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**INHALABLE DUST MEASUREMENTS AS A FIRST APPROACH TO ASSESSING  
OCCUPATIONAL EXPOSURE IN THE PHARMACEUTICAL INDUSTRY**

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## **ABSTRACT**

Occupational exposure to active ingredients in the pharmaceutical industry has been the subject of very few published studies. Nevertheless, operations involving active powdered drugs or dusty operations potentially lead to operator exposure. The aim of this study was to collect occupational exposure data in the pharmaceutical industry for production processes involving powdered active ingredients. While the possibility of assessing drug exposure from dust level is examined, this article focuses on inhalable dust exposure, without taking chemical risk into account. 377 atmospheric (ambient and personal) samples were collected in nine drug production sites (pharmaceutical companies and contract manufacturing organizations) and the dust levels were assessed. For each sample, relevant contextual information was collected. A wide range of results was observed. These were, among others, site- and operation-dependent. Exposure to inhalable dust levels varied from 0.01 mg/m<sup>3</sup> to 135 mg/m<sup>3</sup>. Though restricted to dust exposure, the study highlighted some potentially critical situations or operations, in particular manual tasks (loading, unloading, mechanical actions) performed in open systems. Simple preventive measures such as ventilation, containment and minimization of manual handling should reduce dust emissions and workers' exposure to inhalable dust.

## **KEYWORDS**

Occupational exposure, inhalable dust, pharmaceutical industry, ACCU-CAP<sup>TM</sup>

## INTRODUCTION

In France, the pharmaceutical industry employs approximately 110,000 people, over a third being involved in production. Pharmaceutical production workers may be exposed to active pharmaceutical ingredients (APIs) via different pathways (airborne and cutaneous). Indeed, some adverse health effects have long been recognized, and different reviews have summarized the studies published on this subject.<sup>(1-7)</sup> The potential for airborne exposure appears to be more significant when the API is in powder form.<sup>(3)</sup> Workers must therefore be protected from the potential harmful effects of APIs, and this is a relevant challenge in the manufacture of pharmaceuticals, particularly in the production of final dosage form of drugs.

A document intended for the pharmaceutical industry and prevention partners was published in 2001 by one of the French Regional Health Insurance Funds (CRAM- IF: Caisse Régionale d'Assurance Maladie d'Ile de France).<sup>(7)</sup> Among other things, it provided general information about risk assessment and how to assess occupational exposure in the pharmaceutical industry. Some examples of typical dust exposure levels were indicated for various steps in drug production. This document provided an overall picture of what is known about the risk of exposure to drugs during these processes. However, only three field examples assessing exposure were presented, and few details were given.

Control banding can be employed as a useful way to assess potential occupational health hazards in the pharmaceutical industry. Since the 1990s, a great deal of work has been done and several company-specific systems have been developed to classify active ingredients in several categories, generally four<sup>(8)</sup> or five<sup>(9)</sup> according to their toxicity / potency and to their

pharmacological properties.<sup>(10)</sup> Depending on the control banding strategy, these categories are linked to safe handling conditions: level of containment and ventilation engineering; personal protective equipment (PPE). In addition, they can be used to provide occupational exposure limits.<sup>(9-10)</sup> While this methodology has several advantages and interests, it is not within the capabilities of the average hygienist to implement it alone, as it requires a multidisciplinary evaluation of all the available data (pharmacology, medicinal chemistry, safety assessment, clinical research, etc.) to classify a substance without misconceptions.<sup>(8-9)</sup> Moreover, this system has to evolve with new data and new technologies. Besides, air monitoring and wipe tests are recommended to verify that the control measures specified by the control banding strategy are effective and safe. Although it can be considered as useful guidance in achieving a level of control to protect employees, it cannot replace industrial hygiene exposure assessments.<sup>(8)</sup>

More particularly, within the context of risk management, research is being carried out with the intention of developing models that predict a worker's aerosol exposure in the pharmaceutical industry.<sup>(11-13)</sup> These models are supported by a large dataset and relevant contextual information collected in the pharmaceutical industry. They also have to be validated by comparing the results obtained by the model and the measured values. As it is often difficult for those outside the industry to obtain or collect sufficient field data, the pharmaceutical industry alone can develop such models. These expert tools give predictive information on exposure but, like the control banding schemes, they cannot replace the exposure measurements which have to be taken within the framework of an exposure assessment.<sup>(11)</sup>

At an international level, few studies presenting occupational exposure data in the pharmaceutical industry have been published. Among the most recent, a very complete occupational exposure assessment has been conducted during narcotic analgesics production.<sup>(14-</sup>

<sup>15)</sup> Generally, for practical reasons, studies focus on one active substance, and sometimes on its structural analogues, and measure exposures on only a few pharmaceutical sites. While pharmaceutical groups have certainly worked on occupational exposure and have collected data, few studies have been published and information is not available outside the industry.

At the time of designing this study, the French National Research and Safety Institute, INRS (Institut National de Recherche et de Sécurité), and the Regional Health Insurance Funds (Caisses régionales d'assurance retraite et de la santé au travail, (CARSAT), and the Caisses régionales d'assurance maladie, (CRAMs)), all occupational risk prevention partners, had relatively few available data on the French pharmaceutical industry. Indeed, as monitoring in the pharmaceutical industry is not widespread practice <sup>(16)</sup>, their knowledge of assessing occupational exposures to active ingredients remained limited.

The aims of this study were to provide a comprehensive picture of airborne exposure levels in secondary production, to identify problematic operations and to provide some suggestions for risk management. The first step in assessing exposure was to quantify the inhalable dust levels. This yielded useful information about the range of dust concentrations present during the operations involved in the production of pharmaceuticals.

Although determining the inhalable dust level by gravimetry was a simple initial approach, (one sampling device and a simple analytical method), it provided original data on occupational exposure. The interest of these results was above all to identify potentially critical situations linked to dust exposure. To assess occupational exposure in the pharmaceutical industry, a chemical risk assessment is undoubtedly more relevant, as it encompasses the determination of airborne API concentrations. Indeed, in this sector of activity, the main chemical risk is linked to

the presence of API. Its percentage in the formulation and in the dust samples varies and furthermore, both toxicity and OEL are substance-dependent. Airborne API concentrations can either be estimated from the dust concentrations or assessed by direct drug analysis. Ideally a sampling and analytical method is required for each drug of concern. However as the samples of this study encompassed about 50 APIs, the resources available were insufficient to develop specific methods for each. For some samples (about 160), the inhalable dust measurements were completed by quantifying the active substances present in the dust samples after developing six specific analytical methods. The part of this paper concerning the analytical determination is deliberately limited in scope to comparing the drug concentrations to the total dust results for only one API. All the API results will be presented in full elsewhere.

## **METHODS**

### **Plant and work description**

Nine secondary manufacturers of pharmaceuticals and secondary sites (either pharmaceutical companies or contract manufacturing organizations) were visited. Information was recorded about the daily activity of the workers, chemicals handled, processes, local exhaust ventilation, personal protective equipment (PPE), etc. Workers directly exposed to powdered active ingredients were selected first for monitoring.

Occupational exposure was assessed in various work situations; these were classed in 13 categories. The following activities were studied over 10 sampling campaigns, which were conducted in nine different workplaces (E1 to E9) that had agreed to participate in this study:

-E1: weighing, mixing, tablet and capsule production, sachet packing, crushing, tablet-press cleaning, blister packaging.

-E2: calibration, tablet-press cleaning, tablet production, sachet packing.

-E3: tablet production, sieving, microgranule production by conventional turbine ( $\mu$ gran CT) and by Fluid Air Bed (FAB) Technologies ( $\mu$ gran (FAB)), weighing.

-E4: tablet production, weighing, sieving, microgranule production by conventional turbine ( $\mu$ gran CT) and by Fluid Air Bed (FAB) technologies ( $\mu$ gran (FAB)), blister packaging.

A second assessment was carried out on production site E4 following changes in equipment and aeraulic conditions:

-E4bis: tablet production, sieving, mixing

-E5: tablet production, tablet-press cleaning, weighing, wet granulation and Fluid Air Bed drying (gran - FAB drying).

-E6: tablet production, crushing, loading - mixing.

-E7: tablet production, wet granulation and Fluid Air Bed drying (gran - FAB drying), tablet film coating.

-E8: weighing, wet granulation and Fluid Air Bed drying (gran - FAB drying), tablet production, mixing, crushing.

-E9: loading-unloading, weighing, unloading after spray drying.

In E7, all the samplings concerned different activities involving the handling of powders composed of excipients and one API, the antidiabetic API1 (the author is bound by law to keep the identification of this drug confidential). The presented results are focused on the different productions steps of identically dosed tablets.



## **Sample collection**

Personal exposure to inhalable dust was measured using a 37 mm diameter closed face cassette (CFC) (Millipore model) fitted with an ACCU-CAP<sup>TM</sup> insert (MEC: 37 mm/0.8 µm or PVC: 37mm/5 µm, Arelco) attached to an MSA air sampler (Escort ELF). Standard gravimetric methods were used to assess the weight concentration of aerosols, in accordance with Metropol protocol 002, as recommended by INRS.<sup>(17)</sup> The ACCU-CAP<sup>TM</sup> is an accessory sampling capsule rather than a complete sampler. It can be inserted into the 37 mm diameter cassette to prevent loss of particles due to aerosol deposits on the inner cassette walls. This capsule is used with a two-piece cassette and support pad. The dome-shaped ACCU-CAP<sup>TM</sup> capsule is molded from clear, static-dissipative plastic and is heat-sealed to the sampling filter.

Airflow was set to 2.0 l.min<sup>-1</sup>. The sampling head was positioned within the breathing zone. When a respiratory protective device was part of the operator's PPE, the sampling head was placed outside the face piece. In parallel, ambient air samples (near the workers and the potential emission source) were taken using a similar set-up. Both the work shift and the sampling period generally lasted 8 hours. Only work shift exposures are presented in the results section. All samples were collected during a full workday but were interrupted during lunch and coffee breaks; they typically lasted from 350 to 500 minutes. For each batch of ACCU-CAP<sup>TM</sup> (~20 to 25), an average of six field blanks were taken. The number of blanks ranged from 6 for site E8 (number of samples: 20) to 13 for site E3 (number of samples: 70). The laboratory analysis detection limit ranged from 45 to 113 µg per sample.

## **Dust sample analysis**

The mass of sampled particles was determined by weighing the ACCU-CAP™ before and after particle sampling using an electronic balance (Mettler Toledo, model MX5) to determine the mass concentrations sampled. Prior to weighing, if compatible with the manufacturer's recommendations for the stability of the active ingredients, the ACCU-CAP™ were placed in a non-vacuumed dessicator and dried at 50 °C for at least 4 hours to remove moisture, and then left for at least one night in the weighing room. Weight differences between the second and first weighing operations were corrected using variations in the field blanks. The same transportation, storage and weighing procedures were used for the blanks and the samplers.

Data below the detection limit (DL) were replaced by a 0.5 DL to allow an estimation of geometric means (GM), geometric standard deviation (GSD) and median values (med).

### **API1 sample analysis**

Briefly, each sample collected in E7 was also analysed for API1 after an extraction step without disassembling the cassette, by percolating 5 ml of a specific extraction solution twice. Based on methods found in the literature, the drug was quantified by High Pressure Liquid Chromatography (HPLC) with an Uptisphere PHA column (20X0.32 cm, 5 µm), UV detection being set to 235 nm. Recovery ranged from 0.94 to 1.06. The linearity of the method was verified with standards over the range 0.2 – 100 µg/ml ( $r=1$ ).

## **RESULTS**

Nine pharmaceutical sector sites were surveyed during the study. This allowed a wide range of handling activities, representative of exposure scenarios found in the secondary pharmaceutical

industry, to be monitored. Exposure to inhalable dust was measured by means of 377 atmospheric samples (193 ambient and 184 personal samples). Site E3 provided the largest number of samples (personal and ambient,  $n = 70$ ). Few data are censored. Eleven out of 193 ambient values (6%) are below the limit of detection. No individual concentration is below the limit of detection.

### **Dust levels for each pharmaceutical site**

Table 1 presents the individual data obtained on the different pharmaceutical sites, with  $n$  the number of measurements on each site.

Considering the median, exposure to inhalable dust was lowest on site E6 (med =  $0.21 \text{ mg/m}^3$ ) and highest on sites E2, E3, and E4bis (med = 2.8, 3 and  $3.4 \text{ mg/m}^3$  respectively). The distribution of the values was assessed by the percentage of values lower than  $1 \text{ mg/m}^3$ , values between 1 and  $10 \text{ mg/m}^3$  and values higher than  $10 \text{ mg/m}^3$ . As in most European countries, France has set the occupational exposure limit for inhalable dust “without specific effect” (meaning without effects linked to the chemical properties of the dust) at  $10 \text{ mg/m}^3$ .<sup>(18, 19)</sup> This value was used arbitrarily as an indicative reference to discriminate between situations, and one tenth of this value was used as a second threshold.

Although the median values were all relatively low compared to the  $10 \text{ mg/m}^3$  threshold (the highest being  $3.4 \text{ mg/m}^3$  for E4 bis), concentrations exceeding  $10 \text{ mg/m}^3$  were recorded for five of the nine sites: E2, E3, E7, E8 and E9. For site E4, where two sampling campaigns were conducted, the two sets of values were different: all the values were below  $10 \text{ mg/m}^3$  in both cases, but they were higher in the second campaign for the median, the maximum and the distribution of the values. The highest exposure level,  $135 \text{ mg/m}^3$ , was recorded for site E3

during the production of microgranules by conventional turbine involving manual powder supply, brewing, and open vibrating screen sieving operations.

This value was extremely high, but was correlated with the observations: visible dust emissions, very dusty area, high quantity of airborne particles, etc.

### **Dust levels as a function of main activity**

To get a more accurate picture, data were classed as a function of the main tasks (or the dustier ones). Tables 2 and 3, for ambient and individual samplings respectively, indicate the number of values, the median, the range, the geometric mean and the geometric standard deviation. The last two values are the parameters of a log normal distribution. The reduced sample size does not allow a rigorous log normality test, nevertheless, since the data are right-skewed and since this hypothesis is well admitted, this assumption is considered reasonable<sup>(20)</sup> The abbreviations used to identify the activities are reported in the Methods section.

The geometric means and median values were relatively low compared to the 10 mg/m<sup>3</sup> threshold, for ambient and individual samplings. Comparison of the data presented in Tables 2 and 3 clearly highlights that individual values tend to be higher than ambient ones (geometric mean, median and maximum values). As expected, the geometric means for ambient and personal exposures were correlated ( $R^2=0.64$ ). For the ambient measurements, the highest geometric means and medians were observed for sieving and production of microgranules by conventional turbine, whereas the highest maximum values were obtained for compression (31 mg/m<sup>3</sup>), microgranule production by conventional turbine (8.7 mg/m<sup>3</sup>) and weighing (6.1 mg/m<sup>3</sup>). For the individual measurements, the highest dust exposure levels were measured for the following activities: crushing-calibration (med = 7.1 mg/m<sup>3</sup>), wet granulation-drying (med = 4.4 mg/m<sup>3</sup>),

sieving (med = 4.1 mg/m<sup>3</sup>), and microgranule production by conventional turbine (med = 4.1 mg/m<sup>3</sup>) (Table 3). The maximum values indicate high dust concentrations exceeding 10 mg/m<sup>3</sup> for the above-mentioned activities, loading-mixing and compression. Globally, dust exposures were relatively low for blister packaging, microgranule production with FAB, film coating, and sachet packing (medians of 0.1, 0.3, 0.4 and 0.5 mg/m<sup>3</sup> for individual measurements respectively). Apart from compression, the highest dust exposures were measured for activities involving manual operations performed in a non-confined system and requiring frequent manual powder handling (e.g.: sieving and microgranule production by conventional turbine). In these work configurations, the operators were directly exposed to dust, and powder capture systems were either absent or inadequate. During some sampling campaigns, in addition to the main task, they were also responsible for cleaning, potentially leading to dust reaerosolization.

For several tasks, very high GSDs (>5) were observed (Tables 2 and 3). For some operations, namely crushing-calibration and capsule production, the restrictive number of data (less than 7) may be an explanation. As for weighing and loading-mixing, different ways of handling powders were grouped in each of these task categories. For example, weighing corresponded to either automated or manual weighing, with different kinds of tools, and was applied to various quantities of powder ranging from several grams to several hundred kilograms. There were either active substances or excipients in powder form. This is why the variability of the operations recorded in this task category may explain the variability of the results and the high GSDs.

For compression, a lower GSD could be expected as this operation was more or less the same, whatever the site and type of production. It was generally fully automated, with the feed system placed above a fully contained press system. On exiting the press, the tablets were routed through a deduster. As a rule, the deduster and the containment equipment were connected to vacuum

systems. Problems occurred during some shifts such as clogging in the magnesium stearate (lubricant) feed system, use of compressed air to transport tablets and deduster malfunction, corresponding to degraded mode compressions. In addition, production was also sometimes stopped to clean or dismantle the press. Based on a field assessment, the compression data were divided into three categories: nominal mode production, degraded mode production and cleaning-dismantling operations. Comparison of the geometric means clearly illustrated that the highest dust levels were measured during degraded mode compression for ambient (Table 4) and individual data (Table 5). In spite of this, the GSD remained very high for ambient samples.

### **Relationship between API1 and dust concentrations**

Figures 1, 2 and 3 illustrate the very good linear correlation ( $R^2 = 0.96$ ) between API1 and dust concentrations for tablet production, granulation-FAB drying and tablet film coating respectively.

## **DISCUSSION**

The results presented in this article are representative of the work conditions encountered during sampling. The dust levels were influenced by the efficiency of the ventilation, containment and capture systems. Although the sampling did not take PPE into account, when assessing occupational exposure, it is important to point out that workers wearing respiratory protection were not exposed to the levels indicated. Real exposure levels depended on RPE efficiency, how it was worn, etc.

To our knowledge, this study is the first publication giving detailed results of exposure to inhalable dust in several pharmaceutical plants during different operations. It also forms the basis of a database intended for the various prevention partners working in France. Moreover, while

these data are unlikely to yield any information about chemical exposure, they are still relevant to the identification of certain potentially critical dust exposure situations.

It should be noted that the individual dust exposures varied according to workplace, (Table 1) and that values higher than  $10 \text{ mg/m}^3$  were observed in five plants. The current occupational exposure limit for inhalable dust “without specific effects” is  $10 \text{ mg/m}^3$  in France. However, active substances are present in the pharmaceutical industry, making this limit inappropriate for risk assessment. Thus while inhalable dust values below  $10 \text{ mg/m}^3$  do not guarantee the absence of chemical risk for workers, values higher than  $10 \text{ mg/m}^3$  indicate at least some risk of adverse health effects due to dust. This value was therefore used as an indicative reference to compare among situations. Higher dust concentrations were measured for individual samples. In fact, this phenomenon was also observed for a given task, particularly tasks involving frequent powder handling by the operators. This can be explained by the movements of the operators when performing these various tasks, and by their position close to the dust emission sources. The ambient samples depended on the location of the sampling unit chosen, which was dictated by various constraints (available space, obstacles, etc.).

On the whole, apart from compression, the highest individual dust exposures were measured for manual operations performed in non-confined systems involving frequent manual powder handling, in particular: crushing-calibration, wet granulation-fluid air bed drying, sieving operations and microgranule production by conventional turbine. Indeed, during these operations, potentially critical situations were likely to occur.

For example, the granulator and dryer were closed during production. However, they were frequently opened for manual operations such as powder transfer and unloading / loading, all involving direct operator exposure to the powder. Moreover, cleaning the installations (scraping

the granulator) and some specific interventions on the dryer (maintenance or replacement of dusty filter bags) contributed to dust exposure. Regarding microgranule production by conventional turbine, which involves numerous manual operations (brewing and open vibrating sieving), it should be noted that there was a difference between the exposure levels measured with a manual powder supply (for individual data, GM = 11.4 mg/m<sup>3</sup>, n = 12) and an automated powder supply (for individual data, GM = 1 mg/m<sup>3</sup>, n = 11). Moreover, the seven values higher than 10 mg/m<sup>3</sup> were measured in set-ups using a manual powder supply. These activities may thus be particularly critical in terms of the amount of dust emitted and, as a result, of occupational exposure.

Although comparing our data with other published data is not easy, the dust exposure range provided by one pharmaceutical group is nearly identical to ours for similar activities.<sup>(7)</sup> Nevertheless, the maximum values for compression presented in this article go beyond the bounds of the typical dust exposure levels presented in Note technique n°21 published by CRAMIF.<sup>(7)</sup> This difference is probably due to the higher dust exposures obtained for degraded mode production (see Results section). Other published studies mention inhalable dust measurements from 5.10<sup>-7</sup> to 200 mg/m<sup>3</sup> (n = 381)<sup>(11)</sup> and 5.10<sup>-5</sup> to 12 mg/m<sup>3</sup> (n = 192)<sup>(13)</sup> in a multinational pharmaceutical company. The results are classed by scenario: activity, quantity, powder or granule and presence or absence of local exhaust ventilation. Detailed results are given for some scenarios. Despite the interest of these results, they cannot be compared to the present results as the scenarios cannot easily be associated with a main activity in the present study. Furthermore, contrary to the present study, these are task-based exposure measurements with a very short sampling time (median = 28 min).



It is important to note that the critical operations identified in this study are not specific to the pharmaceutical industry, but are typical of powder handling. Although the type of activity influenced the dust level, this was not the only parameter. The characteristics of the powder (granulometry and dustiness in particular) and the type of collective protective device employed, including the ventilation and containment systems, may also significantly influence results. As the operations are mainly manual and as the worker frequently intervenes in the process, there is also a strong likelihood of worker behavior influencing the results.

As a general rule, tried and tested prevention solutions exist to reduce dust emissions.<sup>(21)</sup> It is not possible to present specific prevention solutions in the present article as several parameters must be taken into account in each specific case, including the existing equipment, the particularities of the pharmaceutical industry, the manufacturing process, etc. Some modifications to the installations (process, ventilation or containment) may require validation before re-starting production. It therefore seems relevant to try to include these steps as early as possible, preferably at the industrial and pharmaceutical development stage of new drugs.

According to the results presented in figures 1, 2 and 3, measuring inhalable dust could be a good way to estimate active ingredient concentrations. However, these investigations are limited because the results are based on a single workplace and a single active substance with only one dosage. A more exhaustive and thorough work <sup>(22)</sup> suggests the drug concentration may be estimated for activities like compression as only mixed powders are handled. For other activities such as the granulation and drying process, this is not possible as the active substance and the excipients are sometimes handled separately. While it can constitute a useful way to determine drug exposure, depending on the process used, the sensitivity of the gravimetric method can be insufficient to assess low dust exposure and low drug exposure, in the order of a few  $\mu\text{g}/\text{m}^3$  or

less. This monitoring strategy will not provide the accuracy of drug analysis assessment, notably in this particular case.

## **CONCLUSIONS**

In the pharmaceutical industry, several tasks are still performed manually in open systems. Some may be a cause for concern in terms of dust and therefore of operator exposure, if personal protective systems are inadequate, not used or worn incorrectly. These include: manual transfer of powders; and mechanical actions on powders or solids in open systems, sieving, calibration, crushing and brewing in conventional turbines, etc.

The data presented show no evidence to suggest cleaning and maintenance operations are critical since few airborne samples were taken for these tasks alone. However, some other measurement methods (not presented) have shown that these activities produce emission peaks or high background noise. In particular, the use of compressed air as a cleaning tool, observed on several sites, should be prohibited. For automated operations and when powders are confined the situations are generally less problematic, except when there is a break in containment (unloading, cleaning and maintenance) or a malfunction.

In this study, 4 % of the inhalable dust exposure concentrations were higher than the current French occupational exposure limit for inhalable dust “without specific effect”. This should be a matter of concern for hygienists, especially since dust containing active substances should have a lower exposure limit. Simple preventive measures such as ventilation, containment and, where necessary or in addition to collective protection, the use of appropriate personal protective

equipment should be included at the design stage of the process in order to try to reduce worker exposures to inhalable dust.

As a first step in assessing drug exposure in pharmaceutical companies, the total inhalable dust can also be used to provide a rough but satisfactory estimate of inhalable API, depending on the process.

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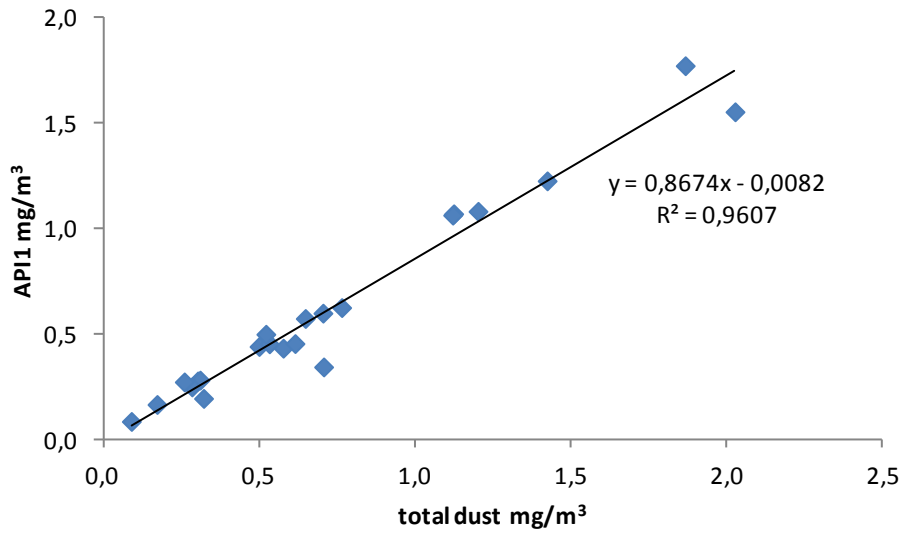


FIGURE 1. Relationship between total dust and API1 concentrations for compression - individual and ambient samplings, n = 22



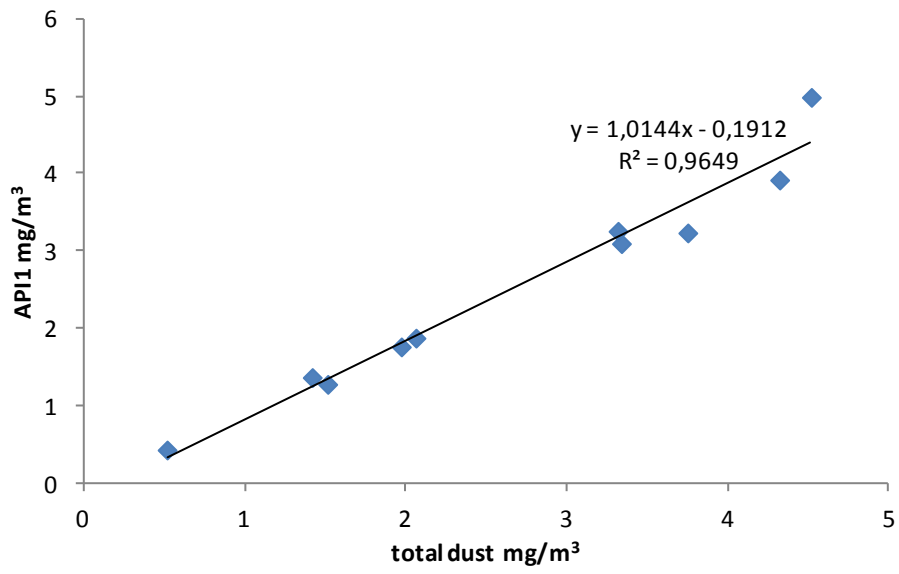


FIGURE 2. Relationship between total dust and API1 concentrations for granulation – FAB drying - individual and ambient samplings, n = 10

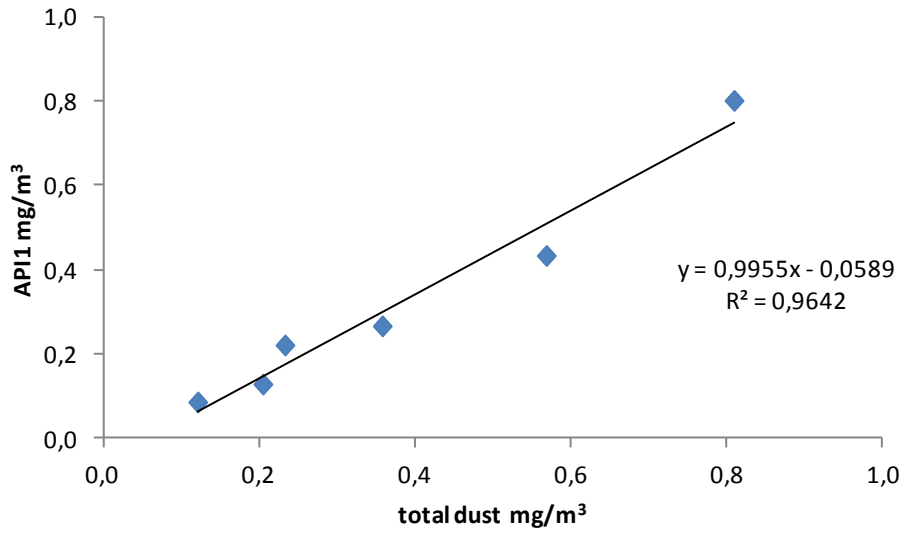


FIGURE 3. Relationship between total dust and API1 concentrations for tablet film coating - individual and ambient samplings, n = 6

TABLE I. Inhalable dust levels measured on the nine production sites – individual samples, n=184.

<b>Production sites</b>	<b>E1</b>	<b>E2</b>	<b>E3</b>	<b>E4</b>	<b>E5</b>	<b>E6</b>	<b>E7</b>	<b>E8</b>	<b>E9</b>	<b>E4bis</b>
<b>n</b>	17	18	24	28	16	16	18	16	16	16
<b>median (mg/m<sup>3</sup>)</b>	0.52	2.8	3	0.57	1.65	0.21	0.70	1.75	1.79	3.4
<b>minimum (mg/m<sup>3</sup>)</b>	0.07	0.38	0.04	0.01	0.14	0.01	0.2	0.07	0.46	0.07
<b>maximum (mg/m<sup>3</sup>)</b>	2.56	23.9	135	5.8	8.3	0.47	13.19	11.7	15.9	9
<b>data &lt;1mg/m<sup>3</sup> (%)</b>	88	23	35	72	38	100	58	38	38	43
<b>data 1&lt; &lt;10 mg/m<sup>3</sup> (%)</b>	12	54	42	28	63	0	38	50	56	57
<b>data ≥ 10 mg/m<sup>3</sup> (%)</b>	0	23	23	0	0	0	4	13	6	0

TABLE II. Inhalable dust levels classed by activity – ambient samples, n = 193

<b>Activity</b>	<b>n</b>	<b>GM (mg/m<sup>3</sup>)</b>	<b>GSD</b>	<b>median (mg/m<sup>3</sup>)</b>	<b>range (mg/m<sup>3</sup>)</b>
weighing	22	0.2	5.6	0.1	0 – 6.1
crushing-calibration	7	0.3	5.6	0.6	0 – 1.3
sieving	4	1.4	2.0	1.1	0.8 – 3.8
compression	62	0.3	7.2	0.3	0 - 31
capsule production	5	0.4	7.0	0.4	0.1 – 4.5
blister packaging	5	0.1	2.3	0.1	0 – 0.3
sachet packing	8	0.5	2.0	0.5	0.2 – 1.3
µgran CT	17	1.1	3.7	1.1	0.1 – 8.7
µgran FAB	23	0.2	2.7	0.2	0 – 0.8
gran-FAB drying	15	0.8	3.5	0.7	0.1 - 4
loading-mixing	15	0.1	5.1	0.1	0 – 2.8
film coating	3	0.3	2.6	0.2	0.1 – 0.8
unloading after spray drying	7	0.5	2.6	0.7	0.1 – 1.5

TABLE III. Inhalable dust levels classed by activity – individual samples, n = 184.

<b>Activity</b>	<b>n</b>	<b>GM (mg/m<sup>3</sup>)</b>	<b>GSD</b>	<b>median (mg/m<sup>3</sup>)</b>	<b>range (mg/m<sup>3</sup>)</b>
weighing	22	1.1	3.2	0.9	0.3 – 9.7
crushing-calibration	7	3.7	5.9	7.1	0.2 - 22
sieving	6	4.7	1.4	4.1	3.4 - 9
compression	55	0.7	3.2	0.6	0.1 – 23.9
capsule production	3	1.8	4.8	2.8	0.3 – 6.6
blister packaging	5	0.1	1.6	0.1	0.1 – 0.2
sachet packing	7	0.5	1.3	0.5	0.3 – 0.7
µgran CT	23	3.5	5.0	4.1	0.2 - 135
µgran FAB	23	0.3	3.5	0.3	0 - 3
gran-FAB drying	12	3.7	2.6	4.4	0.4 – 13.2
loading-mixing	11	0.6	8.3	0.7	0 – 15.9
film coating	3	0.3	1.7	0.4	0.2 – 0.6
unloading after spray drying	7	2.0	2.1	2.2	0.6 - 5

TABLE IV. Inhalable dust levels for compression classed by categories – ambient samples, n = 62

<b>Activity</b>	<b>n</b>	<b>GM (mg/m<sup>3</sup>)</b>	<b>GSD</b>	<b>median (mg/m<sup>3</sup>)</b>	<b>range (mg/m<sup>3</sup>)</b>
nominal mode production	44	0.2	5.6	0.3	0 - 9
degraded mode production	9	3.2	6.3	9.0	0.1 - 31
press cleaning/dismantling	9	0.2	3.9	0.2	0 – 0.9

TABLE V. Inhalable dust levels for compression classed by categories – individual samples, n =

<b>Activity</b>	<b>n</b>	<b>GM (mg/m<sup>3</sup>)</b>	<b>GSD</b>	<b>median (mg/m<sup>3</sup>)</b>	<b>range (mg/m<sup>3</sup>)</b>
nominal mode production	41	0.5	3.1	0.5	0.1 – 23.9
degraded mode production	8	2.3	2.3	2.3	0.5 – 7.7
press cleaning/dismantling	6	0.9	2.1	1.0	0.3 – 2.0