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A REVIEW ON ALTERNATE VENDOR DEVELOPMENT

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ABSTRACT

Alternate Vendor Development is an important strategy followed by Pharmaceutical industries in order to meet the continuous demand of materials for production of dosage forms. This article reviews the reasons and requirements for AVD, changes in pharmaceutical formulation and API which are inevitable and procedure for evaluating those changes. It also describes advantages over the development of AVD.

KEYWORDS

AVD, Pharmaceutical formulations, API and Dosage forms.

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INTRODUCTION[1,2]

Alternate Vendor Development is an important strategy followed by Pharmaceutical industries in order to meet the continuous demand of materials for production of dosage forms. Multiple resources will come into hand when a company asks for a material. The important step now is to select the material from this group of vendors such that they meet the company's desired specification.

Two of the important responsibilities for the **Purchasing executive are**

1. To select the right source of supply.
2. To develop new suppliers.

In other words, supplier selection and new source development are major contributions of the purchasing function and so should have properly planned approach. A good supplier actively participates and helps the purchase to meet his customer's requirements.

Suppliers also contribute their specialized knowledge and help build quality into the purchasing company's products. For the selection, it is easy for purchaser to work out a preference pattern based on price, quality, and delivery, service land his geographic allocation, his technical ability and knowledge. The suppliers may be large, medium or small, who supplies raw materials, component, equipment, etc.

Reasons for the AVD

- To break the monopoly of the existing product.
- To reduce the cost of the product.
- To improve the Quality of the product
- To reach the continuous market demand of the product.
- To maintain the supply of the product for consumer in time.

AVD is very important in pharmaceutical industry because of the changes occurred in the manufacturing of pharmaceutical products

Changes to the Approved Drug Product[2,3]:

- Changes are inevitable in pharmaceutical industry in fact they are very much necessary for the continuous Quality improvement of the product.
- Frequently, changes are made to the chemistry and manufacturing controls of drug product and continue throughout the life of the product.
- Changes to pharmaceutical products after the original regulatory approval can be initiated for a number of reasons, i.e., revised market forecast affecting batch size requirements, qualification of a new active pharmaceutical ingredient source, optimization of the manufacturing process, upgrade of the container-closure system, or enhancement of the analytical test methods and specifications.
- For technical advancements, there may be situations which demand/ necessitate modifications for an approved drug product.
- Some of these changes may be significant while others are minor. The changes can be major, moderate or minor depending on the changes likely to affect the quality, safety and efficacy of the product.
- The changes made must be in conformance with the regulatory requirements. Irrespective of the category of the changes, every change is to be brought to the notice of the regulatory authorities in the recommended formats.
- Company change control procedures will detail how these changes are evaluated and implemented. The regul atory group will determine the strategy for submission based on a review of the technical assessment of the change and the appropriate regulatory guidance. The strategy may be more complex if the product is marketed globally.
- The Scale Up and Post Approval Change Guidance (SUPAC) and the Changes to an Approved NDA or ANDA offer a significant amount of information. Similarly, for global changes various guidance available provides requirements for various types of changes.
- Type I (minor) and type II (major) variations guidance provide the requirements for the product changes in Europe. Similar guidance is provided by the Who using equivalent definitions for minor and major changes.
- In the US, the current regulations around changes are covered in 21CFR314.70 and indicate that "The applicant shall notify the FDA about each change in each condition established in an approved application beyond the variations already provided for in the application".
- By a thorough understanding of the relevant regulatory requirements and the related guidance documents, the necessary changes can be evaluated for the impact of the change on the Quality attributes of the final product and implemented.

Types of Changes

The available guidance defines the types of changes, recommended control tests for each type of change and recommended documentation that should required supporting the change. The changes that can affect the identity, strength, quality, purity or potency of the drug product are categorically reported as.

Major Changes

- A major change is a change that has a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.
- Such changes include reformulation, new test methods, new or relaxed specifications, packaging changes to a less protective package, new packages, new strengths outside of the approved range, new API synthesis, critical excipient changes, etc.

Moderate Changes

- A moderate change is a change that has a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product.
- Changes in this category include a manufacturing site change to a new location, which uses the same procedures and equivalent equipment, more significant changes to raw material composition, testing site change etc.

Minor Changes

- A minor change is a change that has minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product.
- Such changes include change in manufacturing location within the same facility, scale-up of batch size using equipment of the same operational principle, secondary packaging site changes, simple process changes, small changes in excipient composition, deletion of colorant or flavour etc.

The classification of various types of changes and the examples for each type of change in each category is given below:

Manufacturing Changes[3,4]

Manufacturing changes include changes to equipment, process, scale, and site. Each change needs to be evaluated for its potential adverse effect on the quality of the finished product. Changed batches need to be assessed for their equivalence. Typically, this is assessed through testing to determine if the product's identity, strength, quality, purity, and potency were affected.

A) Site changes

Site changes consist of changes in location of the site of manufacture, packaging operations, *labeling operations* and/or analytical *testing sites*. They do not include any scale-up changes, changes in manufacturing (including process and/or equipment), or changes in components or composition. A typical site change includes a move to a different manufacturing site that involves other changes (e.g., process, equipment) and hence it should be evaluated as a multiple related change.

Major Changes

- A change in manufacturing site to a different manufacturing site
- For the manufacture, processing, or primary packaging of drug products when the primary packaging components control the dose delivered to the patient or when the formulation modifies the rate or extent of availability of the drug; or
- For the manufacture or processing of in-process materials with modified-release characteristics; examples of these types of drug products include modified-release solid oral dosage forms, transdermal systems, liposomal products, depot products, oral and nasal metered-dose inhalers, dry powder inhalers and nasal spray pumps.
- Transfer of the manufacture of a finished product sterilized by terminal process to a newly constructed facility at a different manufacturing site.

Moderate Changes

- Consist of site changes between facilities in adjacent city blocks, where the same equipment, SOP's, environmental conditions (e.g., temperature and humidity) and controls, and personnel common to both manufacturing sites are used, and where no changes are made to the manufacturing batch records.
- A move to a different manufacturing site for the primary packaging of (1) any drug product that is not otherwise listed as a major change and of (2) modified-release solid oral dosage-form products.
- A move to a different manufacturing site for the testing.

Minor Changes

- Consist of site changes within a single facility where the same equipment, standard operating procedures (SOP's), environmental conditions (e.g., temperature and humidity) and controls, and personnel common to both manufacturing sites are used, and where no changes are made to the manufacturing batch records.
- A move to a different manufacturing site for secondary packaging, labeling and ink imprinting of solid dosage form products.
- A transfer of the manufacture of a finished product sterilized by terminal process to a newly constructed building or existing building at the same manufacturing site.

B) Process Changes

Manufacturing changes may involve the manufacturing process itself (critical manufacturing variable). For modified release solid oral dosage forms, consideration should be given as to whether or not the change in manufacturing process is critical to drug release (critical processing variable).

Major Changes

- Change in the type of process used in the manufacture of the product, such as a change from wet granulation to direct compression of dry powder.
- Changes that may affect the controlled (or modified) release, metering, or other characteristics (e.g., particle size) of the dose delivered to the patient, including the addition or deletion of a code imprint by embossing, debossing or engraving on a modified-release solid oral dosage form.
- Changes that may affect the product sterility assurance and the sterile packaging components like
- Changes in the sterilization method (e.g., gas, dry heat, irradiation)
- Addition, deletion, or substitution of sterilization steps or procedures for handling sterile materials in an aseptic operation.
- Changes in materials or pore size of filters used in aseptic processing.

Moderate Changes

- Changes of equipment operating conditions such as mixing times and operating speeds outside of validation ranges.
- For sterile drug products, elimination of in-process filtration performed as part of the manufacture of a terminally sterilized product.
- Filtration process changes like change from single to dual product sterilizing filters in series or repeated filtration of a bulk.
- Changes to filtration parameters for aseptic processing (including flow rate, pressure, time or volume but not filter materials or pore size rating) that require additional validation studies for new parameters.

Minor Changes

- Process changes such as mixing times and operating speeds within validation ranges.
- Addition or deletion of a code imprint by embossing, debossing or engraving on a solid dosage-form drug product other than a modified-release dosage form.
- A change in the order of addition of ingredients for solution dosage forms or solutions used in unit operations. (e.g., granulation solutions).

Equipment Changes

Manufacturing changes also involve the equipment used in the manufacturing process (critical manufacturing variable). For a change in manufacturing equipment that is not identical in every respect to the original manufacturing

equipment, appropriate validation studies should be conducted to demonstrate that the new equipment is similar to the original equipment.

Major Changes

- Change in equipment to a different design and different operating principles.
- Replacing sterilizers that operate by one set of principles with the sterilizers that operate by another principle (e.g., substituting a gravity-displacement steam process with a process using superheated water spray).
- Addition to an aseptic processing line of new equipment made of different materials (e.g., stainless steel vs. glass, changes between plastics) that will come in contact with sterilized bulk solution or sterile drug components, or deletion of equipment from an aseptic processing line.
- Replacement or addition of lyophilization equipment of a different size that uses different operating parameters or lengthens the overall process time.

Moderate Changes

- Change to alternative equipment with that of similar, but not identical, design and operating principle that does not affect the process methodology or process operating parameters.

Minor Changes

- Change from non-automated or non-mechanical equipment to automated or mechanical equipment to move ingredients.
- Change to alternative equipment of the same design and operating principles of the same or of a different capacity.

Scale Changes

Major Changes

- Changes in batch size beyond a factor of ten times the size of the pilot/biobatch, where:
- The equipment used to produce the test batch(es) is of the same design and operating principles;
- The batch(es) is (are) manufactured in full compliance with cGMPs
- The same SOP's and controls as well as the same formulation and manufacturing procedures are used on the test batch and on the full-scale production batch (es).
- Changes in aseptic processing methods, including scale that extends the total processing, including bulk storage time, by more than 50% beyond the validated limits.

Moderate Changes

- Change in batch size, up to and including a factor of 10 times the size of the pilot/biobatch, where:
- The equipment used to produce the test batch(es) is of the same design and operating principles
- The batch(es) is (are) manufactured in full compliance with CGMP's
- The same standard operating procedures (SOP's) and controls, as well as the same formulation and manufacturing procedures, are used on the test batch (es) and on the full-scale production batch (es).
- Changes in scale of manufacturing for terminally sterilized products that increase the bulk solution storage time by more than 50% beyond the validated limits.

Minor Changes

- Changes in scale of manufacturing for terminally sterilized products that increase the bulk solution storage time by no more than 50% beyond the validated limits.

FORMULATION CHANGES[5,6]

Product Reformulation

Reformulation of the drug product could lead to changes in the product stability. For example, the current formulation may contain an ingredient (inactive or another active) which is reacting with the API or causing the API to form a degradation product which increases over time. Therefore, a new formulation (with different excipients) is developed. An acceptable reformulation should have an improved degradation profile versus the original formulation. Changes in the qualitative or quantitative formulation, including inactive ingredients are considered as major changes and should be evaluated. A similar approach would likely be taken for a change in the critical excipient (rate-controlling) of an extended release or

transdermal dosage form. In this case the potential event triggering the re-formulation may be a decrease in dissolution results on stability as the formulation ages causing out-of-specification (OOS) results and/or a shortening of the expiration date. Thus the successful re-formulation may yield several benefits from a compliance perspective as well as a supply standpoint, such as improved dissolution performance on stability, an extension of the expiration date, and a decrease in rejected batches at release, since the internal requirements for dissolution may be relaxed.

The available guidance provides the information on excipient changes within certain ranges and also describes requirements for critical and non-critical excipients.

Changes in Non-Critical Excipient / Non-Release Controlling Excipient

Major Changes

- Addition or deletion of excipient(s)
- Changes in the excipient(s), expressed as percentage (w/w) of total excipient(s) in the formulation, greater than 10% w/w of total excipient content in the solid oral dosage form.

Moderate Changes

- Change in the technical grade and/ or specifications of an excipient (non-release controlling excipient). (Example: Avicel PH102 vs. Avicel PH200.).
- Changes in excipients expressed as percent (w/w) of total formulation, greater than those listed for a Minor change but less than or equal to the following percent ranges in the following Table No. 1.

Table No.1: Excipient and its Percentage

S.No	Excipient	Percent excipient (w/w) out of total dosage form weight
1	Filler	±10
2	Disintegrant Starch Other	 ±6 ±2
3	Binder	±1
4	Lubricant Ca or Mg Stearate Other	 ±0. 5 ±2
5	Glidant Talc Other	 ±2 ±0.2
6	Film coat	±2

Minor Changes

- Deletion or partial deletion of an ingredient intended to affect the color or flavor of the drug product; or change in the ingredient of the printing ink to another approved ingredient.
- Changes in excipients (non-release controlling excipient in case of Modified Release dosage form), expressed as percentage (w/w) of total formulation, less than or equal to the following percent ranges in Table No.2.

Table No.2: Excipient and its Percentage

S.No	Excipient	Percent excipient (w/w) out of total dosage form weight
1	Filler	±5
2	Disintegrant Starch Other	 ±3 ±1
3	Binder	±0.5
4	Lubricant Ca or Mg Stearate Other	 ±0.25 ±1
5	Glidant Talc Other	 ±1 ±0.1
6	Film coat	±1

Changes in Critical Excipient / Release Controlling Excipient

Major Changes

- Addition or deletion of release controlling excipient(s) (e.g., release controlling polymer/plasticizer).
- Changes in the release controlling excipient(s), expressed as percentage (w/w) of total release controlling excipient(s) in the formulation, greater than those listed for a Moderate change (i.e., greater than 10% w/w of total release controlling excipient content in the modified release solid oral dosage form).

Moderate Changes

- Change in the technical grade and/or specifications of the release controlling excipient(s). Example: Eudragit RS-100 vs. Eudragit RL-100.
- Changes in the release controlling excipient(s), expressed as percentage (w/w) of total release controlling excipient(s) in the formulation, greater than those listed for a Minor change, but less than or equal to 10% w/w of total release controlling excipient content in the modified release solid oral dosage form.

Minor Changes

Changes in the release controlling excipient(s), expressed as percentage (w/w) of total release controlling excipient(s) in the formulation less than or equal to 5% w/w of total release controlling excipient content in the modified release solid oral dosage form.

PACKAGING CHANGES[6]

The potential for adverse effect on the product when making a change to or in the container closure system is generally dependent on the route of administration of the drug product, performance of the container closure system and likelihood of interaction between the packaging component and the dosage form.

Changes to the container/closure system need to be evaluated for potential for impact on the product stability profile. Typically, only changes to the primary packaging component (product contact materials) have the potential to affect the product stability. Changes to secondary packaging such as cartons or a change in the packaging site do not directly impact product stability. However, deletion of a secondary packaging component that provides additional protection (e.g. light, moisture, or oxygen) may affect the product stability.

Major Changes

- For liquid (e.g., solution, suspension, elixir) and semisolid (e.g., creams, ointments) dosage forms, a change to or in Polymeric materials (e.g., plastic, rubber) of primary packaging components or in permeable or semi-permeable

container closure systems a change to an ink or an adhesive used on the permeable or semi-permeable packaging component.

- A change in the primary packaging components for any product when the primary packaging components control the dose delivered to the patient (e.g., the valve or actuator of a metered-dose inhaler).
- For sterile products, any other change that may affect product sterility, such as:
- A change from a glass ampoule to a glass vial with an elastomeric closure
- A change from single-unit-dose container to a multiple-dose container system;
- Changes that add or delete silicone treatments to container closure systems (such as elastomeric closures or syringe barrels)
- Adding a pre-filled syringe dosage form
- Changing to a flexible bag (large volume parenteral-LVP) from another container system
- Change in the size or shape of a container for a sterile drug product
- Deletion of a secondary packaging component intended to provide additional protection to the drug product (e.g., carton to protect from light, overwrap to limit transmission of moisture or gases)

Moderate Changes

- A change in or addition or deletion of a desiccant
- A change in the size or shape of a container for a non-sterile drug product, except for solid dosage forms

Minor Changes

- A change in the size or shape of a container containing the same number of dose units, for a non-sterile solid dosage form
- For solid oral dosage forms: adding or changing a child-resistant closure, changing from a plastic to metal screw cap or vice versa, changes in packaging materials used to control odour (e.g., charcoal packets), a change in or addition of a seal (e.g., heat induction seal), a change in an antioxidant, colorant or stabilizer for production of the container or closure etc.
- Similarly for liquid and semisolid dosage forms: adding or changing a child-resistant closure, changing from a plastic to metal screw cap or vice versa, a change in or addition of a cap liner or seal etc.

CHANGES TO ACTIVE PHARMACEUTICAL INGREDIENT (API)

Selection of API phase is one of the important decisions in the formulation development process. Subsequent to phase selection, the focus shifts to the API properties i.e., characterization of the chemical and physical properties of the drug substance. Chemical properties especially the identification of impurities is very important. In addition, the physical properties such as solubility, polymorphism, hygroscopicity, particle size, density, etc. must be addressed.

In the recent years, there has been a steady increase in the number of low solubility compounds in drug development. It is estimated that up to 90% of new chemical entities would be categorized as BCS class II or IV compounds. However, with the increase in the number of compounds in development and the shortened timelines for formulation development, focus now mainly sifted to development of better formulations with the existing drug substances. Optimization of API chemical (e.g., salt formation) and physical (e.g., particle size reduction through milling) properties is oftentimes employed to improve oral bioavailability of insoluble compounds. Such properties are closely monitored throughout the drug development and after the drug product approval, as they can have a direct impact on the formulation bio-performance.

Major Changes

- Transfer of manufacturing of an aseptically processed sterile drug substance to a newly constructed or refurbished aseptic processing facility or area or an existing aseptic processing facility that does not manufacture similar products.
- Process changes for sterile drug substances like change in sterilization methods; addition, deletion or substitution of sterilization steps etc

- Changes in the source material (e.g., microorganism, plant) or cell line
- Filtration to centrifugation, or vice versa change in the route of synthesis
- Any process change made after the final intermediate processing step
- Changes in the synthesis or manufacture if the drug substance that may affect its impurity profile or the physical, chemical or biological properties.
- Establishing a new procedure for reprocessing a batch of drug substance that fails to meet the approved specification.

Moderate Changes

- A move to a different manufacturing site for the manufacture or processing of the final intermediate.
- In increase or decrease in production scale during finishing steps that involves new or different equipment
- Changes in the size or shape of a container for a sterile drug substance.
- An addition to a specification that provides increased assurance that the drug substance will have the characteristics of identity, strength, purity or potency that it purports to or is represented to possess; for example, adding a new test and associated analytical procedure and acceptance criterion.

Minor Changes

- A move to a different manufacturing site for the manufacture or processing of drug substance intermediates, other than the final intermediate.
- The addition, deletion or revision of an alternative analytical procedure that provides the same or greater level of assurance of identity, strength, purity or potency of the material being tested.

MISCELLANEOUS CHANGES

A) Specification changes

Specifications (i.e., tests, analytical procedures and acceptance criteria) are the quality standards provided in an approved application to confirm the quality of drug substances, drug products, intermediates, raw materials, reagents and other components, including container and closure systems and in-process materials.

Major changes:

- Relaxing an acceptance criteria
- Deleting any part of specification
- Establishing a new regulatory analytical procedure
- A change in an analytical procedure used for testing.

Moderate changes

- Relaxing an in-process acceptance criterion associated with microbiological monitoring of the production environment, materials and components.
- An addition to a specification that provides increased assurance that the drug product will have the characteristics of identity, strength, purity or potency that it purports to or is represented to possess; for example, adding a new test and associated analytical procedure and acceptance criterion.

Minor changes

- Any change in a specification made to comply with an official compendium.
- Tightening of acceptance criteria.

B) Labelling Changes

A drug product labeling change includes changes in the package insert, package labeling or container label.

Major changes

- Changes based on post marketing study results, including, but not limited to, labeling changes associated with new indications and usage.
- Changes based on data from preclinical studies
- Claims of superiority to another product
- Change in the labeled storage conditions, unless exempted by regulation or guidance.

Moderate changes

- Addition of a precaution arising out of a post marketing study
- Addition of an adverse event

Minor changes

- Changes in the layout of the package or container label that is consistent with the regulations without a change in the content of the labeling.
- Editorial changes, such as adding a distributors' name
- Labeling changes made to comply with an official compendium

C) Others

Major changes

- Addition of or changes to a stability protocol
- Addition of an expiration dating period based on data obtained under new or revised stability testing protocol

Moderate changes

- Reduction of an expiration dating period to provide increased assurance of the identity, strength, quality, purity or potency of the drug product.

Minor changes

- An extension of an expiration dating period based on full shelf life data on full production batches
- Addition of time points to the stability protocol or deletion of time points beyond the approved expiration dating period.
- A change from previously approved stability storage conditions to storage conditions recommended in ICH guidance.

II. CHANGE IN API SOURCE

Often changes to the API source are proposed and implemented after product approval. Equivalence of impurity profile, chemical and physical properties is shown by testing three batches according to the approved specifications and utilizing the appropriate testing (e.g., X-ray powder diffraction, solid state NMR) to establish that the polymorph and crystal habit are unchanged.

On the other hand, many changes do involve synthetic and/or process equipment changes by the approved source. Changes early in the synthesis may have less impact on the final drug substance as compared to changes later in the synthesis. A change in the synthesis after the final intermediate step is typically considered a major change. Any change that may impact the physical properties of the API or the impurity profile needs to be evaluated from a stability perspective as well as the potential effect to the finished product.

The safety of the drug may be based upon the type and level of impurities and different physical characteristics may affect dissolution or content uniformity. Consequently, changes to the manufacturing process for the drug substance may change the purity profile or physical characteristics and thus cause problems with the finished dosage form.

Physical characteristics of raw materials can vary among manufacturers of drug substances and sometimes will vary from lot-to-lot from the same manufacturer. Chemical properties of the new drug substance lead to a chemical and/or physical stability decrease in the drug product, including an increase in the impurity levels. In the case of sterile drug products, increased endotoxins from the new drug substance will lead to increased endotoxins in the drug product.

Typically, a change from one drug substance source to another involves more than simply a site change. In most cases, there will be additional differences (e.g., route of synthesis, process, solvents, and equipment). Without extensive knowledge of the new and old sources (e.g., access to the drug master file), an applicant cannot adequately describe the differences between the sources or evaluate the multiple change.

Often during qualifying a new API source (new supplier), the synthesis procedure will be different from that of the approved source. This change would necessitate a complete evaluation of the API from a release and stability testing perspective.

Need for Changing API Source

Following are some of the intentions behind changing source for any material:

- To improve the quality of the drug product.
- To get the cost effective material. This would ultimately reduce the input material cost and subsequently the finished product.

- To get the material with superior quality (applicable in case of product specific requirements).
- To find a source (vendor) having better regulatory compliance.
- To ensure timely material availability with minimum lead times.
- To break the monopoly of the existing approved source.
- To ensure material availability for production even if the existing approved supplier stops supplying.

GENERAL PROCEDURE FOR EVALUATING CHANGES

- After the product approval, we may make changes in the drug formulation, batch size, process, equipment or manufacturing site, which affects the identity, strength, quality, purity and potency of the finished product.
- Therefore, any change must be fully evaluated prior to implementation to determine its impact on the quality of the finished product.

Assessment of the Effects of the Change

The effects of the change must be measured or assessed since these changes may relate to affect the safety or effectiveness of the drug product. The assessment of the effects of the change on the identity, strength, quality, purity and potency of the drug product can be done by

Conformance to specifications

- An assessment of the effects of a change should include a determination that the drug substance, in-process materials, and or drug product affected by the change conform to the approved specifications.
- A specification is a quality standard (i.e., tests, analytical procedures, and acceptance criteria) to confirm the quality of drug substances, drug products.
- Acceptance criteria are numerical limits, ranges, or other criteria for the tests described.
- Conformance to a specification means that the specification, will meet the listed acceptance criteria.

Additional testing

- In addition to confirming that the material affected by the changes continues to meet its specification, it is recommended to perform additional testing, when appropriate, to assess the impact of the change.
- The assessment should include, as appropriate, evaluation of any changes in the chemical, physical, microbiological, biological, bioavailability and/or stability profiles.
- This additional assessment could involve testing of the post change drug product itself or, if appropriate, the material directly affected by the change.
- The type of additional testing that should be performed would depend on the type of change, the type of drug substance and/or drug product and the effect of the change on the quality of the drug product. For an Instance: Evaluation of the hardness or friability of a tablet after certain changes.

Equivalence

- On testing, we should usually assess the extent to which the change has impact on the identity, strength, quality, purity, and potency of the drug product.
- Usually, this is accomplished by comparing test results from before and Post change material and determining if the test results are equivalent or not.

Adverse effect

- A change within a given parameter can have varied adverse effects depending on the type of dosage form and route of administration of the product.

For example:

- A change in the container-closure system of a solid oral dosage form will have less impact on the drug product than it would for a semisolid or oral liquid dosage form where the primary packaging component becomes critical for the shelf life of the finished product.
- A process change recommended could cause the formation of a new degradant that requires qualification or identification. Therefore we

- Must assess the change and get appropriate information that supports the continued safety and efficacy of the drug product.
- A small change in the concentration ratio of an inactive ingredient may have less impact on an immediate release drug product than it would for a modified release product, where that same ingredient may adversely affect the release rate, thereby impacting bioequivalence.

CONCLUSION

Alternate vendor development is a necessary for maintaining the continuous supply of the demanded product in the market. Before making AVD we have to look the changes and the evaluation of those changes and also reasons for changes. The regulatory authorities should overlook the appropriate documentation for the changes of vendor from old to new. Selecting and evaluating the right suppliers is the quintessential aspect of strategic purchasing and supply chain management that can affect manufacturing firms. The primary objectives of supplier selection and evaluation include reducing costs, attaining real-time delivery, ensuring world-class quality, mitigating risks, and receiving better services.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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