentration level. If this measurements is possible, the 100:1-recovery time can be directly estimates from the measured data.

The recovery rate has been introduced because, sometimes, it's not possible to perform the direct measure of the recovery time; firstly, because sometimes it not possible to bring the initial concentration to values sufficiently high with respect to the arrival values, other times because the

concentration of the decontamination curve tends really slow towards the final cleanliness level. In this case the recovery rate can give important information on the decontamination kinetics.

Unfortunately the standard does not focus too much on the fact that reliable measurements can be done only in the concentration intervals in which the total contamination curve is comparable to the decontamination curve only, hence in the intervals in which the impact of the internal source of contaminants is negligible.

In the standard are defined two procedures, one for the *recovery rate* and one for the 100:1 *recovery time*.

a) Direct measure of 100:1 recovery time

This measure can be performed when it is possible to increase by a factor of 100 times the initial concentration level (for example the contamination class *at rest*) and when the decontamination curve obtained from the measured data is always decreasing. It is advisable, in order to avoid coincidence errors in the DPC, to perform the test using the measuring instrument set at its highest reading channel which detects the minimum particle diameter measurable by the instrument itself. It is also good, before starting the test, to calculate if the highest concentration that has to be measured is inside the measure limits of the instrument. If this is not possible, it should be either measured the recovery rate or changed the instrument or used a diluter.

The execution modality of the test is:

i)   prearrange the instrument according to the constructor instructions and the calibration certificate's instructions;
ii) locate the DPC probe at the sampling point. The sampling location and the number of samplings shall be determined by agreement between the customer and supplier. The sampling location shall not be located under the device for the air introduction, air-vent or filter;
iii) utilize the same sample volume used for the determination of the cleanliness class. The delay time between measures shall not exceed more than 10s.
iv) the particle diameters used for the measures shall be the same as for the measure of the contamination class. In a case of two diameters have been utilized for the class, it is advisable to use the smallest one. For avoiding problems with non iso-kinetic samplings it is advisable to use diameters less than 1 micron.
v)   The cleanroom area shall be contaminated by means of aerosol with the air ventilation system in function.

Note: the recovery time is normally different from the "clean-up" period described in the Eu cGMP Only for cleanroom Grade B the clean-up period and the recovery time are coincident if we measure the recovery time between "Operational" and "At Rest" conditions.

Estimation of 100:1- recovery time ($t_{0,01}$)

The measured data for every location shall reported on a rectangular charts with time on the abscissa and the concentration on the ordinates. The time scale will be linear, while the concentration scale logarithmic. As many diagrams as the number of sampling locations (points) shall be obtained. The recovery time 100:1 for every sampling location as defined above, can be obtained from the relative diagram.

b) Measure of recovery rate

The test is performed with same modalities and shrewdness as already seen for the recovery time, with the exception that now it is not necessary to achieve such high initial counting concentration. The decontamination diagrams, also in this case, can be built for every single location with the same modalities used for the recovery time.
The estimation is performed in this way:

i- the slope of the decontamination curve shall be estimated for every diagram
ii- the slope represents the recovery rate

This value can also be mathematically assessed as it is done by the equations extracted from Equation (12):

$$n = -2,303 \times \frac{1}{t_1} \log\left(\frac{C_1}{C_0}\right)$$

Where:
n = recovery rate,
C_1 = concentration after time t_1
C_0 = concentration at time "0".

From "n" is, then, possible to obtain recovery time: (out of standard)

$$n = 4,606 \times \frac{1}{t_{0.01}}$$

In the last version of the standard there are no methods for the evaluation of the recovery time for the entire cleanroom.
As one can see, aside from the contamination modalities, there is no theoretical difference between the cleansing coefficient $t_{(100)i}$ and the $t_{0,01}$ recovery time

During the test execution attention to the contamination modality shall be put, because, performing the test with the ventilation system in function, if all the area surrounding the sampling location is not sufficiently saturated with the contaminant, the measured value of recovery time can be quite different from the real one.
During the test it's also necessary to control the degree of sub-cooling, because this parameter have direct connection with the cleansing coefficient.

1.4.4)- Method for the estimation of the cleansing coefficient of a cleanroom from data of single locations

A cleanroom can be thought as constituted of many volumes "v_a" and relatives mixing zones. For this reason, it's split-up in "n" elementary cells each one characterized by a volume v_a, a recirculation ratio and a self induced flow rate so that the cleansing coefficient for each one is:

$$t'_{(100)i} = \frac{v_a}{W}(1+b)4{,}6 = \frac{4{,}6}{K_i} = t_i$$

where K_i are the effective recirculations, less than the real ones. So it gives:

$$K_i = \frac{4{,}6}{t_i} \quad \text{with} \quad K_i = E_s R$$

The mean value for the effective recirculations for all the cleanroom, is:

$$\overline{K}v = \sum_i (Kv)_i \implies \quad \overline{K} = \frac{1}{v}\sum_i (Kv)_i$$

If v_i is equal to v/n, one has:

$$\overline{K} = \frac{1}{n}\sum_i (K)_i$$

One can also write the cleansing coefficient for the entire room as:

$$t'_{(100)i} = \frac{4{,}6}{\overline{K}} = \frac{n\,4{,}6}{\sum_i (k)_i} = \frac{n}{\sum_i \left(\frac{1}{t}\right)_i}$$

2) - Consequences in clean room design and control

2.1) – Choice of sampling locations of the cleanliness class

The ISO 14644/1 standard defines the cleanliness classes by a classification number "N" representative of the maximum allowable concentration, in each sampling location, valuated as the average of the measurements performed at the location. In the current version, a statistical evaluation based on the T–student, is requested if the number of sampling locations are less than 9. Actually, a revision of the standard is on work, and surely the statistical verification will rightly be eliminated. The important thing to highlight is that the cleanliness class is determined by the maximum measured concentration, even if as mean value, in each sampling location. All standards published till nowadays (F.S.; B.S.; JACA; A.S. etc.) accepted this criteria. If this is true, the other logical deduction is that in whatever location the measure is done the condition shall be respected inasmuch the certification of a classification cannot depend on the chosen locations. Till many years ago this principle was well known to technicians and specialists of this field. As a result of that the latest versions of FS 209 defined the number of sampling locations in function of the expected class, this led to a sampling location density of more than $1/m^2$ for the class M3,5 (ISO5). Unfortunately this procedure is slightly changed with the publication of the new ISO standard where the choice of the sampling locations ($n = A^{0{,}5}$) is not intended with same clear aim as before, but only by means of a not always representative geometrical condition.
In the previous chapter it was shown that a mixed flow cleanroom can be considered as group of "dirty" and clean volumes. A correct choice of the sampling locations, should, therefore, interest only the dirty volumes because they are, in principle, the only sensible for the evaluation of the contamination class of air in an environment with controlled contamination.

The previous analysis becomes important for the contamination transport within the unidirectional fluxes for the protection of critical areas, especially taking in to account the new tendencies in controlling and managing of such kind of systems, based on the risk analysis. Often, this transportation is made, during normal working conditions, by direct intervention of the personnel whose degree of "non-cleanliness" depends on the contamination of the dirty volumes where they have passed through. A wrong evaluation of the contamination class would lead to a wrong evaluation of this type of impact over the quality of the final product and to a wrong deviation analysis /9/. For the sampling locations a correct approach should be based on the evaluation of the locations and their positioning in function of the dirty volumes, as well, taking into consideration the minimum number established by the Standard.

Furthermore, from the two flux model one can infer why the statistical verification of the contamination class in the ISO 14644/1 will probably be eliminated. The two flux model simply demonstrates the contemporaneous presence within a cleanroom of clean and dirty areas, well distinguished and affected by different contamination phenomenologies. In the dirty areas the transportation and removal of contaminants occur by means of the induced flow rate Wa, while in the clean areas, underneath the filters, it is caused by the introduced flow rate W whose degree of contamination is fixed and depends on the filtration efficiency of the final filter.

It is clear how regarding the contamination the two things are distinguished and separated, and therefore the measured data cannot satisfy the normal distribution of probability which is necessary for applying the T student distribution. On the contrary, it is thinkable that in stationary conditions, which is quite simple to reach without working activity inside, in the sampling points close to the volumes v_a this distribution is applicable.

It appears clear, from the previous analyses, that the criteria for choosing the control points for the contamination shall be different depending on if the class in unidirectional flows or the class in the entire air of the cleanroom is the parameter to determine. The presence of the mixing volume in the border zones of the unidirectional fluxes make problematic for the latest one too a selection criteria purely geometric.

It would be proper that during the operational qualification the entity and the geometry of these zones were verified, for example by means of smoke tracers, with the purpose of individuating the real useful "core" as clean zone for critical operations.

In the recent edition of the European guide line concerning the good manufacturing of drugs, has been introduced, in practice, the almost continuous contamination monitoring for critical area (class A) and for the surrounding environments (class B). Some problems exist for the choice of the sampling locations for class B and C, while there are no problem for the critical areas. As criterion of choice can be suggested of measuring in a point of the dirtiest volume where the operator ,which can interact with critical areas, passes through. The determination of this volume v_a can simply be done by the analysis of the data used for the valuation of the class if the sampling locations have been selected as suggested above. Moreover, the position of the probe does not have to be strictly positioned close to the working plane, because the volume v_a affects the entire height of the cleanroom, therefore it can be positioned also close to the ceiling. The data eventually collected can be utilized in an eventual deviation analysis.

2.2) – Issues connected with the flux inversion

Normally cleanrooms, in operational status, work with an high degree of sub-cooling higher than one degree Celsius, also in winter periods. The problem of inversion would seem inexistent for these applications, specially for air intake velocities higher than 0,4 m/s.
 Two conditions, in which the inversion can occur, exist:

- heating in winter conditions at rest conditions
- operational conditions with heat released by devices

In the first case the occurrence of this phenomenon can lead to a different values of the $t_{0,01}$ measured in winter conditions with respect to the summer conditions.

In particular, it can happen that the cleanroom increases its removal efficiency of airborne contaminants (decreasing of $t_{0,01}$), this never happens in practice because in operational conditions the sub-cooling degree increases and the system goes away from the inversion conditions.
In order to avoid useless and wrong actions for the determining causes of a presupposed anomalous functioning, it would be appropriate to measure, together with the recovery time also the degree of sub-cooling due to the important influence that it can have in the evaluation of $t_{0,01}$, and therefore in the contamination class. Particular attention shall be given to the cleanrooms where the environmental loads are negligible. In this particular condition the inversion phenomenon can happen also in operational conditions causing the modification of the aerodynamic paths of the working areas. As result of this, it would happen that the critical areas would not be anymore Class A environments.

The second case, even if intuitively simple to comprehend, needs some further explanation.
During the normal sub-cooling process the air goes out from the filter with a certain velocity and temperature. The forces that push the air towards the foor of the rooms are, in this case, two: the gravitational force (the entering air have different density than the air in the environment) and the dynamic pressure caused by the initial velocity.

During the heating process the entering air is lighter than the environmental air therefore the gravitational effect will change in an upwards buoyancy effect in opposition to the dynamic pressure caused by the inlet velocity. Namely, it is like if the over-heating of the air decreases the inlet velocity.
In simple way, when the static pressure caused by the density difference between the environment air and the entering air equals the dynamic pressure of the entering air, the last one will no longer continue its path towards the floor and will be forced to deviate. The distance from the emitting filter to where this phenomenon takes place can be estimated in the following way:

$$z = \frac{\rho \, v^2}{2 \, g \, (\rho' - \rho)}$$

Where z represents the distance from the filter, ρ' e ρ the density of the environment and inlet air. The inversion phenomenon starts when the value of "z" becomes smaller than the "h", height of chamber, and becomes predominant for small values of "z".

In the specific case of one device that release heat inside a unidirectional flux it is possible to achieve an analogous modification of the aerodynamic paths as the one generated by the phenomenon of the inversion. For matter of simplicity is considered the isothermal case, namely that environment and inlet air are at the same temperature. If the device produces one warm zone of height, "h", the up-thrust that it will exert per unit of surface will be:

$$p_h \; = \; z \, (\rho' - \rho_h)$$

Where, this time, ρ' is the density of the environment air equal to the inlet air, and ρ_h will be the density of the air heated by the device. If p_h is equal to the dynamic pressure of the inlet air, it means that the inlet air will not continue downwards but it will be forced to deviate. The over-heating caused by devices can be of many degrees Celsius, thus p_h can result notably higher than the dynamic pressure of air at the inlet. Even though is generated in a different way, the final effect that is reached is analogous to the inversion phenomenon, with the difference that it can be generated independently from the heating/cooling regimes and most probably during working conditions.

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