DESIGNING MODEL OF BIOLOGIC PRODUCT BUILDINGS

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ABSTRACT
The physical health of the human kind and the environment around including medium or direct elements serving to him is one of the main factors of the life of the humanity. Since many years ago the medical sciences has been developing applying new technology and sciences every day. Today, other sciences and new technologies support the sciences of the health branch in line with meeting the welfare and safe life needs of the humanity. Similarly, architecture has taken effective steps with the suitable designing of the biologic spaces in this relation.Diagnosis of infections, prevention of infections and taking care of patients each one has it own special method discovered during years by the expert and professionals of this science, who were used to do this with the help of the other science. On the other hand, for the creation of the new solution and issuance of new methods, a suitable structural space is needed in line with meeting the needs of the collection. For reaching this purpose that is the same called "Good architectural at the service of industry and medical section", the architectural engineers should apply their best in designing an applied collection having dominance on the performed activity and application of the advanced production systems in order to supply the safe working environment for the personnel with the creation of fascinating and diverse spaces which motivate the personnel giving them comfort at the same time.It was almost several years ago that W.H.O[i] has compiled G.M.P[ii] rules in line with the health of community and quality and safety of the products and introduced it being enforceable in all the related centers. The above- mentioned standards have believed that the building and installations engineering has a great role in reaching the optimized quality.

Keywords: biological spaces, biologic product, GMP, clean room, movement path, final materials.

1. INTRODUCTION:

Diagnosis, prevention them, caring of diseases each has its special method discovered by the experts and professionals in this field during years and centuries who perform it with the help of the other sciences. On the other hand, for the establishment of novel solutions, presentation, and issuance of new methods, a suitable space is required in line with meeting the needs of the complex. For the realization of this goal, i.e. the good architecture at the service of industry and medicine, an architectural engineer (designer) should apply his best of efforts to establish an applied collection with the dominance on the accomplished activities and to design applying some advanced production systems in order to establish some attractive work spaces contributing to the motivation of personnel and ensuring safe and healthy work conditions for them.

In relation with the treatment and prevention of diseases, sometime, the chemical and biological materials play highly effective role. Production of every material has its special process. However, the group known as biologic materials have complex production process and since there are some biologic factors including the aerobe and non-aerobe bacteria, parasites, fungus, and/or some effective infectious factors that the deal with each one of

them requires special necessities a part of which necessities is available with the attendance of a good architect and establishment of a good architecture.

For designing buildings for the production of the biologic products, first of all we should reach a general concept about the product, production process, and needs of that complex similar to any other production centers. Such recognition ends in different performance domains and their general relation with each other. With its development, a comprehensive view is acquired concerning all effective factors in designing a special project, structuring, arrangement of the building, and the preliminary design. This preliminary design should be provided with the precise and full cooperation between the designer (specialists in building affairs), process specialists, and specialists in the field of installations.

In the meantime, it must be noted that all the production centers of the biologic products similar to any other architecture should be designed based on the needs of the user and in line with reaching special objectives of the project and similar to any other erection they must be formed based on special standards and principles. The only difference in this connection is that in the production complexes producing variety of medical products, especially those of biologic type, attendance and practice of such standards and principles finds much importance in the designing and formation of the erection[iii].

Higher focus on the special standards and principles in case of all production centers is because of the fact that all the production processes are in relation with the establishment of comfort for the sake of the human life and deficiency in any stage of production will directly or indirectly cause disorder or risk the life of the humankind. In this connection, collection of standards, principles, and rules are compiled under the title of Good Manufacturing Practice (GMP) for the presentation of the desirable production methods. GMP is a part of Quality Control of Product and insures that products are continuously controlled based on the quality standards in relation with the expected consumption and authorized consumptive necessities are produced and controlled.

Purpose from the practice of such standards is the reduction of the probable risks on the way of production that may not be controlled with the mere control of the final products. In this collection of principles and standards required for the production matter, two issues are discussed separately: a) management, and b) facilities (building, installations, and equipment), and include all productions of the car making industries, wood industries, agricultural industries, medical industries, food industries, etc.

World Health Organization (WHO) has became responsible to supervise the chemical and biologic medical industries as of several years ago, which organization has compiled

the GMP regulations in line with the social health, quality, and health of products and has made them enforceable for all the related centers. Such standards have introduced the role of civil engineering and installations being very effective in having products with higher quality.

This collection of principles and standards (GLP and GMP) has presented regulations for the establishment of ideal and desirable situations in the production centers that the related executive instructions are compiled through interaction with the specialist groups in the field of contraction and installations.

2. Designing Model of Biologic Product Buildings

2.1 Principles and basics ruling on architecture:

For reaching a general layout of the building, It should specify the sitting of each one of spaces in relation with each other and in every realm. Such sitting is done with the consideration of all needs related to the process in every domain, movement of materials, personnel, needs related to equipment and installation requirements of the common and clean spaces.

2.2 Identification of product and biologic product:

The first and the most effective factor in the composition of the biologic production spaces is the specifications of the biologic materials worked with. The true understanding of the production process, lifespan of the biologic factor and its biological specifications, as well as the production course of the product has a big role in the formation of spaces and the relation between them.

2.3 Moving Flow:

One of the other effective factors in the laboratory designing of the biologic products is the movement flow. The moving style of every production factor in a laboratory may have different specifications and models. In the production building, the most important of such flows is related to the production process. Stages that products leave behind in the production process are the most important factors in the formation of buildings such that the other factors are designed in line with the optimized execution of it. Course of the shortest path, suitable alternation of spaces, avoiding unnecessary comes and goes, avoiding creation of any cross contamination and consideration of the G.M.P. principles are of cases that must be taken into account in the production process.

The moving materials flow required by different sections in the production process should take a path different from that of the production process. These materials may include consumptive materials in every section or space as well as wastes resulted from the production process. Two models can be selected in the movement of materials from the storages to the source spaces and from spaces to the sections related to the discharge of wastes: a) Unilateral movement flow and b) Bilateral movement.

In the unilateral movement, input and output of materials is done through two separate and non-crisscross courses. Non-contamination of the raw material, nonexistence of cross between the course and the polluted points, and existence of entrance and exit independent from the passing path of the personnel are of matters that should be considered in the materials flow.

Movement and access of personnel to all the laboratory spaces follows special predetermined model and order. This model differs depending on its activity type, criticality of the work area, (BSL)[iv] Movement of personnel throughout the laboratory or within the critical spaces and areas should be designed in unilateral fashion in terms of either the weather class or (BSL) such that the site and the entrance current and the dress change order while entering are fully independent from the exit course and site and dress change order. Accesses and the movement paths to the clean spaces should be away from the polluted points and without interchange with the courses in relation, by one way or another, with the polluted spaces.

The last debate considered in this section is the movement of devices and equipment. Devices and equipment used in the production laboratory are divided to two big groups including the *big equipment* the transfer of which is rarely done, and the *consumptive equipment* used in different production and packing sections. In cased of the consumptive equipment such as small containers and devices, bottles, and the related accessories, the access courses and the movement current should be considered such that an optimal course is passed through from the storage of sterilized devices to the site and to sterilization section from there, if necessary, to the washing and autoclave and wastes discharge sections. For this purpose, the access courses from storages to the considered spaces and to the washing and sterilization and waste discharge sections should be independent from each other and without interchange or cross with each other. Entrance of clean devices and exit of the polluted ones from the working spaces should be done through separate vents. The passing course of the clean equipment

should be away from the polluted region or courses. The return course of the polluted equipment should independent from the clean spaces.

2.4 Stages of Critical Process and Clean Work Regions:

The production process of a biologic product includes different stages. These stages that are done with special alternation start from raw materials and end in the final product. Considering the type of the product, production stages, and specifications required by it in every section of the process have some predetermined conditions. Some of these stages are very sensitive. Therefore, they require some controlled environmental conditions. These production stages are called the *critical zone*[v]. Such operations are done in a space called the Clean Room.

2.5 Classifying the cleanness level of air and the control methods of contamination:

The cleanness level of air for room or a clean area is the maximum number of the allowed particles per m^3 of air for the said measurements and in the form of Air Classes A, B, C, and D.

Four distinguish degrees are introduced for the air class according to the following table:

Table 1- Air purity degrees according to the standards of Federal E-209[vi]:

Maximum of the particles per foot m^3/lit * 5-micron and bigger particles	Purity degree (metric)	Maximum of the particles per foot m^3/lit * %5-micron and bigger particles
10 (0.35)	100 (3.5)	100 (3.5)
10 (0.35)	1000 (35)	1000 (35)
35 (2.3)	10000 (350)	10000 (350)
700 (25)	100000 (3500)	100000 (3500)

- Numbers within brackets are in terms of metric unit.

2.6 Air Pollution, Contamination Sources, and Control Methods:

In the medicine and food materials production factories, consideration of the cleanness and neatness is obligatory and for the establishment of a suitable work or production environment, the input courses of contamination should be dammed and the existing contaminations must be removed through the application of special approaches. Such contaminations in a Clean Room include the transferred contaminations and contaminations of the space itself.[vii]

For the economic, technical, and operational reasons, the clean areas are usually surrounded by the other area with lower neatness scale. In this connection, we can

minimize the scale of areas with higher neatness degree. Since the transposition of materials and personnel between the adjacent clean spaces may increase the risk of contamination transfer, therefore, the arrangement and management details of the movement of materials and personnel should be precisely considered.

For the pass and transfer of bigger and small equipment to laboratory through locations in which the transfer and pass box equipped with the air shower is installed must be used. At the time of transferring the consumptive materials in laboratories, the transfer and transposition of the contamination sources and contaminator particles is avoided through making use of suitable and proper packing.

Figure1. Sample of clean room

From: URL2-mecart.com-2006

Number of the openings connecting the clean room to the outer space or the adjacent spaces should be minimized. For minimizing the contamination resulted from the input and output of personnel, materials, or air stream, some effective methods should be applied. Entering to/existing to the clean room for the sake of personnel and materials is done through air lock.[viii]

The air locks and pass boxes are used usually for the preservation of the pressure variation and unity of the controlled space while entering and exiting.

The cautious proceedings should be taken to make sure that opening of the entering and exiting doors and the vent of the air lock are not open at the same time.

In designing settings of spaces in clean areas, the sitting order of spaces should be considered. For instance, for designing a space with the Air Class C, we should enter the controlled area first, and then the Air Class D, and then the considered space last of all.

This matter besides the creation of special and step-by-step order for entering the cleaner spaces results in the reduced expenses resulted from the filtration and making sure of the consideration of the conditions of clean room.

A collection of clean rooms may include various rooms with different necessities for the control of contamination. The designing objective may be the preservation of production process, preservation of product and, in some occasions, a combination of such necessities. For protecting the clean rooms against the adjacent spaces with lower purity, the clean room should be kept in a higher static pressure compared to the adjacent spaces or, instead, the controllable (variable) air speed should be used in the air leakage areas from the clean space to the space with less purity. The reverse current may be dangerous. In both situations, a non-penetrable physical dam may be used as a substitute method.

The pressure change between the clean rooms or the adjacent clean spaces with different purity degrees is usually adjusted in the range of 5p – 20p in order to provide the possibility of opening doors with no difficulty and to avoid the creation of unwanted cross s and noise contamination sometimes. The dress change rooms are kinds of special air locks for the entrance and exit of the personnel of the clean rooms.

Special equipment used for controlling contamination such as air showers, sticking doormats, scrappers, etc may be used in the incoming and outgoing points. You should make sure of the separation of the personnel entering the clean room and those exiting it. These rooms, suitable with their function, should have enough space and depending on the quality of the clean room should include a space for dressing and taking off special cloths, or they shall include the antiseptic locations, etc.

This matter can be done through the time separation or installation of the separate input and output courses. When dangerous materials are processed, a distinguished path should be used for changing closes and avoiding the contamination.

2.7 INSTALAITIONS OF THE CLEAN ROOM:

For having access to the desirable physical conditions in a Clean Room, strategies should be adopted in favor of the installations that are related to the mechanical installations and the electric ones and the executive facilities and possibilities of which should be taken into account at the time of designing the building.

In the electric installations section, type of color and intensity of light is considered. Generally, supply of a suitable space and environment is crucial not only in the clean

room but also in the other space and this matter is more serious in case of the controlled and special spaces.

In the calculation of installations, the matter of temperature in measurement labs equipped with the measurement systems with the precision rate at micron scale, the temperature change may have some undesirable effects on the output of the system. Existence of openings and windows, even the double glass type, cause the higher consumption of energy for adjusting temperature due to the existence of the generation possibility of temperature variations. For this reason, it is considered as one of the main issues in the calculation and designing of buildings.

3. MATERIALS AND CONSTRUCTION:

One of the main and effective factors in the preservation of the controlled conditions of the production laboratory spaces and its clean spaces is materials and the final coating of the surfaces of these spaces.

Materials used in the establishment of the clean complexes should be selected and applied in compliance with the necessities of the clean complex and the following matters should be considered in this connection:

A) Purity Degree;
B) Effect of abrasion and strike;
C) Cleaning and disinfection methods and its alternation; and
D) Corrosion and chemical/microbiological damages.

Materials that may collapse or generate particles can be used only when they are muffled and preserved properly.

The chemical compatibility of all the used materials with the operational necessities of the clean complex should be considered.[ix] The external surface of equipment, fittings and materials entered to the inside of the clean room or the clean space should have parameters similar to the façade structural works in the clean complex.

All the exterior materials should be suitable for cleaning and effective and cyclic pesticide and do not cause spongy or hard surfaces that can cause the accumulation of unit or chemical contamination or development of microbic infections such that they must stay non-spongy all the time and they should be resistant against corrosion and fraction. Walls, flooring, and ceiling in the clean rooms and clean spaces should be designed

such that their surface can be easily accessed for cleaning. In a clean room, walls, flooring, ceiling doors, the entrance section of the air vents to the inside of the rooms, swabs of wastewaters and so on are subject to this precondition.

Figure2. curve corner to clean easily
From:
URL-portafab.com-2005

Figure3. samples of door & window in clean room
From:
ULR-MECARt.com-2006

Angles and corners, especially in the connection site of flooring to wall and wall to wall, should be done in inclined fashion to provide the possibility of an effective cleaning.

For avoiding the staring reflection of light, the interaction of the color of surface and its rendition taking into account the illumination situations should be considered. Air locks, dress change rooms, and passages of materials should usually include the minimum necessities required for the clean spaces supported by them.

The ceiling vents for avoiding the entrance of particles existing in air or the other contaminators should be completely air tightened and the evenness of the air locks of

the passages designated for the necessary installations or the other penetration spaces should be granted with much attention.

In places that installations of glasses for walls or doors is required, the used glasses should be of non-opening type. Use of double glass with full air tightening quality should be considered such that they should generate completely even surfaces. If straight curtain or Venetian blind is used for reaching the required shadow, it must be installed out of the clean space or between the double glass windows. Minimization of the brims and protrusions at surface of doors and its fittings should be granted with higher attention. Doorsills must be omitted. Where the transfer of contamination is important, use of the pressure plates and automatic openers with suitable orientation for opening doors is recommended.

The apparent surfaces should generate conditions similar to those of the internal space of the clean room and the clean space and some additional qualities may be required in this connection. Save the emergency exits of the clean room, no direct relation must remain with the other spaces including performance or medium spaces and even with the ventilation systems.

Followings are common materials used in the external spaces:

a. For walls and ceilings:

- Antirust steel plates, plated aluminum, polymer plates or coatings (these materials are practiced in the form installation over a layer or suitable structure).

b. For flooring:

- Polymer coatings or plates, square parts with suitable sealants (in addition, flexibility, functioning, stability, beauty, and preservation qualities should also be considered).

4. ARRANGMENT OF EQUIPMENT:

Generally, in the clean spaces and scopes of critical process the minimum tools, equipment, and suites should be used. Existence of any barrier against the air current of the room besides causing disorder in the air stream may create points in which the air has not a suitable current. Such points can be referred as the blind points.

Arrangement of equipment in these spaces should such that a) minimum disorder is caused concerning the air stream and b) any additional movement of personnel should be eliminated through the suitable application.

All devices and containers used in the production cycle are movable and capable of being reused and they must leave behind the primary contamination elision, washing, and sterilization stages. Transfer of the contaminated devices from the consumption site to the washing section is possible through the special one-way paths. These tools should be transferred within suitable and airtight packs.

5. WASTES:

During the production process and in different stages of it, polluted materials and devices are generated that are not used that must be discharged from the building as wastes. Such wastes may be either in liquid or solid states. All the contaminated liquids should be cleaned before being discharged through the wastewater channels.[x]

The solid wastes after being collected and packed within suitable wraps are transferred to the primary autoclaves for removing related contaminations. There, after passing through the said autoclaves and becoming clean from any biologic infection, they are transferred to the out of the building and carried immediately to special place designated for burning them and burnt afterwards. In all stages of carrying wastes, suitable multilayer and resistant packs should be used.

6. ECONOMIC ASPECTS OF THE PLAN

Creation of building and production laboratories for the medical products especially for the sterile biologic products is very expensive. The mechanical equipped and advanced installations systems, developed electronic and electric systems cause higher expenses for the Client the passage boxes and air locks used in these buildings are very expensive. The building materials, especially the final coating materials of surfaces and materials for the construction of the clean rooms and the other related equipment are also expensive items in relation with the construction of such laboratories. Taking this into account, in all designing stages, from the general segmentation and arrangement of laboratory up to the higher details including the arrangement of every space, determination of the air class of the complex, and even the arrangement of the equipment, the economic aspects of the plan must be considered.

Any inconsiderable change in the plan may cause higher expenses. In the meantime any mistake in the designing stage may cause heavy damages in the construction period. Moreover, the unsuitable designing may double the current expenses of the building and production, in consequence, during the utilization period.

The continuous and rising change of the technical production know how and development of the related technologies and equipment used in the field of production causes the need for changes and corrections of building to be deeply felt. Obviously, for reducing the correction and betterment expenses, the flexibility matter of spaces and the possibility of changing with the minimum costs should also be analyzed.

7. Conclusion:

In designing the plan of a production building used for the generation of the biologic products, the come and go path of the personnel, the entrance of the raw materials, course of big equipment and the exit used for carrying out the waste materials should be designed with special conditions in order to yield no contamination connections. Solution of this multi unknown (x) equation is not possible except with the active attendance of an efficient and talented architect. Of course, attendance of the biologic consultants and installation specialist and their role in the execution and fulfillment of the tasks should not be ignored. The higher is the precision granted to designing the higher capacities are used higher quality products will produced and this will be effective for the health of the society in terms of every important aspect. It must not be ignored that admittance of the architects to the designing domain of the biologic spaces may provide a suitable ground for the production of the novel biologic and medical products in the local country.

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[i] World Health Organization

[ii] Good Manufacturing Practices

[iii] In treatment productions complex, that part including the virus and bacteria vaccines, treatment serums, and antigens are called the biologic productions for the type of production. In the production of such products, alive and half- alive viruses and bacteria are used in the preliminary stages and up to the end of the production process sometimes.

[iv] Bio Safety Level

[v] critical zone, may include the distinguished air class or the fully sterilized conditions. Temperature, light, humidity, and other environmental factors should be at a determined and

defined level. Obviously, the input and output method of materials, personnel and equipment has weal models. In addition, other physical and structural factors such as the final materials, doors, and windows should have correct specifications.

[vi] Reference: Zareh Shahneh, Abolghasem (2006), "Designing the Cleaning Room", 1st Edition, Tehran, Farhange Eslami Press.

[vii] The transferable pollutions include the contaminations caused by the humankind, air and material contamination. The human factor is a main source for pollution. Particles are excluded from the mouth and nose of people and yet the physical movements of the humankind general particles. The more is such movements the higher will be the generated particles. If the air is not cooled, it will carry the contaminated particles with itself. The next contamination factor is the consumed materials in laboratories. In case of contamination the origin of which is the space itself, we may introduce the laboratory equipment and tools. In this kind of spaces, we should avoid creation of surfaces, because surfaces absorb contaminations.

[viii] Air Lock Room is a space that functions as a device for establishing relation between the spaces with different classes or different air quality and is designed for this purpose.

[ix] For instance, this matter may have impact on the selection of the sticking and air lock materials of the final work or materials used for sitting and air tightening the air filters.