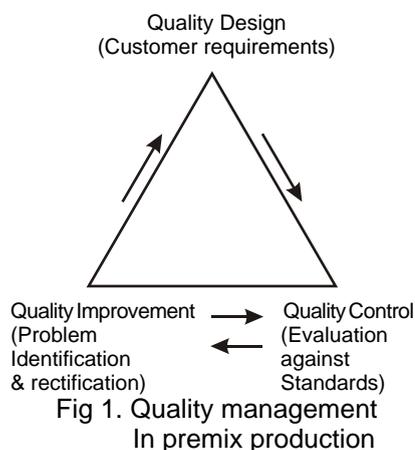


MANUFACTURING A QUALITY PREMIX

A premix is a mixture of vitamins, trace minerals, medicaments, feed supplements and diluents. It is a value added solution for feeds with sustainable safety and quality. The premix industry is charged with the responsibility of manufacturing a high quality premix consistently, efficiently and economically. Its main objective is to deliver the micro ingredients in a manner desired by the consumer.

Premixing has progressed from the simple hand mixing of several ingredients to mechanical mixing, to continuous mixing, and now to computer controlled mixing. However, the basic concept of mixing ingredients together to result in a homogeneous blend has remained unchanged.

The principles of quality management can be applied to improve and sustain the quality of premix. Modern quality management has three interrelated elements i.e. quality design, quality control and quality improvement (Fig. 1).



A quality premix can be manufactured only through a stringent quality assurance programme and current good manufacturing practices (cGMP).

Quality assurance is a proactive, continuous system for monitoring reproducibility and reliability of a product. It encompasses all the activities undertaken to ensure predetermined standards of a quality premix. Good manufacturing practices covers all the areas of the production process like personnel, facilities, raw materials, quality assurance checks, inventory control, processing, mixing, packaging and delivery.

Some premix plants are designed for specific functions, such as making poultry premix exclusively; others are designed for producing a variety of premixes for other segments as well. Regardless of the specific purpose of a premix plant, material flow follows a basic pattern (Fig. 2).

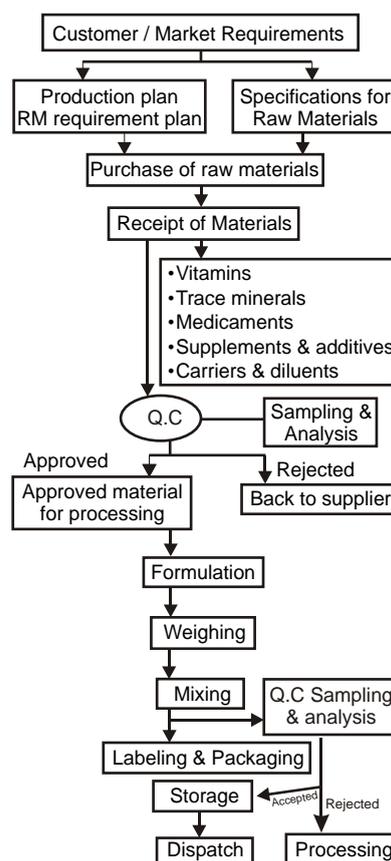


Fig 2: Flow chart of premix production process

Premix manufacturing process comprises:

- A. Raw Materials
 1. Selection & Specifications
 2. Purchase
 3. Receipt & Storage
 4. Sampling & Analysis
 5. Processing
- B. Formulation
- C. Weighing
- D. Mixing
- E. Packaging
- F. Labeling
- G. Storage of Finished Premix

A. RAW MATERIALS

1. Selection & Specifications

Vitamins and trace minerals are available in different forms and their bioavailability varies between sources. Amongst vitamins the stability forms an important criteria whilst bioavailability, potency and reactivity of trace minerals aid in their selection process. The form of ingredient selected must also be easily available, of economic interest and also impart acceptable physical attributes to the premix.

In order to maintain the stability of vitamins throughout their shelf life it is recommended to procure more stable derivatives like coated forms, that are not destroyed even when mixed with trace minerals. The spray-dried form of vitamins improves the flowability of the premix. The list of nutrients with their recommended sources is shown in Table 1.

The specifications for all raw materials should be based on recommendations applicable for particular animal's feed as mentioned by AAFCO, AOAC, AFMA, I.P, U.S.P., etc.

Table 1 : Nutrients and its sources

Nutrient	Sources
Iron	Ferrous sulphate monohydrate Ferrous carbonate
Copper	Copper sulphate pentahydrate Tribasic copper chloride
Zinc	Zinc oxide, Zinc sulphate
Manganese	Manganese oxide, Manganese sulphate
Magnesium	Magnesium oxide
Iodine	Calcium iodate , Potassium iodate
Cobalt	Cobalt carbonate
Molybdenum	Sodium molybdate
Selenium	Sodium selenite
Vitamin A	Retinyl acetate (C)
Vitamin D3	Cholecalciferol (C)
Vitamin E	dl- -tocopherol acetate (S.D.)
Vitamin B1	Thiamine mononitrate (P)
Vitamin B2	Riboflavin (S.D.)
Vitamin B3	Niacin (P)
Vitamin B5	D-calcium pantothenate (P)
Vitamin B6	Pyridoxine HCL (P)
Vitamin B12	Cyanocobalamin (1%)
Vitamin Biotin	Biotin (2%)
Vitamin Folic acid	Folic acid (S.D.)
Vitamin K 3	Menadione Nicotinamide Bisulphite-MNB or Menadione Sodium Bisulphite-MSB (C)

S.D.- spray dried, P-pure, C-coated

2. Purchase of Raw Materials

Raw materials must be procured from approved vendors and should conform to the specifications laid down by the nutritionist. No material should be received without a certificate of analysis.

Purchases should be done periodically taking care that sufficient inventory is maintained at all times. A purchase plan is desirable in accordance with production requirement.

3. Receipt & Storage of Raw Materials

The receiver should have enough information from the quality assurance program to be able to recognize the quality of product. Sacked ingredients should be checked for identification and condition. A reference number should be allotted for each raw material received into the premises. The sacked ingredients must then bear this reference number. Large consignments are to be weighed at weigh bridge whereas small ones

by using electronic balance. The complete details of the raw material along with its reference number must be entered into the stock records.

The raw materials should be logged in after segregation of drugs and other nutrients. Extra care must be taken for labeling. Bags or containers must be stored in a dry location on pallets assigned to them taking care of sufficient space between the pallets for comfort loading and unloading. To prevent development of stacking resistance not more than 10 bags are to be stored on one pallet. Meanwhile stacked stocks should be rotated to minimize lump formation, product degradation, and insect infestation.

The storage area must have sufficient protection from rodents and insects. It should be well ventilated, sanitized and away from direct sunlight. Depending on the stability of raw material they must be stored in environment of controlled temperature and humidity.

The storage area for approved and rejected materials must be distinct in order to prevent any confusion.

4. Sampling & Analysis

Sampling of raw materials is performed following a quality assurance programme. To obtain a representative sample, sampling should be done from bottom, center and top layer of the bag using a sample probe. When large consignments of raw materials are received, it is advisable to mix the raw material in mixer and then analyze each mixed batch to make an accurate assessment.

Instruments like H.P.L.C, flame photometer and spectrophotometer are used for analysis of raw materials to obtain accurate results. Raw materials should be analyzed using official methods by trained personnel.

Approved raw materials may be considered for formulation. If raw materials are differing in their particle size but other parameters are satisfactory then they should be considered for further processing like sieving, milling etc. When they are not meeting the pre-determined specifications in terms of potency or purity then they should be rejected.

5. Processing

Processing seeks to modify the physical properties of raw materials to meet the specifications of premix. Processing basically includes:

- (A) Sieving
- (B) Milling

Sieving is a primary process of removing foreign materials from raw materials as well as separating coarse ingredients. The operation can be carried out in equipments like vibratory or mechanical sifters. Care must be taken that the sifter is cleaned well before and after use to prevent any sort of contamination. The 'overs' obtained in the sieving process may then be ground.

A multimill can be used to reduce particle size to the desired screen analysis. Regular checks should be performed to detect wear of mill screen and blades.

The sieved and milled material is then bagged, weighed, labeled and transferred to the warehouse area for storage.

B. FORMULATION

This is an important and critical step in manufacturing a premix. Qualified personnel possessing knowledge and expertise regarding micro ingredients and powder technology should formulate a premix.

The formulator has to consider source of ingredients based on their physical, chemical characteristics, bioavailability, their interactions when mixed, handling characteristics, and economic implications on the final product before any final conclusion is arrived at.

Table 2 : Physico-chemical characteristics of raw materials

Physical Characteristics	Chemical Characteristics
Particle size	Potency
Particle shape	Purity
Particle density	pH
Flowability	Reactivity
Compressibility	Stability

Physical Characteristics

Particles of uniform size, density and that of spherical shape blend well to form a homogenous mixture. The chance of segregation is thereby minimized. For example trace minerals available in the market are invariably found to be coarse in nature whereas the vitamins are normally fine powders. Achieving a homogenous mixing of these two ingredients would be difficult (sand and pebble effect). However, homogenous mixing can be achieved by processing the trace minerals to the desired particle size and improved flowability.

The flowability of the ingredients plays a vital role while handling the powder i.e. before and after mixing. Poor flowability results in bridging, caking and product loss in the transfer system. Conversely too fluid a product may cause flushing.

Chemical Characteristics

Potency of vitamins, trace minerals and medicaments need to be considered whilst formulating high quality premixes. Based on the customer's requirement the formulator has to include the micronutrients considering their analytical value so that desired amount can be delivered when mixed in the feed. No materials should be incorporated in the premix without analysis since under or over addition may have deleterious effect on the overall performance of the birds consuming the feed.

Selection of carrier and its percentage is important for formulating a quality premix. It is generally preferable to leave sufficient space for a carrier in order to minimize any sort of interactions between the active ingredients. The carrier should serve the functions as depicted below:

- It should neutralize the electrostatic charges present in certain ingredients.
- Chemically inert
- Primarily have the density, particle shape and particle size compatible with other micro ingredients so as to prevent any demixing in the premix.
- Water sequester from other raw materials thereby reducing water activity and improve stability of the premix.
- Impart good flowability.

Types of carrier widely used in the formulation of premix:

- (A) Organic carriers
- (B) Inorganic carriers

Table 3: List of carriers used in premix

Organic Carriers	Inorganic Carriers
Wheat middling	Calcium carbonate
Rice hulls	Dicalcium Phosphate
Corn cobb, ground	Monocalcium phosphate
Soya bean meal	Zeolite
Lactose	Fine dried salt

Better premixes can often be prepared by employing a blend of predetermined ratio of several diluents rather than with just one. The organic carrier absorbs moisture while inorganic carrier contributes towards density of premix.

The formulator has to consider all the above-mentioned parameters whilst preparing the batch control or manufacturing record. The batch manufacturing record serves as a link between the formulator and actual production. While preparing the batch sheet the formulator has to give importance for the following details:

- Nutrient requirements
 - Selection of ingredients
 - Potency of ingredient
 - Process loss
 - Level of free flowing agents
 - Level of antioxidant
 - Percentage of carrier
 - Packing & packaging material
 - Inventory of materials
- The manufacturing of a premix should follow the batch control sheet under the supervision of trained personnel. The batch sheet should comprise following details:
- Name of the premix
 - Code of premix
 - Production date
 - Batch no. of premix
 - Batch size
 - List of ingredients to be mixed
 - Batch no. of ingredients to be mixed
 - Mixing order of ingredients
 - Actual quantity of ingredients to be taken
 - Mixer name and mixing time
 - Instructions regarding packing and mixing
 - Provision for signatures

All the above-mentioned details aid in keeping a track of the premix which may be traced in future with respect to customer complaints or product recall. Thus it serves as a control copy.

C. WEIGHING

Weighing is an important point in manufacturing of a premix. No matter how good the formula is, it is difficult to achieve the desired nutrient levels in the premix without precise weighing. Any extra addition of vitamins may not improve performance but costs extra money, whereas lower levels could depress performance. Precision in weighing is critical for certain ingredients like Selenium, and Roxarsone where mistakes may even prove toxic.

The accuracy of the weighing balance enables precise weighing. The accuracy decreases with increasing size of the scale. As a general rule, a scale is accurate to no more than 0.1% of its total capacity. There is large variation in doses of different micro ingredients added in the premix. So weighing balances need to be sized according to their use as depicted below:

Table 4 : Selection of scales as a function of product

Ingredients	Range of scale (kg)	Precision (g)
Vitamins A, D3, E, Niacin, Calpan Trace minerals	300 to 1	100
Vitamins B, K Cobalt, Iodine, Molybdenum, Selenium	20 to 0.5	20
Amino acids Minerals Carriers	1000 to 100	1000

Assurance in weighing can be achieved by calibrating balances against standard weights. The balances should be preferably calibrated daily in the beginning of weighing and documented accordingly. They should be cleaned before and after use and must be subjected for maintenance twice a year.

D. MIXING

The mixing process is the heart of any premix-manufacturing unit. In a premix the proportion of ingredients vary considerably; hence in order to obtain a homogenous blend the mixing operation should be divided into two steps

A) Micro mixing

B) Macro mixing

A) Micro mixing, as the name suggests, is for mixing micro ingredients which weigh less than one percent of mixer capacity. These ingredients should be initially mixed in a smaller capacity mixer like double cone blender. The micro mix so obtained should be then mixed in the large mixer with all other ingredients.

B) Macro mixing is the actual blending of all components of the premix along with carriers in a batch mixer. The content uniformity of the premix is based on following parameters:

(i) Type of Mixer

(ii) Mixing Time

(iii) Mixing order

(i) Type of mixer

A mixer selected must be able to provide homogenous mixtures of physically adverse particles incorporated at various levels in the mix. Horizontal or vertical mixers can be used. It must meet safety standards and must be properly installed. The requirements of a mixer are:

- Affords good homogeneity with the component included at lowest possible content.
- Short mixing time
- Variable degree of filling, with no loss of mixing efficiency.
- Complete emptying
- Easy Cleaning
- Provision for adding liquids
- Absence of heat during mixing
- Provision to break the lumps
- Less consumption of energy
- Least maintenance cost
- Cost effective

A normal feed mixer is not recommended for premixes. A specialized mixer capable of mixing to a low CV (Coefficient of variation) is the most desired. Specialized Nauta mixers are normally capable of ensuring homogenous mixing.

Examples of mixers: ribbon mixer, conical screw mixer, mass mixer, and cylindrical plough mixer etc.

(ii) Mixing time

The mixing time is also crucial for obtaining a homogenous premix. It is evident that shorter mixing time leads to under mixing while prolonged mixing time results in demixing. By trial and error and also by conducting coefficient of variation studies, optimum-mixing time can be arrived for a particular mixer.

(iii) Mixing order

The sequence of addition of various ingredients while loading the mixer can affect the quality of premix. If proper mixer loading sequence is not followed, oil balls, chemical interactions and particle segregation can result in a premix.

Do's	Don'ts
Clean the mixer before and after use.	Collection of first few bags after mixing
Area must be free of remains of previous batch	Collection of premix in unlabeled bag
Addition of Ingredients when the mixer is on	Collection of premix when the mixer is on.
Note the mixing start and end time	Collection of premix before the specified mixing time
Strict adherence to the mixing order	Addition of reactive materials in the beginning.

Regular mixer evaluation should be accomplished by conducting coefficient of variation studies. C.V value of less than 5% is indicative of excellent mixing. The mean assay value for the tracer should also be within the permissible limits of analytical variation. Any deviation from the expected result indicates any one of the following:

- Improper mixing time
- Irregular mixing order
- Selection of bad mixer
- Improper alignment of mixing aids
- Wear out of internal part
- Larger analytical variations indicative of poor lab analysis

Lack of uniformity in a premix is compounded when mixed into finished feed (multiplier effect). Hence utmost care has to be taken whilst manufacturing a premix.

E. PACKAGING

The primary purpose of packaging for premix is to maintain the stability of micronutrients and to protect the integrity of the premix. Improperly packaged premixes experience considerable loss in the potency of various sensitive ingredients.

Selection or designing of packaging material should be according to the local climatic conditions. It should bear following properties:

- Provides barrier against light, moisture, oxygen
- No chemical interactions with the premix
- Provides good printing surface
- Sturdy enough to withstand the transport pressure.

The different types of packaging materials that could be use are glass containers, aluminium foil, paper and plastics. Ideally, aluminium foil lined multilayered paper bags provides an excellent barrier against light, moisture, oxygen, odour and flavour. Hence for very sensitive ingredients and where cost is not a constraint, aluminium foil package is the material of choice.

F. LABELING

Labeling of premix serves two purposes:

- Provides complete information about the premix
- Gives an identity to the premix and helps in differentiating from other premixes. The premixes for different segments like layer, broiler, breeder and dairy

should bear labels of different colour. This prevents any confusion and mix-ups between the premixes.

A premix label should have following information:

- Name of the premix
- Composition
- Dosage of premix
- Net weight of premix contained in the package (in kg)
- Regulatory/Statutory statements.
- Date of manufacture in month/year
- Date of expiry in month/year
- Batch number
- Storage conditions
- Directions for use
- Name and address of the manufacturer with logo
- Disclaimer note if any

Careful attention must be paid while preparing label since the customer follows the instructions given on the label. Any mistake made will be carried on to the feed and ultimately affect the performance of the birds.

G. STORAGE

The quality of premix is also affected by the storage conditions in the premises until it is transported through distribution channels.

The following steps are recommended during warehouse storage:

- The temperature and humidity of warehouse should be controlled below critical levels.
- Keep the area clean, well lit and ventilated with fresh air.
- Store the premix on the pallet meant for it taking care not to store more than 10 bags on each pallet.
- Design the storage areas to facilitate the FIFO (First in First Out) policy, with bags stored in consecutive order so that oldest can be withdrawn first.

- Make separate provision for storing sale return or expired premix
- Keep floors, walls and walkways clean, dry and free of any obstructions.
- Place sinks and bathrooms away from premix storage area.
- Keep the area free from pests and rodents
- No bag should be stored without any label.

When stored under such conditions the consumer is guaranteed of its label claim.

METHODS OF QUALITY CONTROL

1. For raw materials
2. For production process
3. For finished premix

1. The raw materials must be analysed first and only then incorporated in the premix once it meets all the specifications. The formulator must be strict while considering the nutrient percentage in the raw material. Proper segregation must be done for the approved and rejected materials. Care should be exercised while actually taking the material for production. The raw material must be sieved to omit any foreign and oversized material, if necessary process before use.

2. The Premix production process ensures the precise weighing & inclusion of each required micro-ingredient in the premix. This method must be fool proof and verifiable through a system of physical (weight) and book (record) checks.

A preinclusion check should be performed by quality assurance personnel whereby random check is made for the number of bags, quality of material, their weights, cleanliness of mixer, integrity of packaging material and labeling. If any deviation is observed corrective steps should be taken immediately so that the error is not carried on to the final product.

A post manufacturing check is necessary to assure that premix manufactured is free of lumps and freely flowable.

Cross contamination should be eliminated while manufacturing quality premix. It becomes a matter of concern when drugs get carried over from one premix to another that is meant for another segment and where the contaminated drug is toxic to other species. There are three main methods that can reduce cross contamination in premix:

- a) Flushing- This is a technique whereby an ingredient such as ground grain or any carrier material is run through the system after a batch of medicated premix is produced. This ingredient will pick up much of the contamination in the system and then must be bagged up and used later when premix containing the same medicament is made.
- b) Sequencing-This technique involves the production of feeds containing the same medication at the same time. This reduces the number of times contamination may occur. A run of the medicated premix would then be followed by production

of type of premix that would not be affected by a low level of a contamination.

- c) Mixer cleanout procedures-The mixer must be cleaned thoroughly before and after use with brush and compressed air. A thorough wash out programme must be performed at least once a week. Care should be taken to ensure that the mixer is clean and dry before use.
3. The quality of **finished premix** is assured by analysing the same in the laboratory .The premix must be analysed for physico-chemical properties. The premix should be dispatched only if all the parameters are satisfactory. It may be difficult to analyse each and every batch manufactured for complete analysis and hence a sampling plan must be designed mentioning the analysis frequency of such premixes.

Premix is a critical input in feeds. The use of a quality premix is an important feature in any livestock operation leading to improved safety, reliability and performance.

The production of quality premix thus deserves careful and professional attention. Product quality must be built into and not merely tested in, the product.

Monitoring of all the critical points affecting the quality of premix is the best solution for minimizing the deviations from standards.

It is only through well-organized, adequately staffed and accurately performed process and formulation controls that a desired quality of the premix may be achieved.

References:

1. P. Raven & G. Walker. Food and Agricultural Organization of United Nations, 1980.
2. A. J. Leslie. Quality control in feed milling, procedures for an effective program, ASA.
3. D. Monsalve. Key points in mixing and delivery of micro ingredients in Feed Formulations.
4. Micro ingredient Premixing, Keeping Current. BASF Corporation.
5. Quality assurance as applied to micronutrient fortification. Guidelines for technicians, supervisors and workers concerned with Nutrition. Eds P. Nestel, R. Nalubola, and E. Mayfield.(ILSI)
6. D. Armstrong and K. Behnke. Premixing MF-2056, Dept. of Grain Science and Industry.

