IN-DEPTH SURVEY REPORT:

CONTROL TECHNOLOGY ASSESSMENT OF UNIT OPERATIONS EMPLOYED IN ORAL CONTRACEPTIVE TABLET MAKING OPERATIONS

AT

MEAD JOHNSON AND COMPANY
EVANSVILLE, INDIANA

REPORT WRITTEN BY:
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REPORT DATE:
May 1983

REPORT NO. 105-12a

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
Division of Physical Sciences and Engineering
Engineering Control Technology Branch
4676 Columbia Parkway
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PLANT SURVEYED:	Mead Johnson Evansville, Indiana
STANDARD INDUSTRIAL CLASSIFICATION CODE	Chemical and Allied Products Sector (SIC 28)
SURVEY DATE:	February 7-11, 1983
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INTRODUCTION AND SUMMARY

The Occupational Safety and Health Act of 1970 (PL 91-596) was enacted to "assure safe and healthful working conditions for men and women." The Act established the National Institute for Occupational Safety and Health (NIOSH), which is now in the Department of Health and Human Services. NIOSH was charged by this Act to conduct research and develop criteria for preventing exposure of workers to harmful chemical and physical agents. In response to this legislative mandate, NIOSH has conducted major programs to document, develop, and disseminate information regarding the recognition, evaluation, and control of such agents.

In 1976, NIOSH instituted a major effort to prevent occupational health problems through the assessment and application of control technology in the workplace. This control technology research program involves engineering assessments in which effective options for the solution to employee exposure problems are evaluated and documented. The major goals of the assessment program are to establish a catalogue of solutions by documenting successful applications of control measures, and to foster the more widespread application of these solutions through technology transfer.

Oral contraceptives (OC) have been selected for study because they represent the largest single use of estrogens, and because they are processed using rather typical (but well controlled) pharmaceutical technology. From a control technology point of view, the biological potency of these materials has led manufacturers to implement rigorous control systems. The unit processes employed in manufacturing (preweighing of actives and excipients, mixing and granulation, tableting, and packaging) are common within the pharmaceutical industry. A systematic characterization of the controls used in OC tablet manufacturing is therefore beneficial in batch manufacturing processes wherein similar unit operations and active ingredients of similar potency are employed, both within and outside of the OC processing operations.

In May, 1978, NIOSH conducted a walk-through survey of Mead Johnson's OC tablet-making operation. The survey report[1] concluded that "in general, considerable effort to protect employees from hazardous exposures to estrogenic materials was noted, e.g. -- use of local exhaust ventilation, isolation techniques for packaging as well as compounding and through the use of respiratory protection." Since then, the processing and tableting operations have been relocated and their design and associated controls revised and improved.

PROCESS AND FACILITY DESCRIPTION

GENERAL

Processing and tableting of Ovcon(R) oral contraceptives are performed in the steriod area. Packaging is performed in two rooms that are in a building separate from the steriod area.

PROCESSING

Three workers are involved in the production of Ovcon(R) granulation. Ingredients for several batches, including ethinyl estradiol (EE) and norethindrone (NOR), are weighed at one time. The active ingredients are weighed in a SterilGARD(R) Class II, Type A hood manufactured by The Baker Company. The hood is located in the process weigh room and is shown in Figure 1. Excipients are assembled in the excipient dump room which is directly above the room where the Patterson-Kelly (P-K) blender is located. Each batch of product consists of several hundred pounds of mostly excipients with less than one percent of the active ingredients EE and NOR.

Some excipients are first milled in the excipient dump room in a Fitzmill (Fitzpatrick Mill) shown in Figure 2.[2] The blender is then charged with excipients through a hopper in the excipient dump room fitted with a rotary feeder at the bottom. The hopper is connected to the P-K blender via a flange fitting. After the excipients are charged, the blender is disconnected from the hopper and its discharge opening closed. Active ingredients contained in paper bags are dumped into a small 20-gallon agitated tank containing granulating liquid. A schematic of the tank appears in Figure 3. Nitrogen gas is used to force the solution of the actives to the liquid feeding and agglomerate breaking device contained within the blender (Figure 4).[3] The latter rotates about its axis while liquid is being fed. After wet mixing is completed, the material (called wet granulation) in the blender is emptied into stainless steel drums. The material is then transported in the drums to the oven room and scooped into the hopper of a Fitzmill similar to that shown

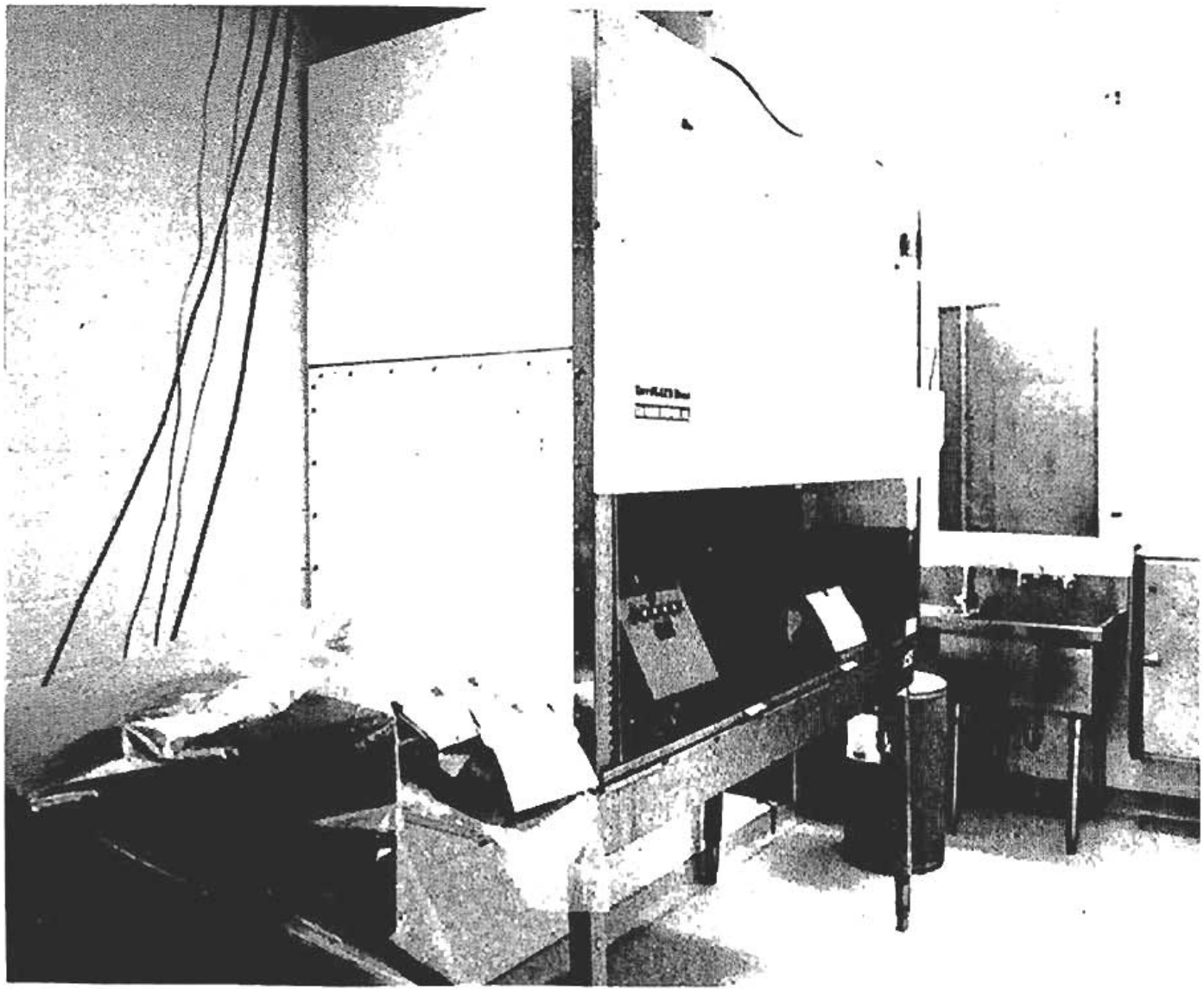


Figure 1 SterilGARD Hood

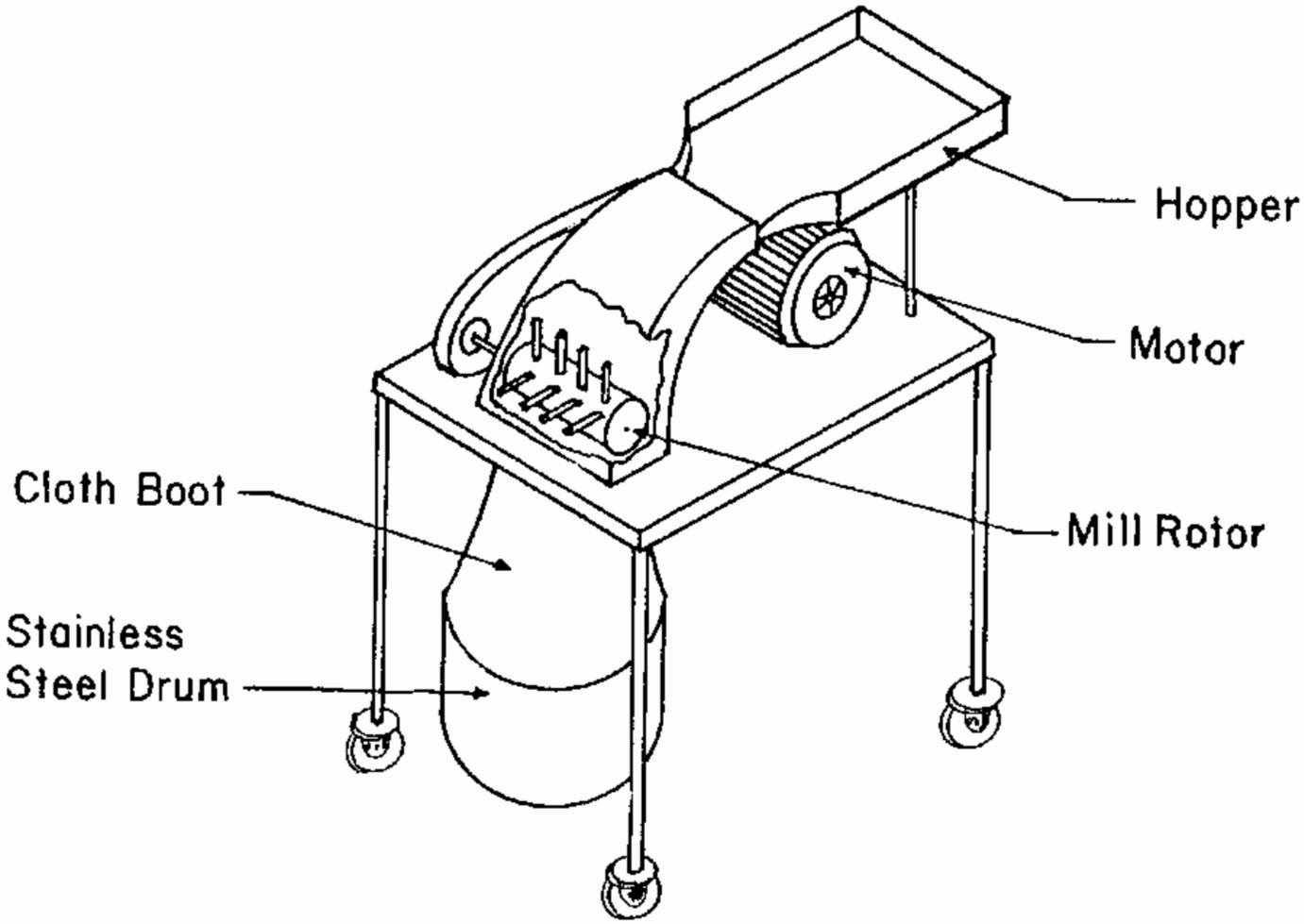


Figure. 2 FITZPATRICK COMMINUTING MILL

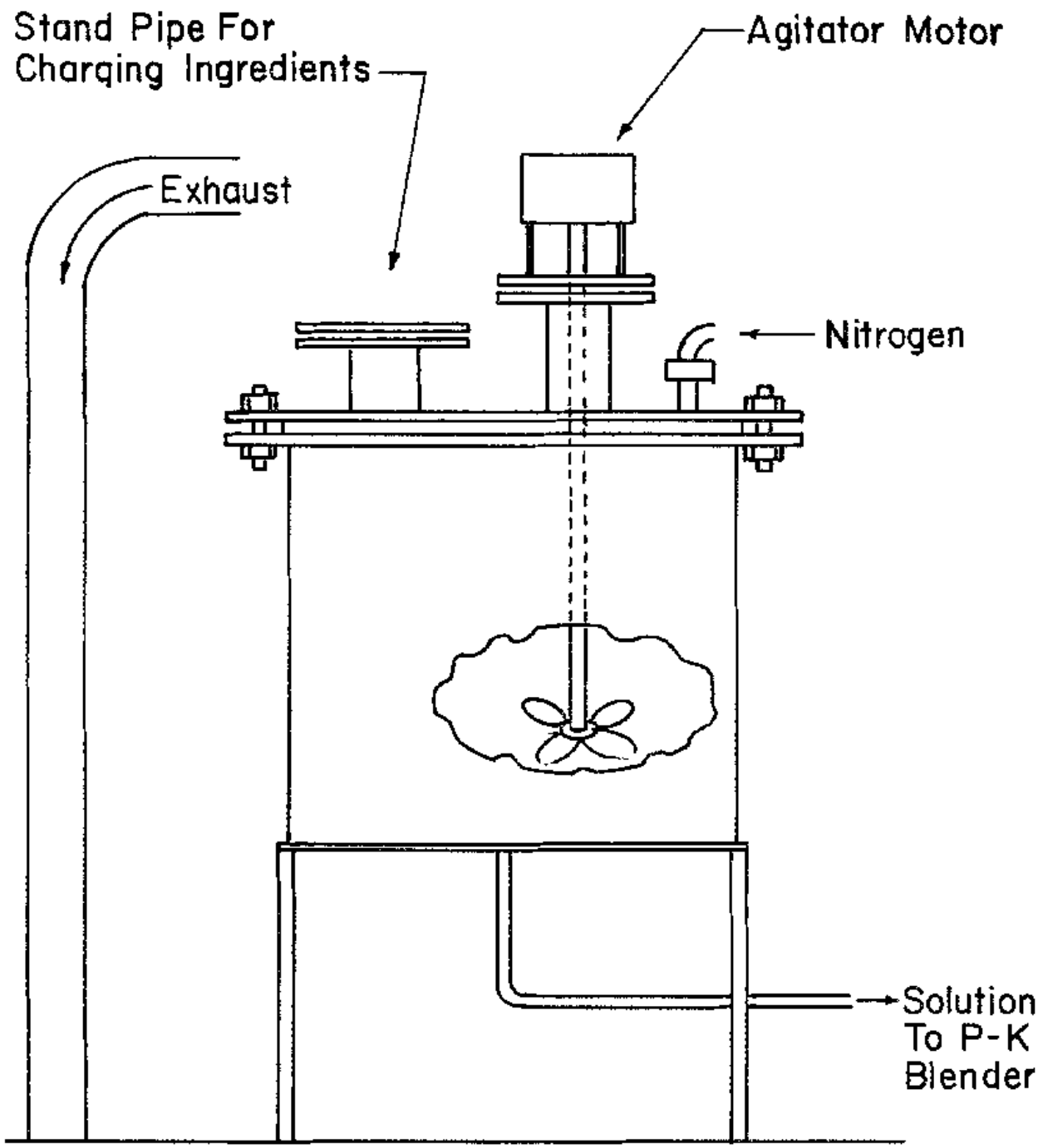


Figure. 3 AGITATED TANK FOR DISSOLUTION OF ACTIVE INGREDIENTS

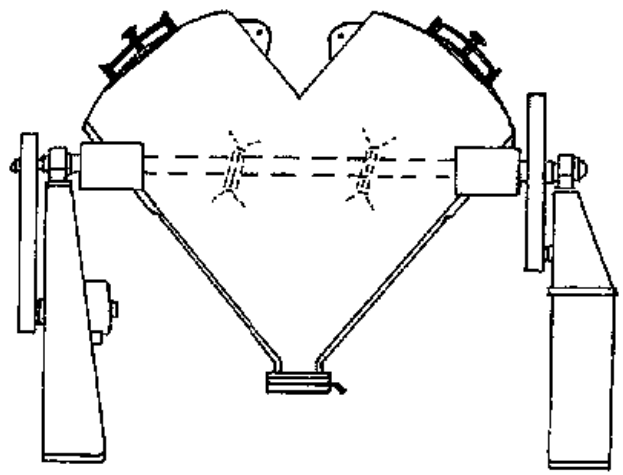


Figure. 4 PATTERSON-KELLY V-BLENDER
(Ref. 3)

in Figure 2. This discharges the wet granulation through a cloth "boot" which is fitted to the discharge end of the mill and also draped across the drum opening. The material is subsequently transferred by scooping and spread into shallow trays lined with paper. The trays are then placed on trucks (or trolleys) which fit into the batch dryers.

The batch dryer (or forced air oven) is schematically represented in Figure 5. Outside air enters at A, through Filter I, combines with recirculated air and is preheated in steam heater E. Fan C forces the air through an air distribution plenum F and air distribution slots G. The air passes over trays mounted on truck H. Part of the air is diverted by means of a damper through exhaust duct B.[4] A separate exhaust fan (J) is used to maintain negative pressure in the oven. Exhausted air is filtered through HEPA filter K.

The granulation in the tray is allowed to dry overnight then transferred, one tray at a time, to the hopper of the Fitzmill. Lubricant is added at this point. The discharge end of the Fitzmill is connected to the Vac-U-Max(R) vacuum transfer system (Figure 6) which transports the granulation to the blender. Vacuum is generated by a pump. A three-way valve is used to connect the filter housing and filter drum to either the return air system or the vacuum pump. When transferring material from the mill, the pump is operating in line with the filter housing and blender. After a certain time of operation in this mode, the filter becomes clogged with powder. The operator at this point turns the three-way valve so that air from the return system flows towards the blender, thus blowing back any material in the filter.

After this transfer is completed, a short blend (few minutes) is performed in the blender. The granulation is then emptied into stainless steel drums and transported to the staging area. Representative samples are taken for quality control analysis prior to releasing for tableting.

Several batches of one product (such as Ovcon 50) are prepared in the course of one week. Typically, steriod processing is carried out over one 8-hour

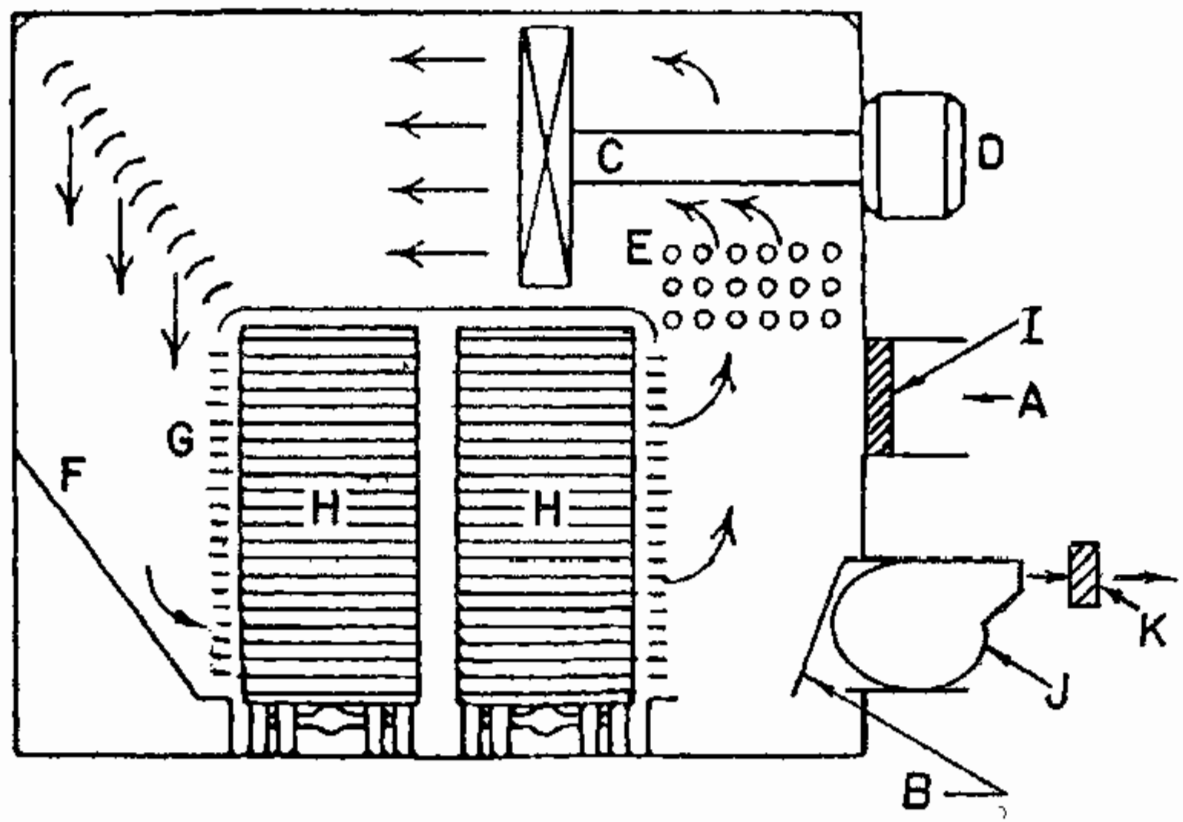


Figure. 5 BATCH DRYER AND TRUCKS (Ref. 4)

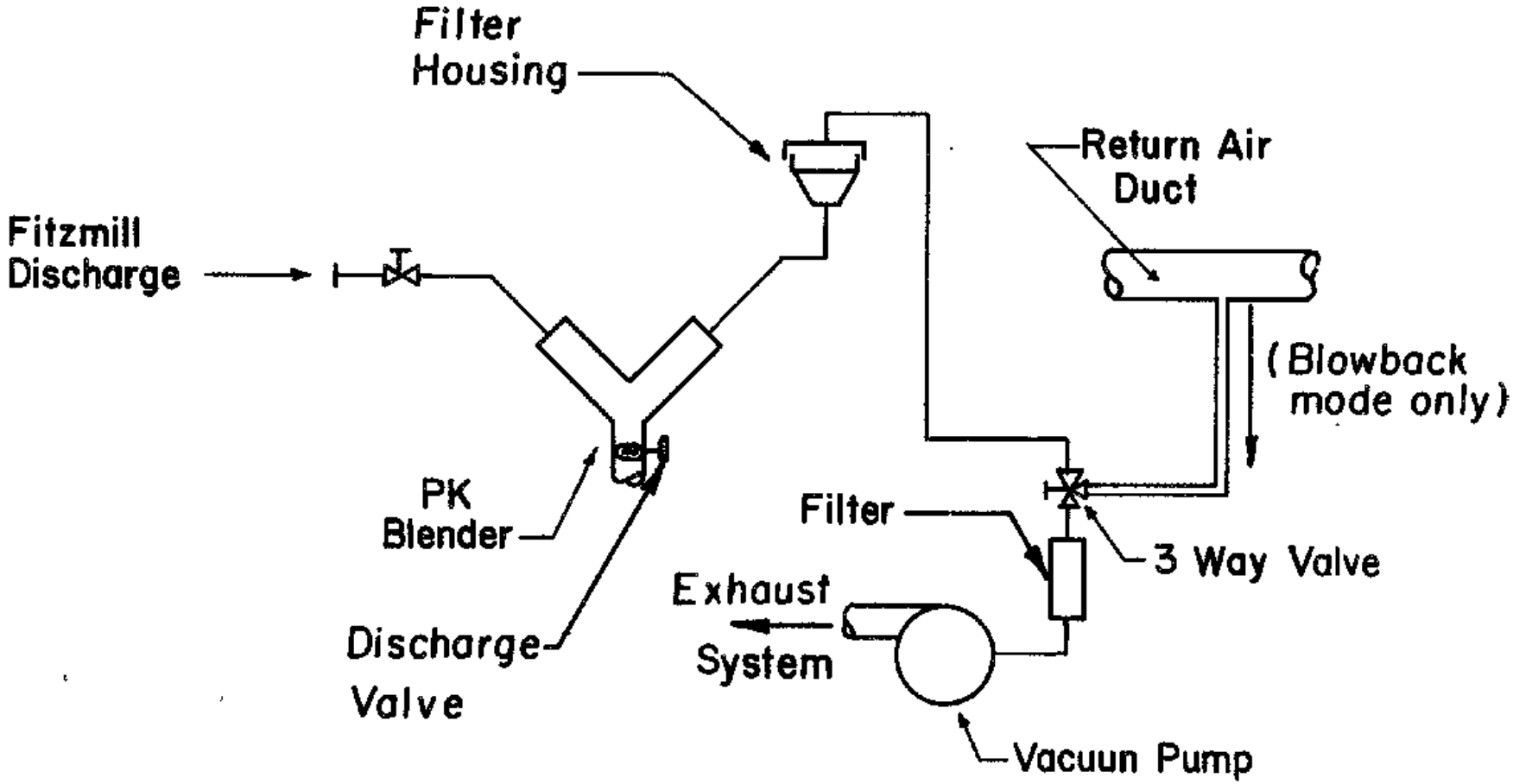


Figure 6 SCHEMATIC OF VAC-U-MAX TRANSFER SYSTEM

shift, Monday through Friday. Processing during one shift in the middle of the week involves dry milling and blending of one batch of granulation (which has been left to dry overnight in the ovens), then wet blending of another batch (including wet milling and loading tray dryers), and finally cleanup of equipment and floor in preparation for the same sequence the next day.

TABLETING

One worker operates two tableting machines in this area. Model BB2 machines (manufactured by Sharples-Stokes Division of Pennwalt) are used to manufacture oral contraceptive tablets. A tableting machine with associated feed systems is shown in Figure 7. Granulation is fed to two feed frames of each machine by two hoppers positioned on opposite sides of the rotary head. The hoppers, in turn, are fed through two flexible hose connections which on the lower side tap into the covers of each hopper and on the upper side join in a common attachment to an adapter fitted with a butterfly valve. The adapter attaches to the drum of granulation via a gasketed recess which fits the rim of the drum. The drum is lifted and securely held in position by a hoist also shown in Figure 7.

The granulation flows from the hopper into the left side of the feed-frame (A) (Figure 8) which has several interconnected compartments. These compartments spread the granulation over a wide area in order to provide time for the dies (B) to fill. The pull-down cam (C) guides the lower punches to the bottom of their vertical travel, allowing the dies to overfill. The punches then pass over a weight-control cam (E), which reduces the fill in the dies to the desired amount. A wipe-off blade (D) at the right end of the feed-frame removes the excess granulation and directs it around the turret and back into the front of the feedframe. Next the lower punches travel to the lower compression roll (F) while simultaneously the upper punches ride beneath the upper compression roll (G). The upper punches enter a fixed (usually) distance into the dies, while the lower punches are raised to squeeze and compact the granulation within the dies. To regulate the upward movement of the lower punches the height of the lower pressure roll is changed. After the

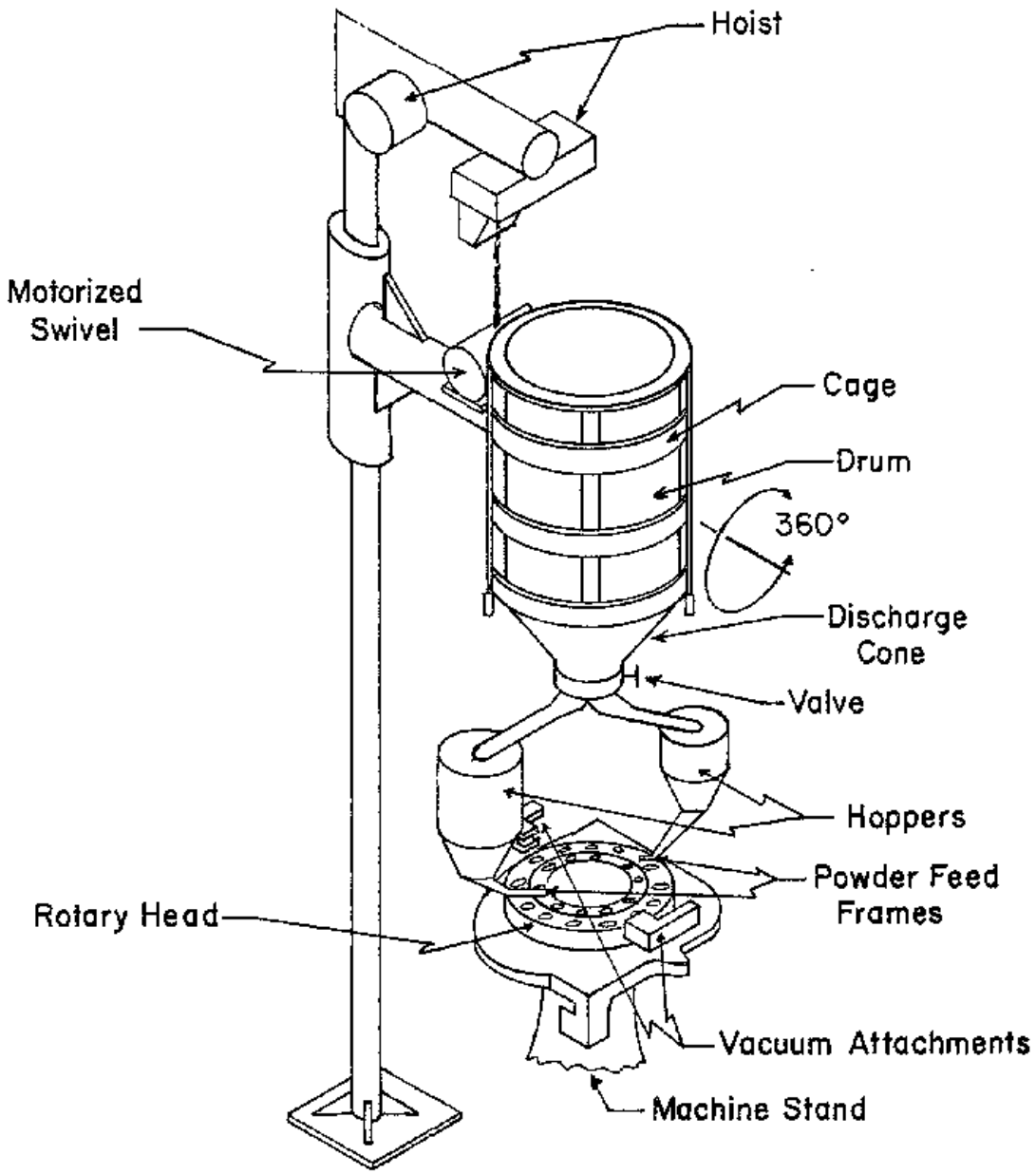


Figure. 7 SCHEMATIC OF TABLET MACHINE AND FEED SYSTEM

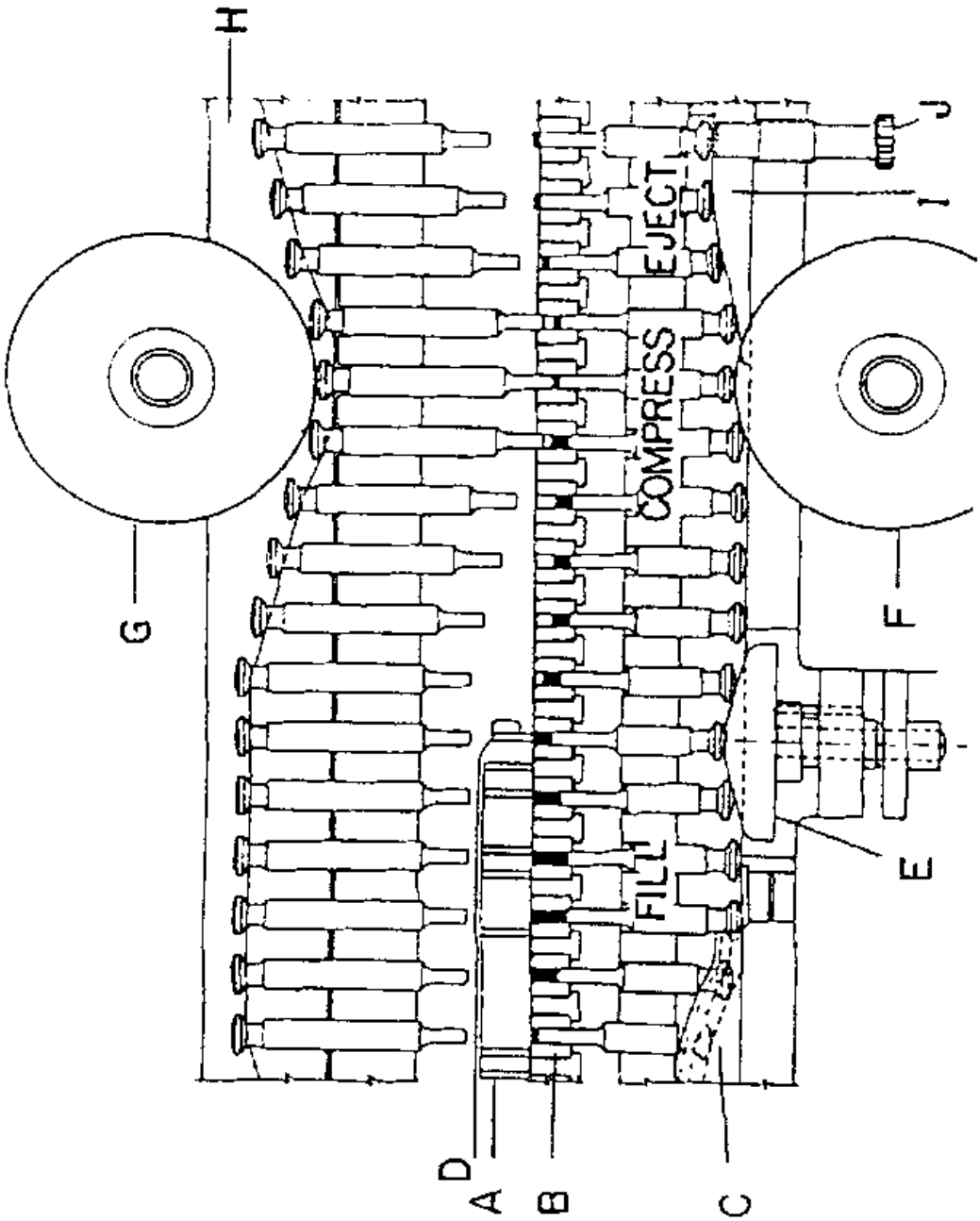


Figure. 8 COMPRESSION CYCLE OF ROTARY PRESS

moment of compression, the upper punches are withdrawn as they follow the upper raising cam (H); the lower punches ride up the cam (I), which brings the tablets flush with or slightly above, the surface of the dies. The exact position is determined by a threaded bolt called the ejector knob (J). The tablets strike a sweep-off blade affixed to the front of the feed-frame (A) and slide down a chute into a hopper which feeds a vibratory conveyor. At the same time, the lower punches re-enter the pulldown cam (C) and the cycle repeats.[5]

PACKAGING

This operation was idle during the NIOSH survey. However, a description is included here for sake of completeness.

Two Hassia machines (Model VAII manufactured by the now defunct Hassia Verpackungsmaschinen of West Germany) are used to produce blister packs. The machines are in separate, but adjacent rooms. Before charging the hopper of the machine with tablets, the operator dedusts them with a vacuum device. Both OC and placebo tablets are conveyed from their respective hoppers to a brush feeder by two vibratory conveyors. The brush feeder consists of two circular recesses with numerous holes at the bottom. Slowly moving brushes sweep the tablets into the holes which feed the blister-type packages. These packs are formed by the machine whereby a plastic sheet is drawn from a roll and continuously thermoformed into tablet-sized pockets as it passes over a roller. The tablets are then inserted and a cover web (aluminum film) is sealed over the thermoformed plastic sheet.

There are three inspectors and an operator assigned to the steroid blistering operation. These employees are supervised by a foreman. The three inspectors rotate positions every 30 minutes. The filler inspector (one person) inspects unsealed blisters for various defects. The filled blister inspector (two persons) perform a second inspection. The blister machine operator de-dusts tablets; keeps the filler hoppers supplied; sets up, operates, and adjusts all parts of the machine; supplies the blister material to the machine; maintains

records of production; and performs routine, intermediate and complete cleanups of the equipment and room.

HEALTH EFFECTS AND SOURCES OF EXPOSURE

Symptoms of overexposure to the estrogen EE and the progestin NOR by both males and females may include: (1) tenderness of nipples or enlargement of breasts; (2) breast discharge; (3) sudden increase in weight; (4) swollen ankles; and (5) skin rashes and/or increased pigmentation of face or nipples. Furthermore, such overexposure may cause decreased libido and sexual potency in males and intermenstural bleeding in women. A summary of toxicological data on both substances may be found in Reference 7 under accession number RC892500 for EE and RC 8975000 for NOR. Briefly, these materials may alter biological activities in organisms in relatively low doses. Some of these materials have also been shown to produce cancer in animals. No Federal standards for exposure are in effect at this time. However, all companies which handle these materials have internal guidelines as to acceptable levels of exposure.

There were several potential emission points associated with the processing equipment. In the P-K blender area such sources include the charging of the mix tank with active ingredients and in emptying the blender (both wet and dry granulation). Sources of exposure in the oven room are: (1) milling wet granulation and loading trays with it; and (2) unloading and milling dry granulation. Possible souces of exposure in the tableting room are: (1) the rotary head at points of powder feeding (feed frames) and the two points at which tablets are formed; and (2) tablet testing.

CHARACTERIZATION OF CONTROLS

A 5-day in-depth survey was conducted by NIOSH between February 7 and February 11, 1983. Monitoring of workers in processing and tableting was conducted between February 8 and 11, 1983. The objectives of the monitoring activities were to determine levels of EE and NOR in the breathing zone of workers outside of the personal protective equipment (i.e., to characterize the engineering containment component of the control system). Actual exposures are, of course, much lower since air supplied suits and air purifying respirators are used as explained in a later section. The methods used by NIOSH for analysis of the materials of interest are detailed in Appendix A. Briefly, air is drawn at a rate of 3.00 lpm through a 37 mm Teflon filter millipore FLAP 37000) mounted in a cassette. The filters were desorbed with acetonitrile and the extract analyzed by high performance liquid chromatography (HPLC). The results of the sampling are given in Appendix B. Side-by-side samples were obtained by company and NIOSH investigators, and these samples were analyzed independently. The results obtained with the Mead Johnson method differed slightly from those obtained with the NIOSH method.

Work practices were observed while the workers performed their job duties and operated process equipment, and while they donned or removed protective clothing and respiratory protective equipment.

Since ventilation is an important control at this site, measurements were conducted to help obtain information on the principles of operation of the ventilation in the steriod processing facility. The objectives of the ventilation measurements were to obtain first-hand information on 1) the techniques used to isolate the steroid facility from surrounding areas by maintaining a negative pressure within the facility, 2) the volumetric rates of ventilation of each area within the steroid facility, and 3) the distribution of the airflow at points where it is supplied and exhausted in each area.

Some of the flow measurements consisted of taking "face" velocity data from air return and exhaust plena using a Kurz Model 441 anemometer. Other flow measurements were made using a FlowHood(R) (Shortridge Instruments) Model CFM-83. The two methods of flow measurement appear to be equivalent. With few exceptions, air was usually exhausted and supplied through perforated (1/4" diameter holes) steel sheet with approximately 40 percent open area. Accurate estimation of the airflows from face velocity data necessitated the performance of experiments to develop factors that are useful in reduction of the data. These experiments and results are described in Appendix C. Typical airflow distributions from large return and exhaust plena are shown in Appendix D.

HAZARD CONTROL TECHNOLOGY

GENERAL CONSIDERATIONS

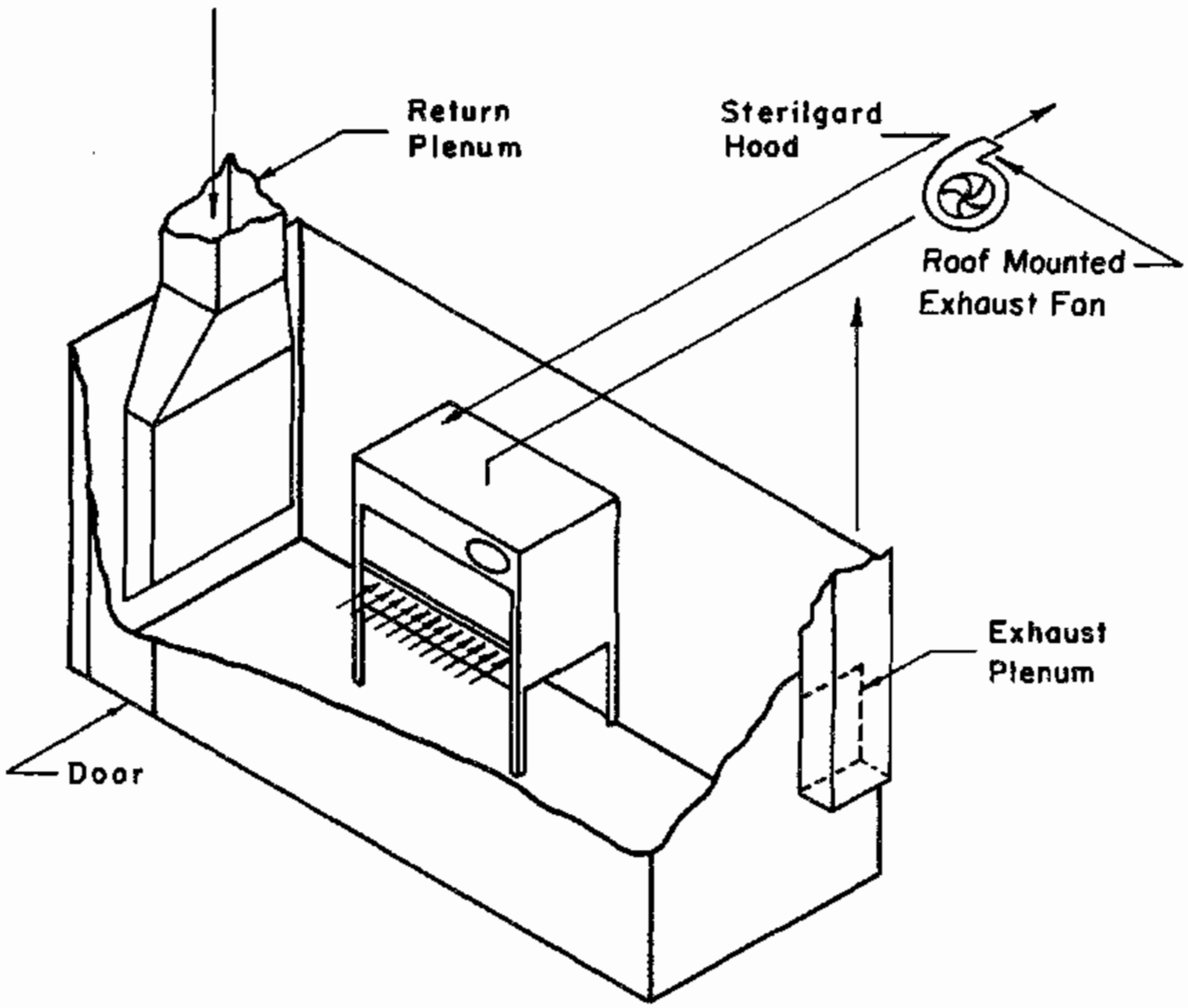
The hazard control techniques of interest are: (1) engineering controls, including isolation, ventilation, and automation; (2) work practices which result in lower exposures; (3) monitoring of worker exposures and their health to detect and correct problems as they occur; and (4) personal protective equipment that is effective in further reducing exposures to levels that are considered acceptable by the company.

ENGINEERING CONTROLS

Granulation

Weighing of active ingredients for several batches occurs in the weigh room within the confines of the SterilGARD(R) hood. In addition to the protection afforded by the hood, general ventilation is also employed. A schematic representation of the weigh room is shown in Figure 9. HEPA filtered return air at the rate of 1.4 room volumes per minute (RVPM) is supplied at one end and exhausted at the rate of 1.3 RVPM at the other end, producing a "laminar" flow. An additional 0.2 RVPM is continuously exhausted through the SterilGARD hood.

The principle of operation of the SterilGARD(R) is shown in Figure 10. Before entering the work area, air passes through a HEPA supply filter that is 99.97 percent efficient in removal of particles with an average diameter of 0.3 um. The filtered air travels vertically through the cabinet at an average velocity of 100 ft/min. Air exits from the work area via two exhaust grilles which extend across the entire width of the cabinet in the rear and in front of the work surface. This air travels back to the motor-filter units through three return air plena located behind the two side walls and the rear wall. Air from one side wall and half of the rear wall plena moves to each of two motor-filter units. All return plena and the two motor-filter units housings



Schematic Representation of the Weigh Room and Controls

Figure 9

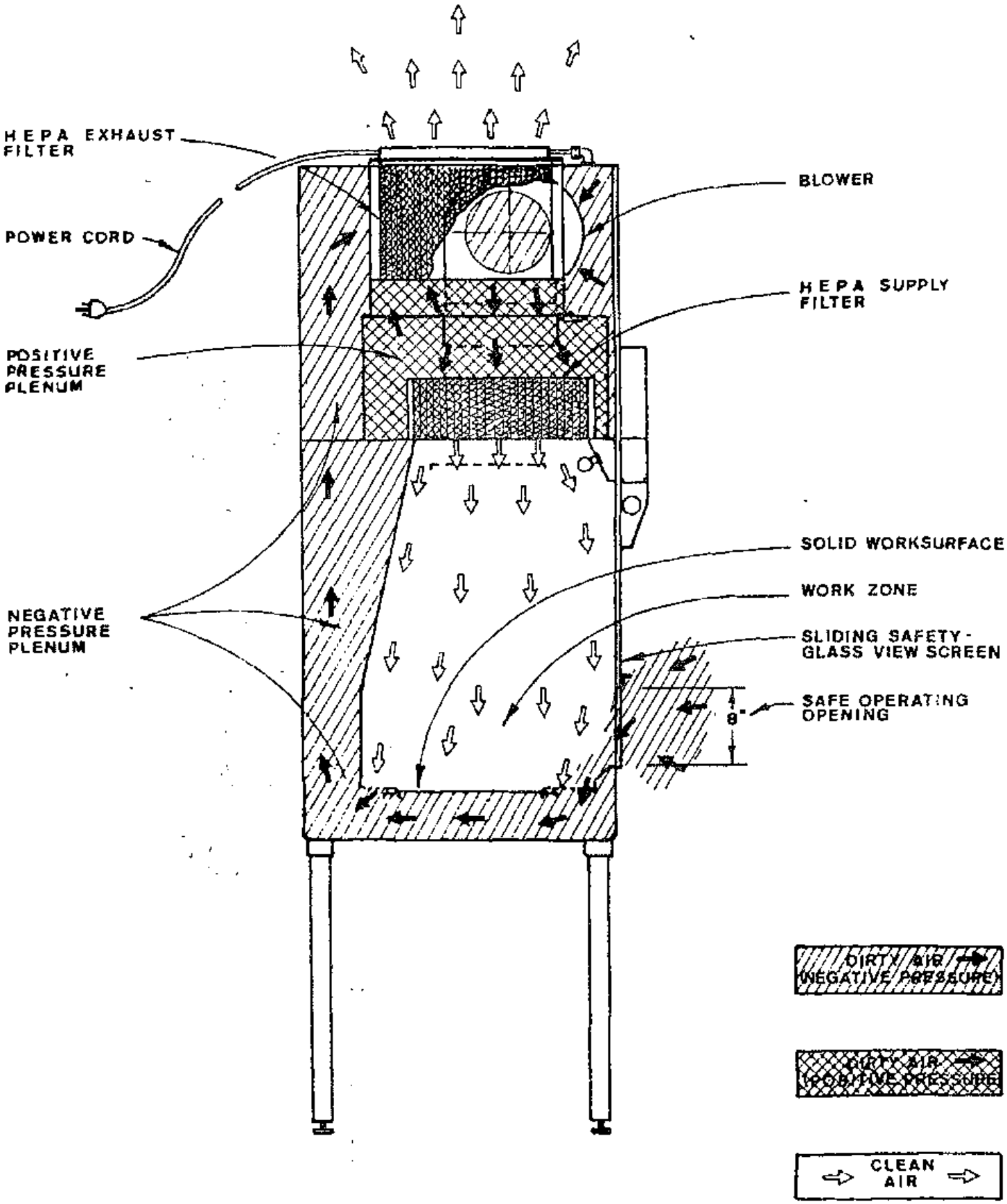


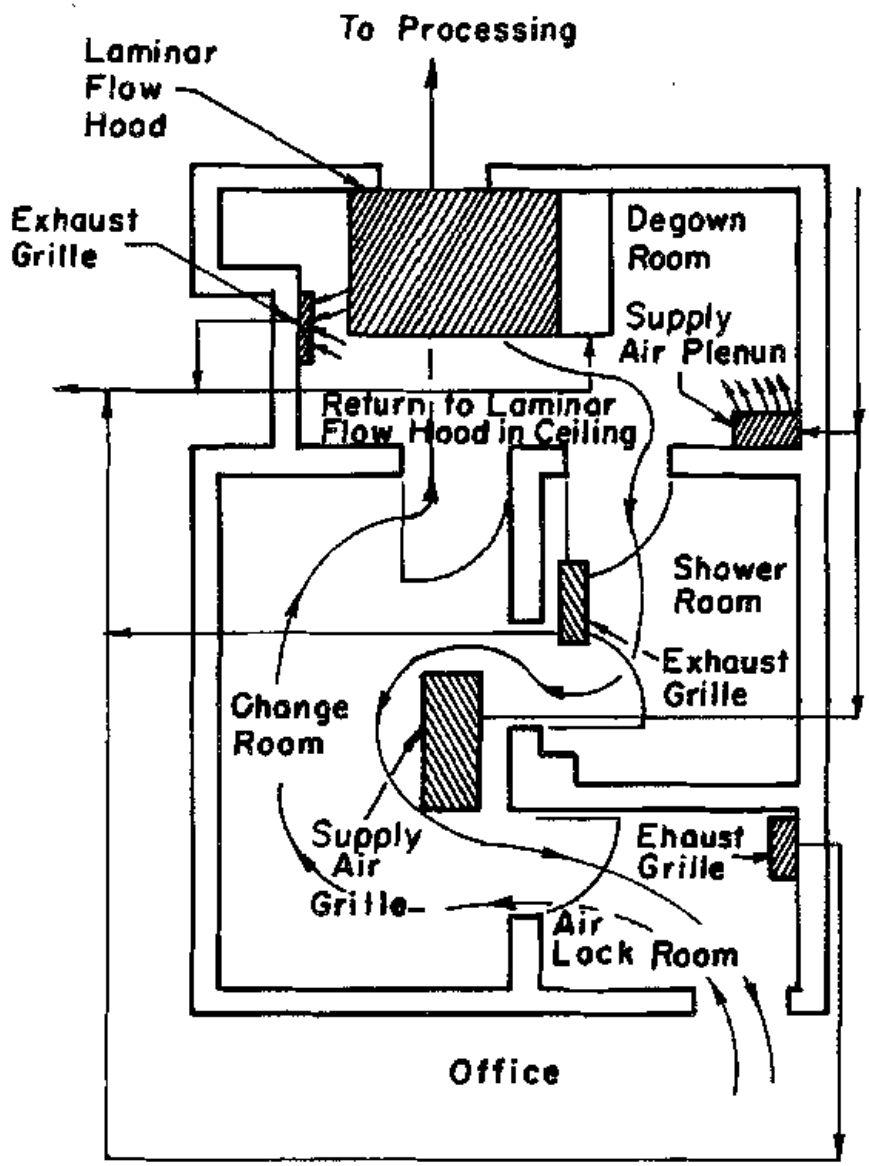
Figure 10. **SterilGARD HOOD**

are under negative pressure. Upon leaving the motor-filter unit housing, the air enters a positive-pressure zone that is surrounded by the negative-pressure plena. Approximately 90 percent of the air in the positive-pressure area passes through the HEPA supply filter to the work area. The remainder (0.4 RVPM) passes through a HEPA exhaust filter. A volume of room air similar to that exhausted is taken into the cabinet at the front opening. This air does not penetrate the work area, but passes into the exhaust grill at the front of the work surface and into the return air plenum.

The cabinet is equipped with a movable front-view window of 0.64-cm safety plate glass that can be raised to a maximal height of 60.9 cm to permit entrance of large items. During working conditions, the window may be raised 20 cm.[6]

Excipients are loaded into the blender under local exhaust. Some of the excipients are milled before loading into the hopper, also under local exhaust. A "portable" hood consisting of a 4-inch flexible hose is used. The room has an independent air exhaust/return general ventilation system which provides approximately 0.6 RVPM. The air that is exhausted is filtered in a prefilter and a HEPA filter, cooled in a cooling coil, and heated in a heating coil (if necessary) before being returned to the room by a fan. About 5 to 10 percent make-up air, drawn from a surrounding staging area, is added to the exhaust before treatment. Granulating liquid is handled in this room. If a spill of this liquid occurs, 100 percent exhaust is employed by closing the damper on the return air duct, and activating an emergency exhaust system consisting of a damper, exhaust fan, and associated duct work.

Access to the processing area (blender room, oven room, and weigh room) is controlled as shown in Figure 11. Workers proceed from the office to the air lock. An alarm sounds when both doors of the air lock are open simultaneously. Workers enter the change room and remove their street clothing, and don protective clothing. They then enter the degown room where they don respirators before entering the processing area. Upon returning from the process area they degown (or remove protective clothing) under the laminar



Controlled Access to Processing Area

Figure II

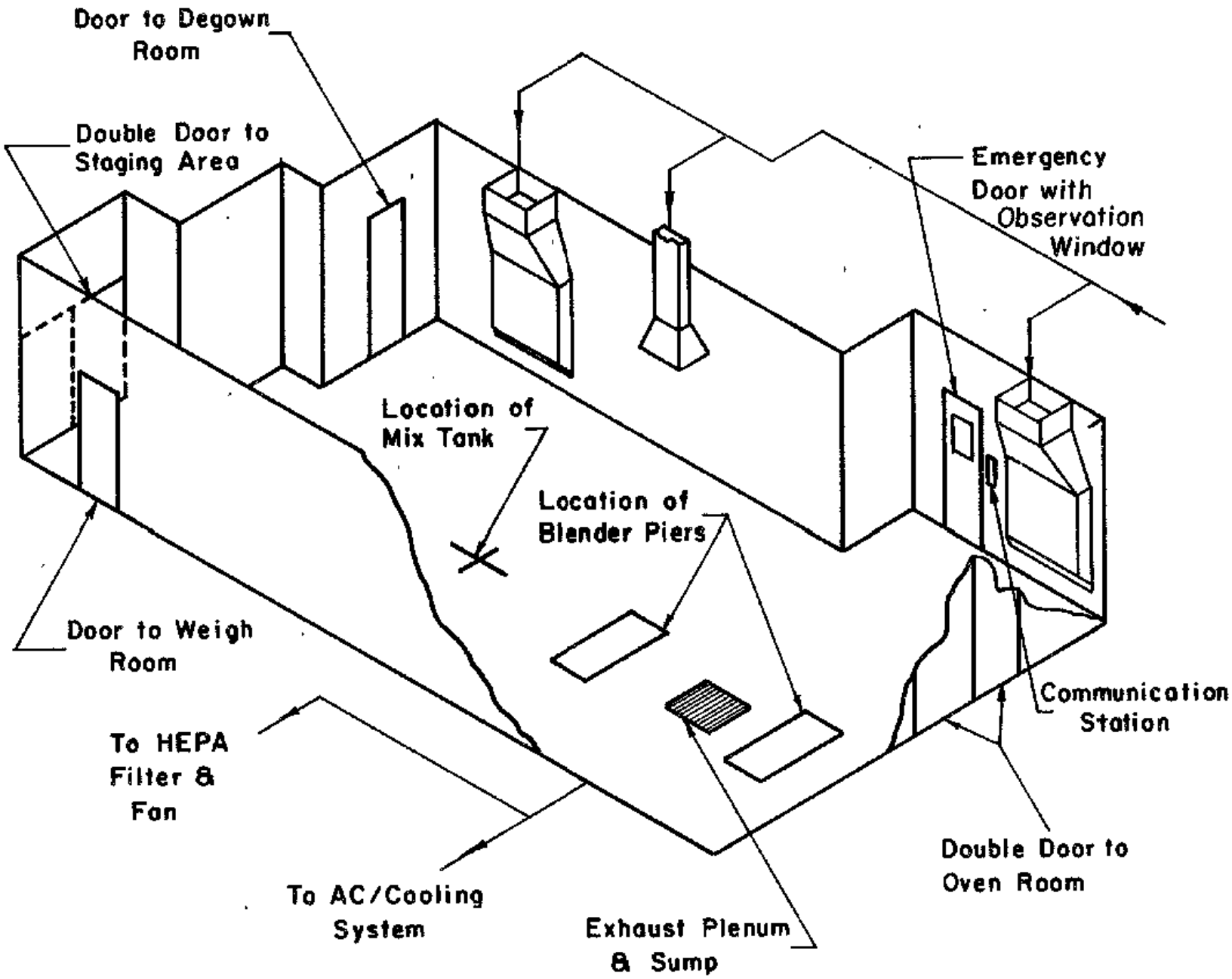
flow hood in the ceiling. They then proceed to the shower room where they are required to take a shower before putting on their street clothes in the change room.

Air is exhausted from the air lock at about 1.0 RVPM (estimated). Air is supplied to the change room at a rate of 0.25 RVPM. Air is exhausted from the shower room at a rate of 0.15 RVPM. The ventilation scheme in the degown room is a company design which simulates an "air shower" to remove dust from outside surfaces of protective clothing and respirators. Air at the rate of 1.0 RVPM is supplied at one end of the room from a plenum. Air is exhausted at the other end of the room (4.0 RVPM). This exhaust air is divided into two parts. One part (2.4 RVPM) is returned to the cooling/air conditioning system while the other part (1.6 RVPM) is recirculated to the laminar flow hood in the ceiling. This hood is fitted with a fan and a HEPA filter and distributes clean air over a 10-square-foot area at the rate of 100 fpm.

Both general and local exhaust ventilation are used in the room where the blender is located. Figure 12 is a schematic representation of the room, equipment placement within the room, and associated controls.

Air at the rate of .5 RVPM is supplied by two plena and a grille in the ceiling. Air is exhausted through a circular, 5-inch, unflanged hood which is designed to control the area where active ingredients are introduced to the mixing tank (Figure 3). Also, a major exhaust point is a grille at floor level between the blender piers. The rate of exhaust is 0.6 RVPM. This floor grille also acts as a water drain when the area is washed down. The major part of the air exhausted is returned after conditioning and removal of particulates in HEPA filters. About 33 percent of air that is exhausted consists of clean air from surrounding areas. This amount of air plus five percent is purged from the system to the outside after passing through HEPA filters. The additional 5 percent consists of fresh outside air.

When wet or dry granulation is discharged from the blender into drums, dust emissions are controlled by the scheme shown in Figure 13. A drum enclosure



V-Blender Room with Associated Controls

Figure 12

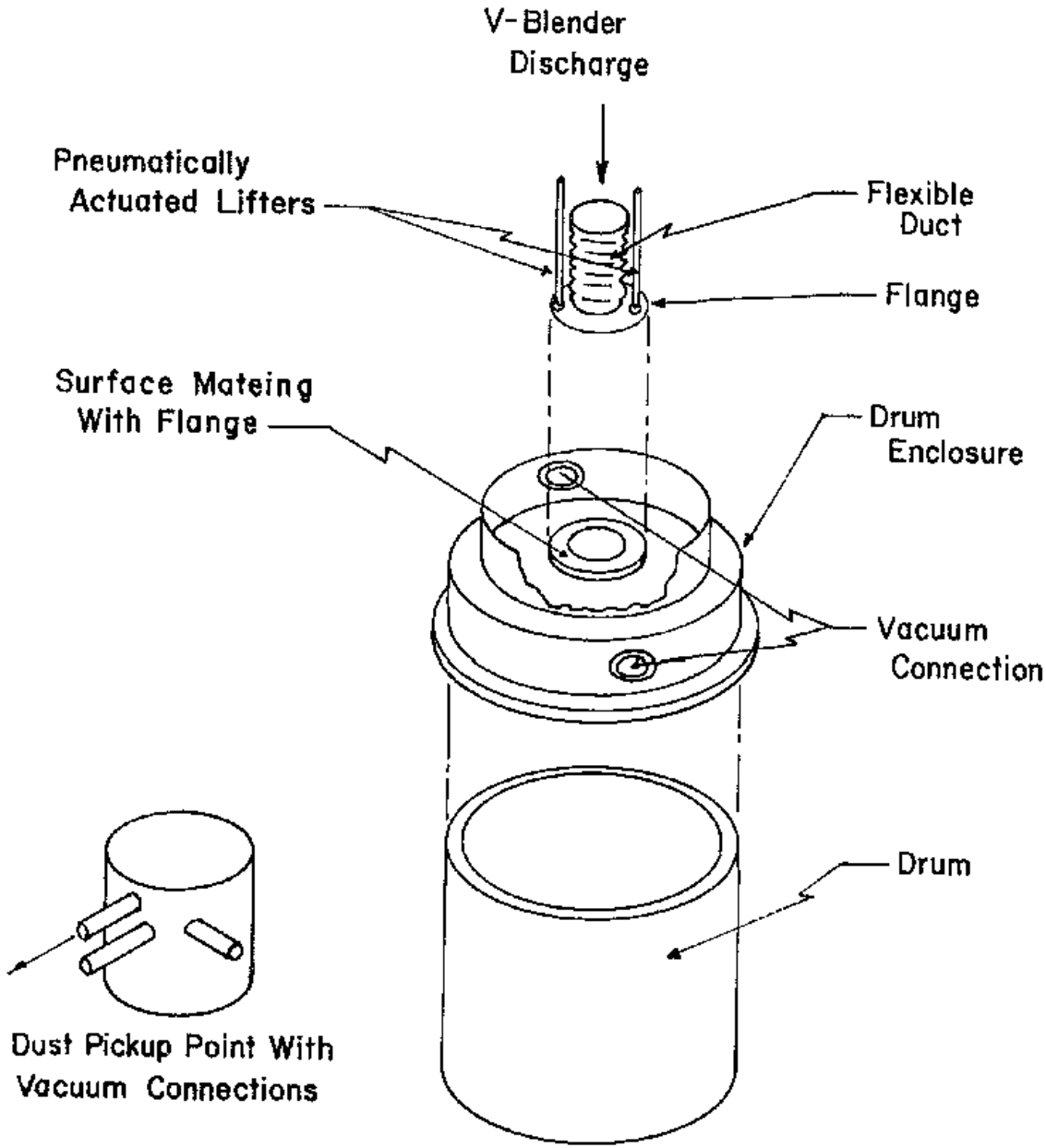


Figure. 13 DUST CONTROLS ASSOCIATED WITH V-BLENDER

with vacuum connections is placed over the drum. The blender flange is lowered by a pneumatically-driven mechanism and presses against a gasketed mating surface located on top of the drum enclosure. Material flow from the blender takes place through a gate valve. The level of material in the steel drum is periodically checked by elevating the blender flange. The total exhaust rate applied to the drum enclosure was estimated at 50 cfm.

A two-way communication station, located near the observation window, is available for workers in the blender room to communicate with the area supervisor who observes activities from the other side of the window.

The oven room is accessed from the blender room as shown in Figure 14. Air from two plena is supplied at the rate of 1.3 RVPM. Air is withdrawn from the room in the exhaust plenum and from the crawl space behind the ovens at the rate of 1.6 RVPM. About 40 percent of the exhausted air (which includes clean air from surrounding areas) is HEPA-filtered before being emitted to the atmosphere. The balance is returned to the air conditioning cooling unit which serves the oven room, blender room, weigh room, and the staging area. This unit consists of HEPA filters, cooling and heating coils, a humidifier, and a damper for the control of pressure drop across the filters. None of the air exhausted from the oven room is returned to A/C cooling unit when granulating liquid is present in the air (when handling wet granulation).

The areas (rooms) served by this unit are maintained at a negative pressure relative to surrounding areas. This is achieved through static pressure control of the inlet vanes on the primary system exhaust fan.

Makeup air for the ovens is obtained from the outside. It is filtered and preheated. Air discharged from the ovens contains granulating liquid and is totally filtered and exhausted to the outside through a high riser.

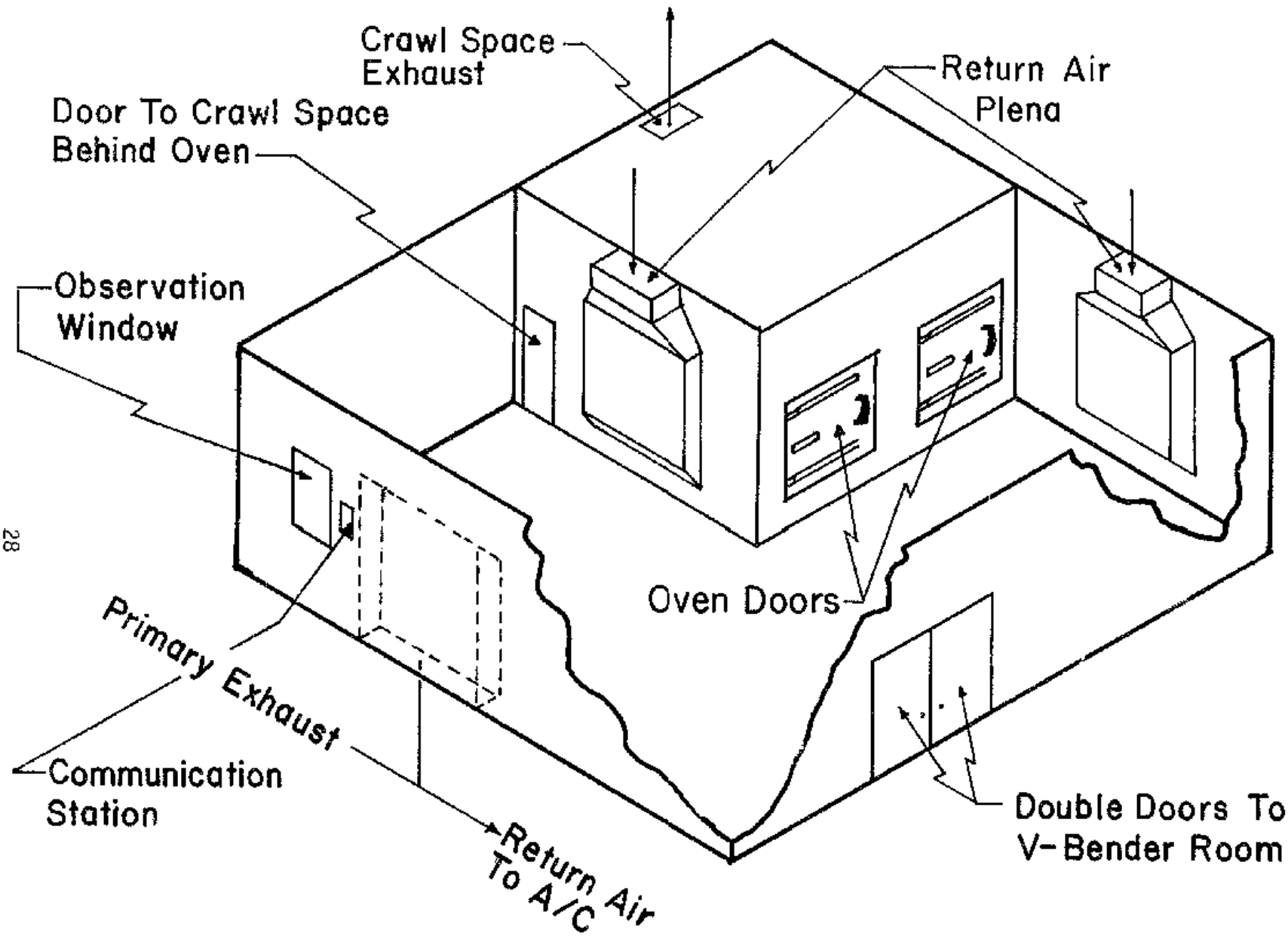


Figure. 14 OVEN ROOM AND ASSOCIATED CONTROLS

Tableting

The controls associated with the tableting operation include general and local exhaust ventilation. The room is schematically shown in Figure 15. This room and the adjacent ones are served by an air conditioning and cooling unit similar to that used for granulation. The room is maintained at negative pressure (ten hundredths of an inch of H_2O minimum) with respect to non-controlled surroundings. Air at a rate of 1.1 RVPM is supplied. About 1.2 RVPM is exhausted by the air plenum on the other side of the room. The area in which the two tableting machines are located is enclosed by curtains made from transparent plastic film. Air within this enclosure is exhausted from a grille in the floor at a rate of 0.45 RVPM. This air is filtered and returned to the overhead plena on top of each tableting machine. One dust pickup point serves each machine and ventilates the two points on each which have the greatest potential for dust generation, namely, the two sectors of the rotary head where tablets are compressed (see Figure 7).

The feed system of each machine has been designed in such a way as to minimize dust generation by enclosing all points where powder is in contact with room air. The only open points are the open ends of the two hoppers where they meet the feed frames. Dust generated by the activities at the tablet testing station is controlled by a laminar flow hood similar to that used in the degown room except that the flow has been reversed. A velocity of approximately 100 fpm in the direction of the wall (away from the worker) is maintained.

Access to the tableting room is through a scheme similar to that shown in Figure 11.

Packaging

The engineering controls in each of two rooms where packaging machines are located include general and local exhaust ventilation, a device for dedusting

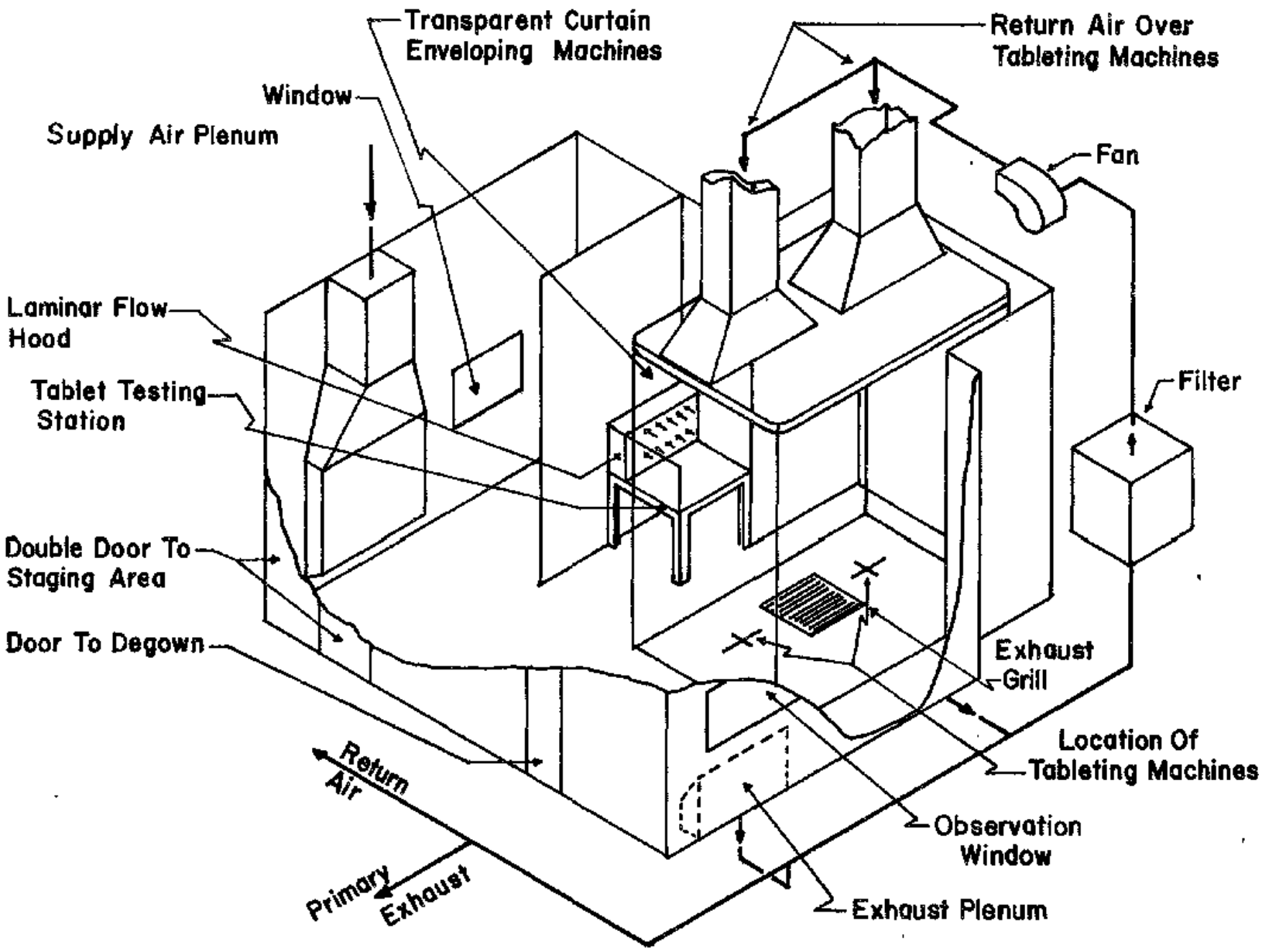


Figure 15 TABLETING ROOM AND CONTROLS

of tablets, and an alarm which indicates whether the negative pressure in the room has been broken.

Air conditioned air is supplied to each room. One hundred percent is exhausted through a Rotoclone(R) to the outside. The Rotoclone(R) consists of a fan in a cast iron housing with an inlet section wherein water sprays remove the dust carried by the air. The room is maintained at a slight negative pressure by exhausting more air than is supplied. A photohelic alarm has been installed to indicate to the operator when negative pressure is not maintained.

A vacuum machine with a filter controls dust at specific areas in the Hassia packaging machines. These points include the vibratory conveyor and the brush feeder.

The dedusting device removes loose dust associated with the tablets. The operator spreads the tablets over the tray with a perforated bottom. Air drawn by vacuum over the tablets and through the bottom of the tray would entrain the loose dust. Lateral exhaust is provided to capture dust that may be generated in the course of dumping and spreading the tablets over the perforated tray.

The packaging machines generate a significant amount of heat which may be stressful to workers in this area in the absence of controls. Additional air cooling units have therefore been installed to reduce air temperature.

WORK PRACTICES

General

Work practices that are effective in reducing or minimizing exposures are the result of effective training and education programs. The company maintains a training center where training sessions for the development of a variety of job-related skills, including those pertaining to performing job duties in a safe manner, are prepared and presented. Permanent staff and modern equipment

and facilities are available for the preparation and presentation of audio/visual materials for training sessions. Also available are special areas where workers may individually study various materials of training sessions.

Procedures that have been written are: (1) the proper use of the steriod facilities (granulation and tableting); (2) proper ingress to, and egress from the facilities; (3) servicing and calibration of the respiratory airline monitor; (4) decontamination of processing areas within the steriod facilities; and (5) personal protective equipment requirements.

Processing

Weighing of active ingredients must be performed within the confines of the SterilGARD(R) hood. The hood is fitted with a velometer which indicates proper airflow into the hood (about 500 cfm). The worker should check the velometer reading before use. Spills are to be cleaned-up and weighed and the foreman notified.

In the areas of the blender and oven room, the negative pressure controls must be checked daily by inspection of the pressure gauges. The ventilation system must be manually switched to total exhaust (no recirculation) whenever granulating liquid is present (wet milling and loading the dryers in the oven room, and wet mixing in the blender room). All Fitzmill boots are to be washed and dried after each batch of similar product is processed. The exterior of drums and tools are to be cleaned before being taken out of the production facility. The house vacuum system for dust collection (dust pickup points) must be started by the operator before entering the processing area.

Each worker in the steriod facility is rotated to other jobs so that exposure to these materials occurs, at most, one day a week.

Protective clothing and respiratory protective equipment (PPE) were donned and checked skillfully. Pant legs were taped to booties and sleeves were taped to

gloves. PPE is not to be reused and no instances of such reuse were observed. The used PPE is dumped into a trash bag lined with plastic. When full it is heat sealed and placed in clearly labelled fiber drums destined for land filling.

Thorough showering with a mild lotion soap is mandatory upon leaving the degown room. The access area is designed so that the shower room cannot be bypassed when going from the degown room to the change room.

Tableting

The requirements in this area are similar to those in processing.

Packaging

Line attendant inspectors are scheduled in the tablet blistering rooms on a rotating basis at a frequency of once every 12 to 13 working days if one line is operating and a frequency of once every 5 days when two lines are operating. The blister packaging equipment operator is not rotated, but permanently assigned to the job.

MONITORING

Company Programs

Periodic monitoring of EE and NOR levels in various areas is performed. An area monitoring system designed by the company is used to monitor concentrations at fixed locations in various areas within the steriod facility. The air samples are drawn through 37-mm glass-fiber filters in cassettes using vacuum generated by a steam jet ejector. Constant airflow is obtained by using critical orifices. The filters are then taken to the laboratory for analyses, in the same manner as standard industrial hygiene samples. This system is useful in detecting departures from expected levels, and in indicating the need for corrective action. Personal breathing zone

levels of active ingredients outside of respiratory protective equipment are occasionally taken by the company. Some of these data are reported in Table 1. Measurements of actual exposures (inside air supplied suits) have, with few exceptions, showed nondetectable levels for both NOR and EE. If actual exposures are assumed to be between zero and the detection limit of about 0.1 micrograms per cubic meters, the protection factors afforded by the respiratory protective equipment that is used in the processing area is estimated in the range of 1,000 to 3,000. On two occasions the levels of EE measured by the company were 0.13 and 0.167 micrograms per cubic meter, respectively, inside the air supplied suit. The corresponding levels for NOR were 0.422 and 0.63.

Table 1. Company-provided data on personal breathing zone levels of active ingredients outside respiratory protective equipment. (Micrograms per cubic meter)

Job and Location	No of Samples	EE		NOR	
		Mean	Range	Mean	Range
Processing blender	2	46.4	13 - 79	79.8	36.5 - 123.00
Processing oven room	4	0.44	0.25 - 0.71	4.00	2.5 - 6.40
Tableting	5	0.58	ND - 1.26	6.55	ND - 14.02
Packaging	35	0.11	ND - 0.37	0.72	0.1 - 1.8

Workers in the steriod facility are provided with periodic physical assessments which include an EKG, an x-ray, pulmonary function test, and a battery of blood tests (SMA-23). This is performed annually for workers over 40 years of age, once every two years for workers that are 30 to 40 years of age, and once every 3 years for workers between 20 and 30 years of age. An

extensive history and physical assessment is performed by company nurses specifically trained for this function at the beginning of employment. Workers in the steriod facility are also examined by a physician once every two weeks specifically for symptoms of overexposure.

Results of Monitoring During NIOSH Survey

Processing--

Breathing zone samples outside respiratory protective equipment were obtained during dry milling and wet milling of granulation and during cleanup. The data is listed in Tables 2, 3, and 4, respectively. Inspection of these data indicates that potential for exposure is highest during dry milling of the granulation. The sources of variability in the data include: (1) differences in work practices between individuals; (2) their proximity to the sources of exposure varies since not every worker in the processing area performs identical tasks; and (3) a minor leakage in some equipment may occur on one day but not on other days. These caveats notwithstanding, the exposure data for the three activities were statistically analyzed with a view to obtaining a geometric mean exposure for workers in this area and a geometric standard deviation which is a measure of the variability of the data. The results of the analysis are given in Table 5.

Table 2. Air concentration levels outside protective equipment during dry milling. (Micrograms per cubic meter)

Day	Worker	NIOSH		Mead-Johnson	
		EE	NOR	EE	NOR
1	A	0.56	9.12	1.12	19.30
	B	0.84	13.40	3.13	64.60
	C	0.52	6.11	2.03	34.90
2	D	4.19	73.40	5.09	78.60
	E	1.23	23.39	1.69	28.80
	F	1.50	29.72	3.39	63.80
3	G	0.83	13.63	2.82	54.20
	H	0.49	7.71	1.81	33.80
	I	1.98	34.90	4.20	81.00
4	J	2.67	45.5	4.46	88.70
	K	3.61	63.92	6.23	139.00
	L	2.55	46.40	2.80	62.40

Table 3. Air concentration levels outside protective equipment during wet milling. (Micrograms per cubic meter)

Day	Worker	NIOSH		Mead-Johnson	
		EE	NOR	EE	NOR
1	A	0.48	12.27	1.28	26.30
	B	0.60	6.53	3.11	37.20
	C	1.2	27.70	2.13	82.00
2	D	0.49	7.96	0.38	7.54
	E	--	--	1.59	21.00
	F	0.34	8.12	0.69	16.20
3	G	2.53	63.84	3.69	52.80
	H	0.40	9.38	14.80	121.00
	I	--	--	2.27	50.9

Table 4. Air concentration levels outside protective equipment during cleanup. (Micrograms per cubic meter)

Day	Worker	NIOSH		Mead-Johnson	
		EE	NOR	EE	NOR
1	A	--	--	--	--
	B	0.31	1.96	0.22*	2.38
	C	0.11*	2.30	0.22*	1.99
2	D	0.12*	0.83	0.26*	2.07
	E	0.28	1.23	0.28	2.99
	F	0.12*	.47	0.26	0.76
3	G	0.75	2.19	0.35*	4.68
	H	0.18*	0.93	0.35	0.99
	I	0.18*	1.91	0.35*	0.67
4	J	0.24*	3.94	0.48*	7.35
	K	1.65	20.36	0.44*	20.1
	L	0.24*	3.08	0.48*	4.8

*Concentration based on half the detection limit which is 50 ng for NIOSH and 100 ng for the company.

Table 5. Geometric means (GM) and geometric standard deviations (GSD) for air concentrations in the processing area.

Activity	NIOSH				MEAD JOHNSON			
	EE		NOR		EE		NOR	
	GM	GSD	GM	GSD	GM	GSD	GM	GSD
Dry milling	1.36	2.14	22.71	2.34	2.89	1.66	54.7	1.74
Wet milling	0.67	2.04	13.60	2.29	1.96	2.84	34.37	2.35
Cleanup	0.26	2.28	2.00	2.68	0.32	1.33	2.67	2.77

Tableting--

Air concentrations outside of protective equipment in tableting are inherently much lower than those in processing. The worker usually spends most of his time performing periodic weight and friability tests on tablets from both machines. He usually enters the enclosed area of the machines to obtain

sample tablets and to perform machine adjustments while the machine is running. Top-of-helmet exposure data were obtained for the tablet machine operator and these are reported in Table 6. Statistical analysis of the data yielded geometric means and geometric standard deviations reported in Table 7.

Table 6. Air concentration levels outside protective equipment in tableting room. (Micrograms per cubic meter)

Day	Worker	NIOSH		Mead-Johnson	
		EE	NOR	EE	NOR
1	M	0.23	0.44	0.07	0.23
2	N	0.05*	0.05*	0.11*	0.16
3	O	0.07	0.15	0.06	0.74
4	P	0.09	1.01	0.10	1.64

*Based on detection limits.

Table 7. Geometric means (GM) and geometric standard deviations (GSD) for air concentrations in the tableting room.

NIOSH				MEAD JOHNSON			
EE		NOR		EE		NOR	
GM	GSD	GM	GSD	GM	GSD	GM	GSD
0.09	1.92	0.24	3.69	0.08	1.33	0.46	2.92

PERSONAL PROTECTIVE EQUIPMENT

Processing

Workers in the excipient dump room wear dust respirators (3M No. 8710) for protection against what is considered to be nuisance dust.

Workers in the processing area must don PPE in the change room and the degown room before entering the blender area, the oven room, or the process weigh room. In the change room the workers remove their street clothing and put on Tyvek undershirts and undershorts. They may, at this point, wear either an unhooded or a hooded Tyvek coverall. If a hooded coverall (American Hospital Supply) is chosen then shoe covers are worn and these should be taped to the legs of the coverall. Then a belt with a vortex cooling assembly (3M, W2862) attached to it is put on. The hooded coveralls are not completely closed while gowning is taking place. The worker proceeds to the degown room and attaches the vortex unit to an air supply to verify that sufficient air flow is obtained. Then a flexible hose attached to the vortex unit at one end is inserted into a side opening in the suit. The suit material and hose are taped at this point to prevent leakage of outside air. Finally, surgical gloves (Derma-Thin, Best Manufacturing Company, No. 1005) are worn and these are taped to the sleeves to prevent leakage. The worker then connects the vortex assembly to an air supply point via a 15- or 20-foot-long rubber hose fitted with quick-disconnect fittings at both ends. This is effectively an air supplied suit. If an unhooded Tyvek coverall is chosen, the worker dons a vest (3M, W2802-6) and a detachable hood (3M, W5220-6, for example), which provides equivalent protection.

Published data on protection factors suggest a protection factor of 2,000 for this combination (Ref 8, p. 54). The company collected data that show a protection factor of 1,000 or better.

When removing the PPE, the worker enters the degown room and removes the detachable hood or opens the hooded coverall. Then the order of removal is: (1) vortex cooling unit; (2) detachable vest (if unhooded coverall is used); (3) coveralls; (4) shoe covers; and (5) gloves. The worker then removes disposable underclothing and enters the shower room.

When wet milling operations are completed, the processing area is hosed down before workers leave for a short break. Only unhooded Tyvek coveralls, shoe

covers, gloves, and dust respirators are required when they re-enter the area for cleanup.

Tableting

Requirements here are similar to those in processing. Underclothing, unhooded Tyvek coveralls, gloves, and overshoes are worn. Respiratory protective equipment consists of a Racal air purifying respirator including a helmet, with a HEPA filter (AS905) blower, and a battery Pak worn also as a back pack. The HEPA filter removes 99.97 percent of particles 0.3 microns in diameter and larger. Theoretically, this should give a protection factor of about 3,300. However, the protection factor of such respirators is compromised by complex turbulent air currents which entrain some particulates back into the breathing zone.

NIOSH has generated field data on such respirators which suggest a protection factor of 205 (geometric mean based on 23 observations).[9] The measurements were made at a lead smelter where both particulates and fumes were found. A lower confidence limit (LCC) of 128 was obtained for the protection factor, while the upper confidence limit was found to be 325. Work conditions in a lead smelter are much more rigorous than those encountered by the tablet machine operator at Mead Johnson, and a higher protection factor may be obtained under these conditions. Mead Johnson-generated data indicate a value of 100 for the protection factor.

CONCLUSIONS

Workplace levels of the highly potent steriods NOR and EE at the Mead Johnson OC manufacturing operation are reduced by a system of controls consisting of engineered safeguards, personal protective equipment, worker training and education, and environmental and medical monitoring.

The processing area potentially contains the highest levels of estrogens. The potential emission sources include weighing of NOR and EE, wet blending and milling of granulation, and dry milling, blending, and drum-filling of dry granulation. With only the engineering controls in place, the mean concentrations of EE and NOR in air were found to be 1.36 and 22.71 micrograms per cubic meter during dry milling; 0.67 and 13.6 during wet milling; and 0.26 and 2.00 during cleanup. Actual exposures, however, are some fraction (possibly between 1/1000th to 1/3000th) of the mean concentrations since the workers don air supplied suits and shower frequently.

The engineering controls and work practices in the area where tableting machines are located resulted in mean concentrations of 0.09 and 0.29 micrograms per cubic meter for EE and NOR, respectively. Use of respiratory protective equipment results in actual exposures that are some fraction (possibly 1/100th) of the mean.

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APPENDIX A

ANALYTICAL PROCEDURES

ANALYTICAL PROCEDURES

HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

Principle of Methods

A known volume of air is drawn through a FALP fiiter to trap estrogens present. The filter is transferred to a small scintillation vial and extracted with acetonitrile. An aliquot of the extracted samples is injected into a liquid chromatographic system. The areas of the resulting peaks are measured with an electronic integrator and quantitatively and qualitatively analyzed using external standards.

Equipment and Materials

17 alpha-ethinylestradiol, mestranol, norethindrone, equilin, estrone, 17 beta-estradiol, megestrol acetate, beta-estradiol 3-benzoate, progesterone, testosterone, testosterone propionate, equilinin, and norethindrone acetate were obtained from a Sigma Chemical Company. Norgestrel and 17 alpha-dihydroequilin were contributed by industries utilizing these compounds. These compounds were chosen in an attempt to investigate all steroids used in the manufacture of oral contraceptives.

Standards and spiking solutions are made by dissolving a known weight of each compound in acetonitrile. Solutions of this stock are diluted and used as analytical standards.

The mobile phase is composed of acetonitrile and water. The acetronitrile is Burdick and Jackson spectrophotometry grade with a UV cutoff at 189 mm. The water is purified in-house with a Millipore system consisting of prefilter, carbon, ion exchange, and post-filter cartridges followed by distillation by a Corning Mega-pure system. All solvents are filtered and degassed prior to use.

The HPLC system consists of 3 Waters 6000A pumps, a Waters WISP 710B sample injector, a Waters 720 system controller, and a reverse phase column (Waters C18 RC, 5 u in a Waters Radial Compression Module). A Waters Model 440 absorbance detector and a Waters Model 450 variable wavelength detector are connected in series. A Waters Model 441 absorbance detector is on order and may replace the Model 450 if gains in sensitivity can be achieved. Recording of chromatograms is made on a Model B-381 Soltec recorder and calculations are performed on a Hewlett Packard 3350 Laboratory Automation System.

Sample Preparation

Upon receipt of the samples in the laboratory, they are logged-in and stored under refrigeration in the sample security room.

At the time of analysis, the chemist analyzing the samples logs them out and takes them to the HPLC laboratory. The FALP filters are removed from the scintillation vial. The absorbent pad is discarded. 2 mL of acetonitile is added to the vial and agitated for 1 hour in a sonic bath. The sample is filtered and 100 microliters is introduced into the HPLC system. As part of NIOSH quality control, filters spiked with the compounds of interest are analyzed with the samples.

Separation

Separation is achieved on a Waters Radial PAK C18, 5u, 5 mm ID pressurized in a Waters Radial Compression Module. The mobile phase is a 40/60 acetronitrile/water mixture at a flowrate of 1 mL per minute for ten minutes followed by a 20 minute linear gradient to 100 percent acetonitrile. This mobile phase is used to analyze the named compounds in a single analytical run. Since the analysis requested will not contain the complete list of compounds, minor modifications will be made to maximize sensitivity of the compounds of interests and minimize the run time. Since the complexity of the samples matrix is unknown, the solvent may need to be modified for greater resolution.

Detection

All seperations are monitored by UV detection. The use of two detectors in series allows greater sensitivity since the lambda maxima of the compounds range from 195 nm to 280 nm. This range is subdivided into the following: 195 nm-208 nm: estradiol benzoate, estradiol, mestranol, ethynylestradiol equilin, 17-dehydroequilin, estrone; 236 nm-239 nm: progesterone, norgestrel, norethindrone acetate, norethindrone testosterone proprionate; and 280 nm: megestrol acetate.

The 195-208 nm group is monitored by the variable wavelength detector set at 200 nm. The 236-239 nm group is monitored by the fixed wavelength detector set at 254 nm. The 280 nm compound is monitored by the fixed wavelength detector set at 280 nm. Inclusion of one compound from each group will necessitate a double run analysis or 3 detectors coupled in series.

Quantitation

Quantitation is accomplished by an external standard. Peak counts are accumulated by the data system and compared to external standards run with the samples. All calculations are made by an internal basic program based on a least square method.

Qualitation

Identification of the compounds is based on the retention data. Absorbance rationing is used to confirm the purity of separation and proper identification.

APPENDIX B

DETAILED LISTING OF MONITORING DATA

Type Sample	Location/ Worker	Date	Process Area	Sample No.	Duration (mins)	ug Per Sample EE	ug Per Sample NOR	Weight, mg Net	NIOSH** EE (mg/m.)	NIOSH** NOR (mg/m.)	M/J** EE (mg/m.)	M/J** NOR (mg/m.)	Sample Volume Liters
Area	Air supply Plenum	2/8	Oven Room	F8	450	0.05*	0.15	0.35	ND	0.11			1395
		2/9		F44	417	0.5*	0.25	-.05	ND	0.19			1293
		2/10		F53	419	0.5*	0.93	0.42	ND	0.72			1299
		2/11		F83	215	0.1	0.99	0.19	0.15	1.49			666
Area	Exhaust Air Plenum	2/8	Oven Room	F15	445	0.06	0.56	0.39	0.04	0.4			1388
		2/9		F40	409	0.05*	0.53	0.24	ND	0.41			1276
		2/10		F57	339	0.4	7.14	0.35	0.38	6.75			1058
				F91	79	0.05*	0.05*	0.23	ND	ND			246
		2/11		F94	214	0.05	2.6	0.23	0.07	3.89			668
Area	Mead Johnson Fixed Location 13	2/8	Oven Room	F92	446	0.13	2.46	0.12	0.09	1.8	0.14	2.39	1369
		2/9		F42	407	0.07	0.94	0.31	0.06	0.75	0.11	1.82	1249
		2/10		F70	344	0.24	3.27	0.24	0.23	3.10	0.67	12.0	1056
				F72	79	0.05*	0.05*	0.22	ND	ND	ND	1.6	242
		2/11		F81	212	0.17	3.22	0.0	0.26	4.95	0.70	15.2	651
Paired Area	Top of Stainless Steel Cabinet	2/8	Oven Room	F12	453	0.05*	0.05*		ND	ND			1431
				F19	453	0.1	0.88		0.07	0.62			1413
		2/9		F43	419	0.41	7.93		0.31	6.0			1324
				F31	419	0.32	6.03		0.24	4.6			1307
		2/10		F67	343	0.05*	1.28		ND	1.18			1084
				F61	343	0.05*	1.96		ND	1.83			1070
				F76	77	0.05*	0.05*		ND	ND			243
				F41	77	0.05*	0.05*		ND	ND			240
		2/11		F93	217	0.05*	0.32		ND	0.47			686
				F78	217	0.13	1.55		0.19	2.29			677
Paired Area	Pier	2/8	V-Blender	F14	456	0.05*	1.22		ND	0.88			1386
		2/8		F39	456	0.05*	0.67		ND	0.46			1468
		2/9		F28	237	0.05*	0.35		ND	0.49			720
				F37	237	0.05*	0.32		ND	0.42			763
				F29	106	0.05*	0.05*		ND	ND			322
				F34	106	0.05*	0.09		ND	0.26			341
		2/10		F75	336	0.05*	0.72		ND	0.7			1021
				F71	336	0.05*	0.8		ND	0.74			1082
				F69	79	0.09	0.22		0.37	0.92			240
				F84	79	0.05*	0.05*		ND	ND			254
		2/11		F79	209	0.07	1.18		0.11	1.86			635
				F97	209	0.05*	1.85		ND	2.75			673
Area	Mead Johnson Fixed Location No. 1 (inside curtain)	2/8	Tableting	F10	489	0.05*	0.21	0.45	ND	0.14			1516
		2/9		F24	407	0.05*	0.05*	0.35	ND	ND	NO	0.16	1262
		2/10		F66	485	0.05*	0.05*	0.35	ND	ND	NO	0.08	1503
		2/11		F87	490	0.05*	0.54	0.46	ND	0.35	ND	0.14	1519

Type Sample	Location/ Worker	Date	Process Area	Sample No.	Duration (mins)	ug Per Sample EE	ug Per Sample NOR	Weight, mg Net	NIOSH** EE (mg/m.)	NIOSH** NOR (mg/m.)	M/J** EE (mg/m.)	M/J** NOR (mg/m.)	Sample Volume Liters
Area	Air Supply Plenum	2/8	Tableting	F13	460	0.05*	0.05*	0.36	ND	ND			1380
		2/9		F30	403	0.05*	0.05*	0.54	ND	ND			1209
		2/10		F64	482	0.05*	0.05*	0.29	ND	ND			1446
		2/11		F86	486	0.05*	0.05*	-0.05	ND	ND			1521
Area	Tablet testing Station Mead Johnson Fixed Location No. 2	2/8	Tableting	F7	464	0.05*	0.05*	0.2	ND	ND	ND	0.38	1438
		2/9		F33	405	0.05*	0.09		ND	0.07	ND	0.06	1255
		2/10		F62	483	0.05*	0.1		ND	0.07	ND	0.08	1497
		2/11		F98	487	0.05*	0.06		ND	0.04	ND	0.06	1510
Personal	M	2/8	Tableting	F11	71	0.11	0.21		0.23	0.44	ND	0.23	213
					62								0
					87								261
	N	2/9	Tableting	F27	96	0.05*	0.05*		ND	ND	ND	0.16	525
					79								
	O	2/10	Tableting	F63	109	0.06	0.13		0.07	0.15	ND	0.74	867
					70								
					39								
					71								
	P	2/11	Tableting	F100	111	0.09	0.99		0.09	1.01	0.10	1.64	975
					92								
					47								
					75								
	A	2/8	Granulation	F23	93	0.16	2.58		0.56	9.12	1.12	19.3	283
				F20	81	0.12	3.03		0.48	12.27	1.28	26.3	247
	B	2/8	Granulation	F59	94	0.24	3.85		0.84	13.4	3.13	64.6	287
				F6	115	0.21	2.30		0.60	6.53	3.11	37.2	352
				F75	75	0.07	0.45		0.31	1.96	ND	2.38	229
	C	2/8	Granulation	F18	89	0.14	1.65		0.52	6.11	2.03	34.9	270
				F51	80	0.29	6.7		1.2	27.7	2.13	82.0	242
				F58	76	0.05*	0.54		ND	2.3	ND	1.99	230
	D	2/9	Granulation	F17	75	0.96	16.82		4.19	73.4	5.09	78.6	229
				F38	106	0.16	2.57		0.49	7.96	0.38	7.54	323
				F32	71	0.05*	0.18		ND	0.83	Trace	2.07	216
	E	2/9	Granulation	F46	78	0.29	5.52		1.23	23.39	1.69	28.8	236
				F48	106	0.05*	0.05*		ND	ND	1.59	21.0	321
				F25	70	0.06	0.26		0.28	1.23	ND	2.99	212
	F	2/9	Granulation	F36	72	0.33	6.54		1.5	29.72	3.39	63.8	220
				F47	68	0.07	1.69		0.34	8.12	0.69	16.2	208
				F35	69	0.05*	0.1		ND	0.47	ND	0.76	211
	G	2/10	Granulation	F68	83	0.21	3.45		0.83	13.63	2.82	54.2	253
				F49	92	0.71	17.94		2.53	63.84	3.69	52.8	281
				F50	48	0.11	0.32		0.75	2.19	ND	4.68	146

Type Sample	Location/ Worker	Date	Process Area	Sample No.	Duration (mins)	ug Per Sample EE	ug Per Sample NOR	Weight, mg Net	NIOSH** EE (mg/m.)	NIOSH** NOR (mg/m.)	M/J** EE (mg/m.)	M/J** NOR (mg/m.)	Sample Volume Liters
	H	2/10	Granulation	F56	81	0.12	1.89		0.49	7.71	1.81	33.8	245
				F26	90	0.11	2.56		0.4	9.38	14.8	121.0	273
				F60	46	0.05*	0.13		ND	0.93	ND	0.99	139
	I	2/10	Granulation	F74	84	0.51	8.98		1.98	34.9	4.2	81	259
				F65	Unk.	0.05*	0.77		ND	Unk.	2.27	50.5	Unk.
				F22	46	0.05*	0.27		ND	1.91	ND	0.67	141
	J	2/11	Granulation	F77	76	0.62	10.56		2.67	45.5	4.46	88.7	232
				F90	34	0.05*	0.41		ND	3.94	ND	7.35	104
	K	2/11	Granulation	F96	75	0.82	14.51		3.61	63.92	6.23	139.0	227
				F80	36	0.18	2.22		1.65	20.36	ND	20.1	109
	L	2/11	Granulation	F95	76	0.61	11.09		2.56	46.4	2.8	62.4	239
				F89	34	0.05*	0.32		ND	3.08	ND	4.8	104
	Blanks			F52		0.05*	0.05*	0.02	ND	ND			
	Blanks			F9		0.05*	0.05*	0.15	ND	ND			
	Blanks			F16		0.05*	0.05*	0.07	ND	ND			
	Blanks			F45		0.05*	0.05*	0.39	ND	ND			
	Blanks			F21		0.05*	0.05*	0.13	ND	ND			
	Blanks			F55		0.05*	0.05*	0.0	ND	ND			
	Blanks			F85		0.05*	0.05*	0.24	ND	ND			
	Blanks			F88		0.05*	0.05*	0.07	ND	ND			
	Blanks			F99		0.05*	0.05*	--	ND	ND			
	Blanks			F54		0.05*	0.05*	0.23	ND	ND			
	Blanks			F82		0.05*	0.05*	0.16	ND	ND			

* Indicates less than detectable value.
** ND - nondetectable.

APPENDIX C

LABORATORY SIMULATION OF VENTILATION MEASUREMENTS

During the site visit, face velocity measurements were obtained from return and exhaust plena. The air is distributed to the work area by perforated (1/4 inch holes) steel sheets with 40 percent open area. Each geometric section of a plenum measured was divided into a number of equal areas. Face velocity in each area was measured with a Kurz Model 441 anemometer by placing the tip of the probe at the centerline of a hole in the middle of the area.

In simulating the measurements, perforated sheets of about 17 inches by 17 inches were placed alternately at the exhaust and discharge end of a wind tunnel. The tunnel was fitted with a calibrated orifice velocity meter. The perforated sheets were divided into 9 equal areas. Velocity measurements were taken as described earlier at three randomly selected holes toward the center of each area. The results of these measurements are given in Tables C-1 and C-2. Calculated flow was obtained by multiplying the average velocity by the gross area. The ratios of actual to calculated flow ranged between 0.65 and 0.69 at the exhaust end and between 0.42 and 0.46 at the discharge end. These factors were used in reducing field data.

Table C-1. Face velocities under exhaust conditions.

Actual Flow (cfm)	Traverse Points									Calculated Flow (cfm)	Ratio of Actual to Calculated Flows
	1	2	3	4	5	6	7	8	9		
638	400	400	400	450	470	430	400	450	420	923	0.69
	410	360	430	450	450	440	490	450	400		
	450	450	480	470	500	400	450	450	380		
Avg.	420	403	437	457	473	423	447	450	400		
422	330	300	280	300	320	290	340	310	250	633	0.67
	340	280	250	310	300	300	300	310	270		
	325	325	280	310	290	310	330	310	220		
Avg.	332	302	270	307	303	300	323	310	247		
216	150	150	150	140	160	150	170	155	140	331	0.65
	175	180	160	160	175	120	170	155	150		
	160	165	175	150	165	140	155	155	125		
Avg.	162	165	162	150	167	137	165	155	138		

Table C-2. Face velocities under supply conditions.

Actual Flow (cfm)	Traverse Points									Calculated Flow (cfm)	Ratio, Actual Calculation
	1	2	3	4	5	6	7	8	9		
216	230	240	250	230	180	225	260	230	230	467	0.46
	260	240	290	230	150	220	240	190	280		
	280	270	300	240	150	190	325	180	190		
Avg.	257	250	280	233	160	212	275	200	233		
422	670	500	500	400	200	420	500	420	600	915	0.46
	600	470	500	550	380	440	450	420	460		
	630	460	470	440	360	420	410	310	430		
Avg.	633	477	490	463	280	427	453	383	497		
634	900	750	800	750	580	700	780	690	900	1491	0.42
	920	730	730	740	560	690	780	620	850		
	1050	780	800	740	570	570	650	700	730		
Avg.	957	753	777	743	570	653	737	670	827		

APPENDIX O

DISTRIBUTION OF FLOW IN SUPPLY AND EXHAUST PLENA

Sector	%Area	%Flow
1	25	12
2	25	10
3	25	15
4	21.5	60
5	1	0.3
6	1	0.3
7	1	1.3
8	0.5	1.1

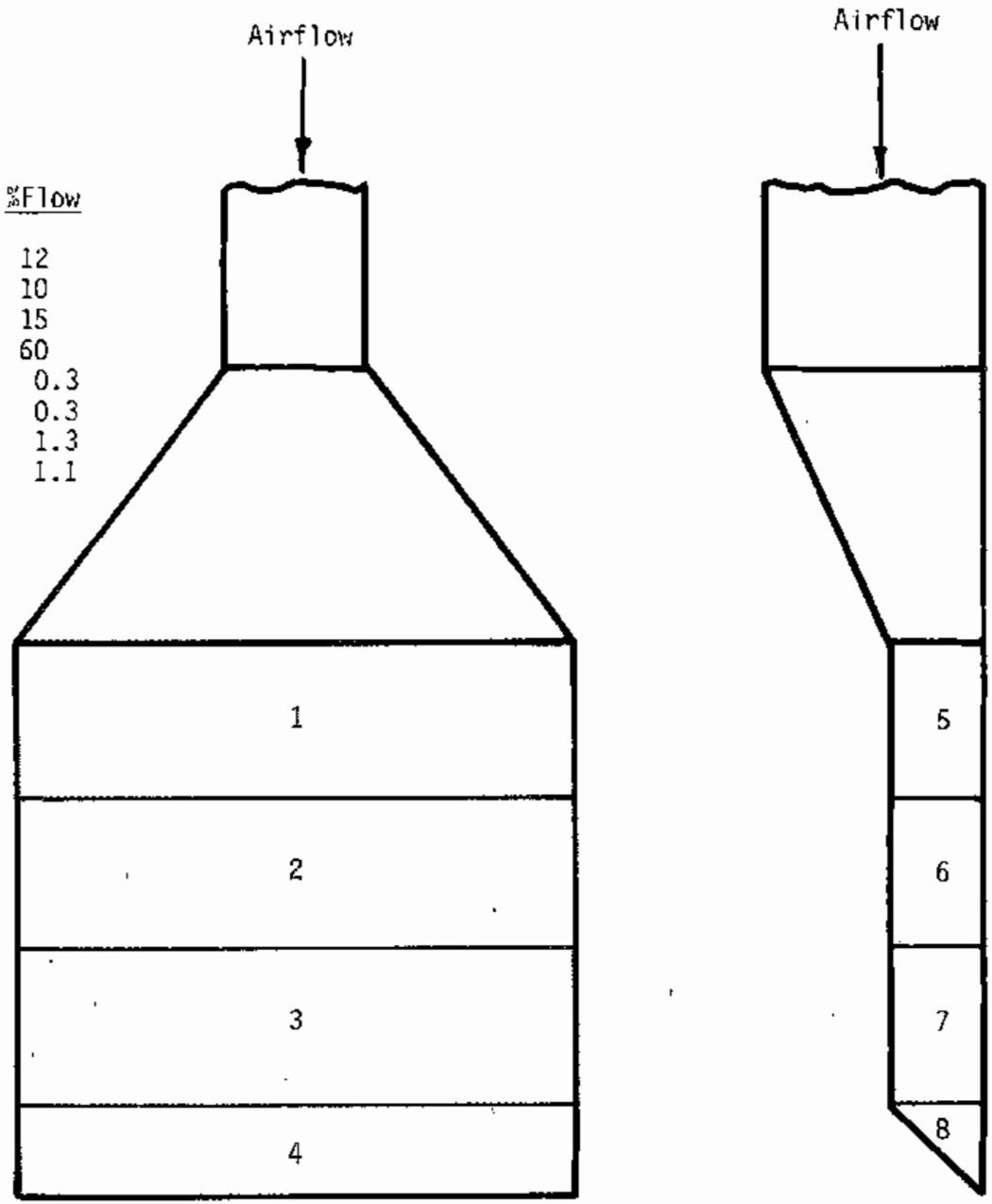

Figure D-1 Typical distribution through return plena

Sector	%Area	%Flow
1	22	15
2	39	31
3	39	54

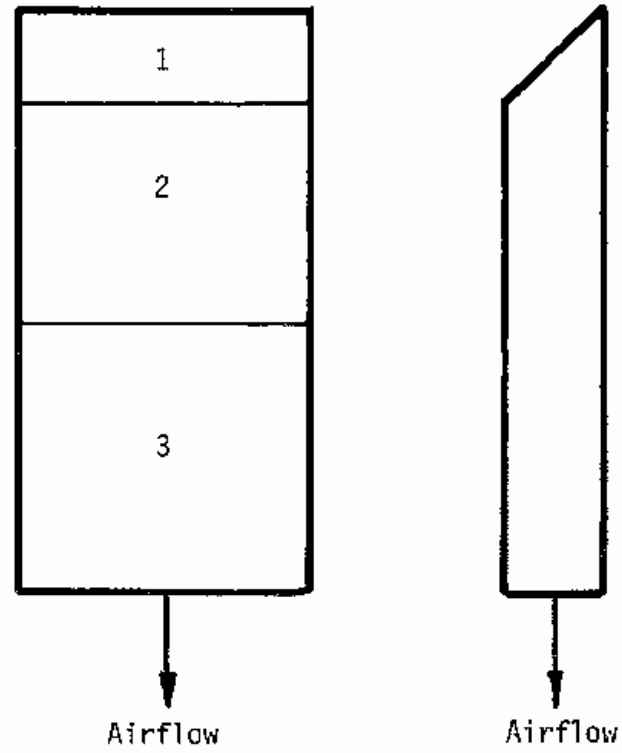

Figure D-2 Typical distribution from exhaust plena