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SILVER JUBILEE YEAR 2016

TAMILNADU PHARMACEUTICALS SCIENCES WELFARE TRUST

25 Years

# Pharma Web

## Newsletter of Tamilnadu Pharmaceutical Sciences Welfare Trust

Jan. - Feb. - Mar. 2017

# Delvin Formulations

*Destiny for Innovation*

# Moving Globally

- R & D and Manufacturing of API
- R & D and Manufacturing of Formulations
- International Marketing
- Domestic Marketing
- Medical Devices
- Surgicals


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Tamilnadu Pharmaceutical Sciences Welfare Trust

# Pharma Web

## Newsletter of Tamilnadu Pharmaceutical Sciences Welfare Trust

ISSUE : 33 Jan. - Feb. - Mar. 2017



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# EDITORIAL

Dear Readers,

First of all we wish all our readers a very Happy Tamil New Year Day.

We are happy to publish the 33rd issue of Pharma Web Newsletter for Jan – Mar 2017.

We are happy to inform our readers, the Pharma Knowledge Training Institute under the Trust conducted series of training programme to the final year B. Pharm students, during this quarter. The lecture programme for these training where held in our Spencer Plaza office premises. We have rearranged our office premises with a seating capacity of 30 trainees with LCD projector as well as modern facilities. The complete programme of the training is inserted in this issue with photos and other events like technical lectures etc.

In this newsletter the following articles are also published

- Ø Quality by Design - by Dr. R. Venkidesh, GM – Quality Control, M/s. Sai Mirra Innopharm Pvt Ltd, Chennai
- Ø Calibration of Quality Control Equipments by Mr. N. Chandar, Pharma Consultant

We have also published the various Gazette Notifications pertaining to the amendment of Drugs & Cosmetics Act & Rules and also important circulars issued by DCGI.

Various events from Pharmacy colleges as well as Association's are highlighted in this issue.

Important news items connected to our Pharmacy profession appeared in various national news papers are published in this issue.

We are very much thankful to M/s. Fourrts (India) Laboratories Pvt. Ltd., M/s. Delvin Formulations, M/s. Medopharm, M/s. Tablets (India) Ltd., for the continuous support by giving advertisement, in order to sustain the cost of publishing of this newsletter.

Hope this Newsletter will benefit our Pharma professionals. Any suggestions to improve our news letter are welcome.

*With Best Regards,*
**R. NARAYANASWAMY**
*Chief Editor*

# ARTICLES

## QUALITY BY DESIGN

by

**Dr. R. Venkidesh, M/s. Sai Mirra Innopharm Pvt. Ltd.**

(Lecture delivered on, 6th March 2017, PKTI - 4th Training Programme)

### Risk Based Formulation Development -QbD

- *The goal of Formulation Development Study is to select the MCC/Lactose ratio and disintegrant level and to understand if there is any interaction of these variables with drug substance particle size distribution. This study is also done to establish the robustness of the proposed formulation.*

- *The **QUALITY TARGET PRODUCT PROFILE (QTPP)** is "a prospective summary of the quality characteristics of a drug product that ideally will be achieved to ensure the desired quality, taking into account safety and efficacy of the drug product."*

- *The QTPP is an essential element of a QbD approach and forms the basis of design of the generic product.*

### QTPP and CQA

- *Initially identify the Quality target Product Profile (QTPP) from the RLD.*

- *This can be done by characterising the RLD, intended patients drug will be given, label of the RLD and on.*

- *Prepare the Critical Quality Attributes (CQA) based on the severity the product would cause if it fails to meet the quality attribute of the product.*

- *The pharmaceutical development must focus on the CQA that will be impacted by the change in the processes or attributes of the API , inactives.*

## QTPP Template Example

| QTPP Elements | | Target | Justification |
|---|---|---|---|
| Dosage Form | | Tablet | Pharmaceutical equivalence requirement: same dosage form |
| Dosage Design | | Immediate release tablet without a score of coating | Immediate release design needed to meet lable claims |
| Route of Administration | | Oral | Pharmaceutical equivalence requirement: same route of administration |
| Dosage Strength | | 20 mg | Pharmaceutical equivalence requirement: same strength |
| Pharmacokinetics | | Immediate release enabling Tmax in 2.5 hours or less; Bioequivalent to RLD | Bioequivalence requirement<br>Needed to ensure rapid onset and efficacy |
| Stability | | At least 24-month shelf-life at room temperature | Equivalent to or better than RLD shelf-life |
| Drug Product Quality Attributes | Physical Attributes | Pharmaceutical equivalence requirement: Must meet the same compendial or other applicable (quality) standards (i.e., identity, assay, purity, and quality) | |
| | Identification | | |
| | Assay | | |
| | Content Uniformity | | |
| | Dissolution | | |
| | Degradation Products | | |
| | Residual Solvents | | |
| | Water Content | | |
| | Microbial Limits | | |
| Container Closure System | | Container closure system qualified as sutiable for this drug product | Needed to achive the target shelf-life and to ensure tablet integrity during shipping |
| Administration / Concurrence with labeling | | Similar food effect as RLD | RLD labeling indicates that a high fat meal increases the AUC and Cmax by 8-12%. The product can be taken without regard to food |
| Alternative methods of Administration | | None | None are listed in the RLD label |

## CQA

- *A critical quality attribute (CQA) is "a physical, chemical, biological, or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality."*

- *The common CQAs are monitored by using the below parameters like:*
  - *Dissolution*
  - *Content Uniformity*
  - *Assay*
  - *Impurities*
  - *Moisture content, etc..*

## CQA Template Example

| Quality Attributes of the Drug Product | | Target | Is this a CQA? | Justification |
|---|---|---|---|---|
| Physical Attributes | Apperance | Colour and Shape acceptable to the patient. No visual tablet defects observed | No | Color, shape and appearnce are not directly linked to safety and efficacy. Therefore they are not critical. The target is set to ensure patient acceptability. |
| | Odor | No unpleasant odor | No | In general, a noticeable odor is not directly linked to safety and efficacy, but odor can affect patient acceptability. For this product, neither the drug substance nor the excipients have an unpleasant odor. No organic solvents will be used in the |
| | Size | Similar to RLD | No | For comparable ease of swallowing as well as patient acceptable and compliance with treatment regimens, the target for table dimensions is set similar to the RLD |
| | Score configuration | Unscored | No | The RLD is an unscored tablet; therefore, the generic tablet will be unscored. Score configuration is not critical for the acetriptan tablet. |
| | Friability | NMT 1.0% w/w | No | Friability is a routine test per compendial requirements for tablets. A target of NMT 1.0% w/w of mean weight loss assures a low impact o patient safety and |
| Friability | | Positive for acetriptan | Yes* | Though identification is critical for safety and efficacy, this CQA can be effectively controlled by the quality management system and will be monitored at drug product release. Formulation and process variables do not impact identity. Therefore, this CQA will not be discussed during formulation and process |
| Assay | | 100% w/w of label claim | Yes | Assay varoability will affect safety and efficacy. Process variables may affect the assay of the drug product. Thus, assay will be evaluated throughout product and |
| Content Uniformity (CU) | | Conforms to USP <905> Uniformity of Dosage Units | Yes | Variability in content uniformity will affect safety and efficacy. Both formulation and process variables impact content uniformity, so this CQA will be evaluated throughout product and process development. |
| Dissolution | | NLT 80% at 30 minutes in 900 mL of 0.1 N HCl with 1.0% w/v SLS using USP apparatus 2 at 75 rpm | Yes | Failure to meet the dissolution specification can impact bioavailability. Both formulation and process variables affect the dissolution profile. This CQA will be investigated throughout formulation and process development. |

## CQA Template example contd..

| Quality Attributes of the Drug Product | Target | Is this a CQA? | Justification |
|---|---|---|---|
| Degradation Products | ACE12345;<br>NMT 0.5%<br>Any unknown impurity<br>NMT 0.2%<br>Total impurities:<br>NMT 1.0% | Yes | Degradation products can impact safety and must be controlled based on compendial / ICH requirements or RLD characterization to limit patient exposure. ACE12345 is a common degradant of acetriptan and its target is based on the level found in near expiry RLD product. The limit for total impurities is also based on RLD analysis. The target for any unknown impurity is set according to the ICH identification threshold for this drug product. Formulation and process variables can impact degradation products. Therefore, degradation products will be assessed during product and process development. |
| Residual Solvents | USP <467> option 1 | Yes* | Residual solvents can impact safety. However, no solvent is used in the drug product manufacturing process and the drug product complies with USP <467> Option 1. Therefore, formulation and process variables are unlikely to impact this CQA. |
| Water Contents | NMT 4.0% w/w | Yes | Generally, water content may affect degradation and microbial growth of the drug product and can be a potential CQA. However, in this case, acetriptan is not sensitive to hydrolysis and moisture will not impact stability. |
| Microbial Limits | Meets relevant pharmcopoeia criteria | Yes* | Non-compliance with microbial limits will impact patient safety. However in this case, the risk of microbial growth is very low because roller compaction (dry granulation) is utilized for this product. Therefore, this CQA will not be discussed in detail during formulation and process development. |
| * Formulation and process variables are unlikely to impact the CQA. Therefore, the CQA will not be investigated and discussed in detail in subsequent risk assessment and pharmaceutical development. However, the CQA remains a target element of the drug product profile and should be addressed accordingly. | | | |

## Pre-Formulation Activities

- ***Pre-Formulation***
  - *Analysis of Reference Listed Drug Product (RLD) (characterise for Description, Coated or uncoated, type of coating, dimension, weight, physical appearance, DT, Assay, Impurities).*
  - *Evaluation of the drug substance properties- Physical properties, description, solid state form (XRD),Solubility in function of pH(BCS class), Hygroscopicity, Density (Bulk, Tapped and True density),Angle of repose, M.P., Eutectic, crystalline nature, thermal analysis, stress analysis, LOD/Moisture, Partition coefficient.*
  - *Excipient Compatibility studies.*
  - *Particle size distribution studies.*

## Design of experiment

- Design of Experiment is done to identify the acceptable ranges in the process steps.
- Identify the Inactive ingredients from PDR or Rx drug index or any other reliable web sites. Now categorise the inactives as below-
- Intra-granular inactives- Lactose, MCC,Starch, DCP, etc.
- Extra- granular inactives-CCS, aerosil,talc,magnesium stearate.
- *Randomization, blocking and replication are the three basic principles of statistical experimental design. By properly randomizing the experiment, the effects of uncontrollable factors that may be present can be "averaged out". Blocking is the arrangement of experimental units into groups (blocks) that are similar to one another. Blocking reduces known but irrelevant sources of variation between groups and thus allows greater precision in the estimation of the source of variation under study. Replication allows the estimation of the pure experimental error for determining whether observed differences in the data are really statistically different.*

## Drug Substance (DS) to Excipient compatibility studies (Binary Mixtures)

| Mixture | Assay (% w/w) | Degradants (% w/w) |
|---|---|---|
| Lactose Monohydrate/DS (1:1) | 99.8% | ND |
| Lactose Anhydrous/DS (1:1) | 99.6% | ND |
| Microcrystalline Cellulose (MCC)/DS(1:1) | 98.4% | ND |
| Dibasic Calcium Phosphate/DS (1:1) | 99.3% | ND |
| Mannitol/DS (1:1) | 101.1% | ND |
| Pregelatinized Starch/DS (1:1) | 100.5% | ND |
| Croscarmellose Sodium (CCS)/DS (1:1) | 99.7% | ND |
| Crospovidone (1:1) | 99.3% | ND |
| Sodium Starch Glycolate (1:1) | 98.8% | ND |
| Talc/DS (1:1) | 99.5% | ND |
| Magnesium Stearate/DS (1:1) | 95.1% | ND |

* Conditions: 40$^{O}$C/75%RH, open container, 1 month

## Drug Substance (DS) to Excipient compatibility studies (Interaction Study)

| Mixture | Assay (% w/w) | Degradants (% w/w) |
|---|---|---|
| All excipients | 99.4% | ND |
| All excipients except Lactose Monohydrate | 99.2% | ND |
| All excipients except Microcrystalline Cellulose (MCC) | 99.8% | ND |
| All excipients except Croscarmellose Sodium (CCS) | 99.9% | ND |
| All excipients except Talc | 99.3% | ND |
| All excipients except Magnesium Stearate | 99.6% | ND |

* Conditions: 40$^{O}$C/75%RH, open container, 1 month

## Stress Study an Example

| Stress Conditions | Assay (% w/w) | Degradants (% w/w) | | | | Solid State Form (% w/w) |
|---|---|---|---|---|---|---|
| | | RC1 | RC2 | RC3 | RC4 | |
| *Untreated* | 99.4 | ND | ND | ND | ND | Crystalline Form III |
| *Saturated Solution* | | | | | | |
| 0.1 N HC1 (RT, 14 days) | 96.9 | ND | 2.3 | 1.1 | ND | N/A |
| 0.1 N NaOH (RT, 14 days) | 97.3 | ND | 2.1 | 0.9 | ND | N/A |
| 3% $H_2O_2$ (RT, 7 days) | 86.7 | ND | 9.9 | 1.3 | ND | N/A |
| Purified water (RT, 14 days) | 96.8 | ND | 1.9 | 1.2 | ND | N/A |
| Photostability (ICH Q1B Option 1) | 90.6 | ND | 7.5 | 2.1 | ND | N/A |
| Heat (60$^{O}$C, 24 h) | 93.4 | ND | 5.2 | ND | 1.5 | N/A |
| *Solid State Material* | | | | | | |
| Humidity (open container, 90% RH, 25$^{O}$C, 7 days) | 99.4 | ND | 0.1 | 0.1 | ND | No change |
| Humidity and Heat (open container, 90% RH, 40$^{O}$C, 7 days) | 99.9 | ND | 0.1 | 0.1 | ND | No change |
| Humidity and Heat (open container, 90% RH, 60$^{O}$C, 7 days) | 95.9 | ND | 2.7 | 0.2 | 1.4 | No change |
| Photostability (ICH Q1B Option 1) | 95.5 | ND | 3.2 | 1.4 | ND | No change |
| Dry Heat (60$^{O}$C, 7 days) | 95.8 | ND | 4.1 | ND | 0.9 | No change |
| Dry Heat (105$^{O}$C, 96 h) | 82.5 | ND | 3.9 | ND | 13.7 | No change |
| Mechanical Strees (Grinding and Compression) | 99.2 | ND | 0.1 | 0.1 | ND | No change |
| ND: Not Detected; N/A: Not Applicable | | | | | | |

## DOE- An Example

| Ingredient | Function | Degradants | |
|---|---|---|---|
| | | (mg per tablet) | (% w/w) |
| Acetriptan | Active | 20.0 | 10.0 |
| Intragranular Excipients | | | |
| Lactose Monohydrate, NF | Filler | 79.0 | 39.5 |
| Microcrystalline Cellulose (MCC), NF | Filler | 79.0 | 39.5 |
| Croscarmellose Sodium (CCS), NF | Disintegrant | 10.0 | 5.0 |
| Talc, NF | Glidant/lubricant | 5.0 | 2.5 |
| Extragranular Excipients | | | |
| Magnesium Stearate, NF | Lubricant | 1.2 | 0.6 |
| Talc, NF | Glidant/lubricant | 5.8 | 2.9 |
| Total Weight | | 200.0 | 100 |

## Excipient Grade and Vendor Selection

- *For Hydrophobic API choose hydrophilic excipeints like Lactose and use MCC for roll compaction for its flake formation, Use CCS in right proportion if the water solubility of the drug is low.*
- *For all the above characteristics, choose from the right vendor which will certify for TSE/BSE free and impurities like mealmine, aldehydes, peroxides, etc..*

## DOE with factorial Levels Example

| Factors : Formulation Variables | | Levels | | |
|---|---|---|---|---|
| | | -1 | 0 | 1 |
| A | Drug substance PSD ($d_{90}$, $\mu$m) | 10 | 20 | 30 |
| B | Disintegrant (%) | 1 | 3 | 5 |
| C | % MMC in MMC/Lactose combination | 33.3 | 50.0 | 66.7 |

| Responses | | Goal | Acceptable Ranges |
|---|---|---|---|
| $Y_1$ | Dissolution at 30 min (%) (with hardness of 12.0 kP) | Maximize | $\geq$ 80% |
| $Y_2$ | Disintegration time (min) (with hardness of 12.0 kP) | Minimize | < 5 Min |
| $Y_3$ | Tablet content uniformity (%RSD) | Minimize % RSD | < 5% |
| $Y_4$ | Assay (%w/w) | Target at 100% w/w | 95.0 - 105.0% w/w |
| $Y_5$ | Powder blend flow function coefficient (ffc) | Maximize | < 6 |
| $Y_6$ | Tablet hardness @ 5 kN (kP) | Maximize | > 5.0 kP |
| $Y_7$ | Tablet hardness @ 10 kN (kP) | Maximize | > 9.0 kP |
| $Y_8$ | Tablet hardness @ 15 kN (kP) | Maximize | > 12.0 kP |
| $Y_9$ | Friability @ 5 kN (%) | Minimize | < 1.0% |
| $Y_{10}$ | Friability @ 10 kN (%) | Minimize | < 1.0% |
| $Y_{11}$ | Friability @ 15 kN (%) | Minimize | < 1.0% |
| $Y_{12}$ | Degradation products (%) (observed at 3 months, 40$^{o}$C/75% RH) | Minimize | ACE12345: NMT 0.5%<br>Any unknown impurity: NMT 0.2%<br>Total impurities: NMT 1.0% |

## DOE comparing Flow Function Coefficient, Hardness with other CQAs

| Batch No. | Factors : Formulation Variables | | | Responses | | | |
|---|---|---|---|---|---|---|---|
| | A: Drug Substance PSD | B: Disintegrant level | C: % MCC in MCC/Lactose combination | $Y_1$ : Dissolution at 30 min | $Y_3$ : CU | $Y_5$ : ffc value | $Y_7$ : Tablet hardness @ 10 kN |
| | ($d_{90}$, μm) | % | % | % | (% RSD) | -- | (kP) |
| 1 | 30 | 1 | 66.7 | 76.0 | 3.8 | 7.56 | 12.5 |
| 2 | 30 | 5 | 66.7 | 84.0 | 4.0 | 7.25 | 13.2 |
| 3 | 20 | 3 | 50.0 | 91.0 | 4.0 | 6.62 | 10.6 |
| 4 | 20 | 3 | 50.0 | 89.4 | 3.9 | 6.66 | 10.9 |
| 5 | 30 | 1 | 33.3 | 77.0 | 2.9 | 8.46 | 8.3 |
| 6 | 10 | 5 | 66.7 | 99.0 | 5.1 | 4.77 | 12.9 |
| 7 | 10 | 1 | 66.7 | 99.0 | 5.0 | 4.97 | 13.5 |
| 8 | 20 | 3 | 50.0 | 92.0 | 4.1 | 6.46 | 11.3 |
| 9 | 30 | 5 | 33.3 | 86.0 | 3.2 | 8.46 | 8.6 |
| 10 | 10 | 1 | 33.3 | 99.5 | 4.1 | 6.16 | 9.1 |
| 11 | 10 | 5 | 33.3 | 98.7 | 4.0 | 6.09 | 9.1 |

## Formulation Development

- Identify the MCC/Lactose ratio, CCS level.
- Effect of extragranular magnesium stearate and talc.
- Use different PSD of the API in pilot bio studies.
- Dissolution testing using USFDA recommended method.
- Developing in-House dissolution method or method validation.
- Monitor the machine parameter variables like, sifter size, multimill screen size, amperage/ voltage in RMG etc. and identify the acceptable ranges.
- Identify the quantity of glident required.
- Monitor blend uniformity activity using NIR (validated method).
- During compression, identify the required hardness or thickness against the fixed weight.

## Process Development

- Now identify the granulation Process
- Type of granulation:
- Roll compaction,
- IPA granulation,
- Direct compression,
- Water Granulation.
- In all of the above processes, the CQAs should be monitored with respect to the change in process attributes.

## Q&Q Formula

| Component | Function | Unit (mg per tablet) | Unit (% w/w) |
|---|---|---|---|
| Acetriptan, USP | Active | 20.0 | 10 |
| Lactose Monohydrate, NF | Filler | 64-86 | 32-43 |
| Microcrystalline Cellulose (MCC), NF | Filler | 72-92 | 36-46 |
| Croscarmellose Sodium (CCS), NF | Disintegrant | 2-10 | 1-5 |
| Magnesium Stearate, NF* | Lubricant | 2-6 | 1-3 |
| Talc, NF | Glidant/Lubricant | 1-10 | 0.5-5 |
| Total tablet weight | | 200 | 100 |

*** Magnesium stearate level estimated by EDTA titration of magnesium.**

## Scale Up

Scale-up principles and plans should be discussed for scaling up from lab (5.0 kg) to pilot scale (50.0 kg) and then proposed for commercial scale (150.0 kg). A 50.0 kg cGMP exhibit batch was manufactured at pilot scale and demonstrated bioequivalence in the pivotal BE study. The operating ranges for identified CPPs at commercial scale were proposed and will be qualified and continually verified during routine commercial manufacture.

## Risk Evaluation-

| Drug Product CQAs | Drug Substance Attributes | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Solid State Form | Particle Size Distribution (PSD) | Hygroscopicity | Solubility | Moisture Content | Residual Solvents | Process Impurities | Chemical Stability | Flow Properties |
| Assay | Low | Medium | Low | Low | Low | Low | Low | High | Medium |
| Content Uniformity | Low | High | Low | Low | Low | Low | Low | Low | High |
| Dissolution | High | High | Low | High | Low | Low | Low | Low | Low |
| Degradation | Medium | Low | Low | Low | Low | Low | Low | High | Low |

## Justification for Risk categorization

| Drug Substance Attributes | Drug Product COAs | Justification |
|---|---|---|
| Solid State Form | Assay | Drug substance solid state form does not affect tablet assay and CU. The risk is low |
| | Content Uniformity | |
| | Dissolution | Different polymorphic forms of the drug substance have different solubility and can impact tablet dissolution. The risk is high<br>Acetriptan polymorphic Form III is the most stable form and the DMF holder consistently provides this form. In addition, pre-formulation studies demonstrated that Form III does not undergo any polymorphic conversion under the various stress conditions tested. Thus, further evaluation of polymorphic form on drug product attributes was not conducted |
| | Degradation Products | Drug substance with different polymorphic forms may have different chemical stability and may impact the degradation products of the tablet. The risk is medium. |
| Particle Size Distribution (PSD) | Assay | A small particle size and a wide PSD may adversely impact blend flowability. In extreme cases, poor flowability may cause an assay failure. The risk is medium. |
| | Content Uniformity | Particle size distribution has a direct impact on drug substance flowability and ultimately on CU. Due to the fact that the drug substance is milled, the risk is high. |
| | Dissolution | The drug substance is a BCS class II compound; therefore, PSD can affect dissolution. The risk is high. |
| | Degradation Products | The effect of particle size reduction on drug substance stability has been evaluated by the DMF holder. The milled drug substance exhibited similar stability as unmilled drug substance. The risk is low. |
| Hygroscopicity | Assay | Acetriptan is not hygroscopic. The risk is low. |
| | Content Uniformity | |
| | Dissolution | |
| | Degradation Products | |
| Solubality | Assay | Solubility does not affect tablet assay, CU and degradation products. Thus, the risk is low. |
| | Content Uniformity | |
| | Degradation Products | |
| | Dissolution | Acetriptan exhibited low (~0.015mg/mL) and constant solubility across the physiological pH range. Drug substance solubility strongly impacts dissolution. The risk is high. Due to pharmaceutical equivalence requirement, the free base of the drug substance must be used in the generic product. The formulation and manufacturing process will be designed to mitigate this risk. |
| Moisture Content | Assay | Moisture is controlled in the drug substance specification (NMT 0.3%). Thus, it is unlikely to impact assat, CU and dissolution. The risk is low. |
| | Content Uniformity | |
| | Dissolution | |
| | Degradation Products | The drug substance is not sensitive to moisture based on forced degradation studies. The risk is low. |

## Risk Assesment

| Formulation Variables | Drug Product COAs | Justification |
|---|---|---|
| Drug Substance PSD | Assay | See Justifications provided in table 13 |
| | Content Uniformity | |
| | Dissolution | |
| | Degradation Products | |
| MCC/Lactose Ratio | Assay | MCC/Lactose ratio can impact the flow properities of the blend. This, in turn, can impact tablet CU. The risk is high. Occasionally, poor CU can also adversely impact assay. The risk is medium |
| | Content Uniformity | |
| | Dissolution | MCC/Lactose ratio can impact dissolution via tablet hardness. However, hardness can be controlled during compression. The risk is medium. |
| | Degradation Products | Since both MCC and Lactose are compatible with the drug substance and will not impact drug product degradation, the risk is low. |
| CCS Level | Assay | Since the level of CCS used is low and its impact on flow is minimal, it is unlikely to impact assay and CU. Thr risk is low |
| | Content Uniformity | |
| | Dissolution | CCS level can impact the disintegration time and, ultimately, dissolution. Since achieving rapid disintegration is important for a drug product containing a BCS class II compound, the risk is high |
| | Degradation Products | CSS is compatible with the drug substance and will not impact drug product degradation. Thus, the risk is low. |
| Talc Level | Assay | Generally, talc enhances blend flowability. A low level of talc is not likely to impact assay and CU. The risk is low. |
| | Content Uniformity | |
| | Dissolution | Compared to magnesium stearate, talc has less impact on disintegration and dissolution. The low level of talc used in the formulation is not expected to impact dissolution. The risk is low. |
| | Degradation Products | Talc is compatible with the drug substance and will not impact degradation products. The risk is low. |

## Risk categorization and Justification

- Categorise the risk for the parameters like those listed below (not only limited to these) with HIGH, MEDIUM, LOW risk and justify the same.
- API Cohesiveness , Flowability and PSD
- Excipient Flowability,PSD, Density,Moisture content.
- Excipient Lot to Lot variation.
- Blender Type, Order of Addition, Rotation Speed, Blending duration, Blender fill capacity, Blender discharge, Drum to Hopper transfer.
- Environment Temp and RH.

## Drug Substance and Flow Related Parameters

| Physical Properities | Interpretation of Data | Lot #1 | Lot #2 | Lot #3 | Lot #4 |
|---|---|---|---|---|---|
| $d_{90}$ (μm) | -- | 10 | 20 | 30 | 45 |
| $d_{50}$ (μm) | -- | 6 | 12 | 24 | 39 |
| $d_{10}$ (μm) | -- | 3.6 | 7.2 | 14.4 | 33.4 |
| Bulk density (g/cc) | -- | 0.26 | 0.27 | 0.28 | 0.29 |
| Tapped density (g/cc) | -- | 0.41 | 0.39 | 0.39 | 0.38 |
| Flow function coefficient (ffc)[6] | ffc < 3.5 poor flow<br>3.5 < ffc < 5.0 marginal flow<br>5.0< ffc < 8.0 good flow<br>ffc > 8.0 excellent flow | 2.88 | 2.95 | 3.17 | 3.21 |
| Compressibility index (%)[6] | < 15 good flow | 36.6 | 30.8 | 28.2 | 23.7 |
| Hausner ratio[7] | < 1.25 fair flow | 1.58 | 1.44 | 1.39 | 1.31 |
| Specific energy (mJ/g) determined by power rheometer[8] | 5 < SE < 10 moderate cohesion<br>SE > 10 high cohesion | 13 | 12 | 10 | 8.5 |

## Statistical Tools, Result and Interpretation

- A univariate method (i.e., one-factor-at -a time (OFAT)) is acceptable in cases where there is no potential interaction between factors. Since this is often not known, a multivariate statistical design (i.e., Design of Experiments (DOE)) is often used and results are evaluated with commercially available statistical software. A sequential strategy is commonly employed when planning a DOE. Initially, a screening DOE can be used to narrow down the extensive list of factors identified during initial risk assessment to a few vital factors. Then, a characterization DOE can be used to understand the main effects and potential interaction(s) between these vital factors. When center points are included in a 2-level factorial DOE, it is possible to test if the curvature effect is significant. Data analysis is done by separating the curvature term from the regression model in an adjusted model. If the **curvature is significant,** the design should be augmented to a response surface DOE to estimate the quadratic terms. On the other hand, if the curvature is not significant, the adjusted model and unadjusted model will be similar. Finally, a verification DOE can be employed to study the robustness of the system by varying the identified critical factors over ranges that are expected to be encountered during routine manufacturing.

- **ANOVA results should accompany all DOE data analysis, especially if conclusions concerning the significance of the model terms are discussed.**

## Other Considerations

- Aanalytical Method Development
- Dissolution Method Development.
- Container closure system
- Compatibility
- Product Life Cycle Management and continuous improvement.

## Further Reading:

- Implementing Quality by Design, by Helen Winkle, FDA
- Implementation of QbD Principles in CMC Review, by Chi-Wan Chen, PhD, Deputy Director, Office of New Drug Chemistry
- Quality-by-Design Case Studies in Pharmaceuticals and Biologics
- Juran.com

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# CALIBRATION OF QC INSTRUMENTS AND EQUIPMENT

by

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(Lecture delivered on, 4th March 2017, PKTI - 4th Training Programme)

## CALIBRATION of QC EQUIPMENT

- PRELUDE
- DEFINITION
- INSTRUMENTS CATEGORIES
- CALIBRATION REQUIREMENTS
- CALIBRATION METHODOLOGY
- CALIBRATION STANDARDS
- CALIBRATION SCHEDULE
- SUMMARY

## CALIBRATION of QC EQUIPMENT - PRELUDE

**Questions**

- What is QC Equipment
- What is Calibration
- Why should it be done
- When to be done
- How to be done
- Who should do it
- What if it is not done

## What is QC Equipment ?

Includes

- Instruments for general use
- Instruments for Qualitative Analysis
- Instruments for Quantitative Analysis
- Measuring Devices and Tool
- Glass Ware with measure mark
- Any thing used to get some value or inference

## What is Calibration ?

An evidence and confirmation that the results/ values you see are correct

## Why should it be done ?

Want to be sure that the results/ values you see are correct and decide on further action

## When to be done ?

Periodically at Definite intervals or as required

## How to be done ?

By a Defined procedure

## Who should do it ?

A Trained and Qualified Person

## What if it is not done ?

- Observations / Results are Wrong
- Decision based on Results are Wrong
- Risk of Non Compliance to Quality Parameter
- Putting the product in doubtful efficacy & Safety
- Leading to Regulatory Non Compliance / Action

## CALIBRATION of QC EQUIPMENT - DEFINITION

- "Operation that, under specified conditions, in a first step, establishes a relation between the quantity values with measurement uncertainties provided by measurement standards and corresponding indications with associated measurement uncertainties (of the calibrated instrument or secondary standard) and, in a second step, uses this information to establish a relation for obtaining a measurement result from an indication."

- This definition states that the calibration process is purely a comparison, but introduces the concept of **Measurement uncertainty** in relating the accuracies of the device under test and the standard.

## CALIBRATION of QC EQUIPMENT - DEFINITION

**ICH**

The demonstration that a particular instrument or device produces results within specified limits by comparison with those produced by a reference or traceable standard over an appropriate range of measurements.

**Calibration** is the process of testing and adjusting an instrument, kit, or test system readout to establish a correlation between the instrument's measurement of the substance being tested and the actual concentration of the substance.

**Calibration verification** means the testing of materials of known concentration in the same manner as patient samples to assure the test system is accurately measuring values **throughout the reportable range.**

## CALIBRATION of QC EQUIPMENT - INSTRUMENTS CATEGORIES

**INSTRUMENT CATEGORIES AND QUALIFICATION**

- Modern laboratories typically include a suite of instruments and equipment varying from simple nitrogen evaporators to complex automated instruments. Therefore, applying a single set of principles to qualifying such dissimilar instruments would be scientifically inappropriate. Users are most capable of establishing the level of qualification needed for an instrument. On the basis of the level needed, it is convenient to categorize instruments into three groups: A, B, and C, Depending on individual user requirements

## CALIBRATION of QC EQUIPMENT - INSTRUMENTS CATEGORIES

**INSTRUMENT CATEGORIES AND QUALIFICATION**

- **Group A**
  Group A includes standard equipment with no measurement capability or usual requirement for calibration, where the manufacturer's specification of basic functionality is accepted as user requirements. Conformance of Group A equipment with user requirements may be verified and documented through visual observation of its operation.

- Examples of equipment in this group are nitrogen evaporators, magnetic stirrers, vortex mixers, and centrifuges.

## CALIBRATION of QC EQUIPMENT - INSTRUMENTS CATEGORIES

**INSTRUMENT CATEGORIES AND QUALIFICATION**

- **Group B**
  Group B includes standard equipment and instruments providing measured values as well as equipment controlling physical parameters (such as temperature, pressure, or flow) that need calibration, where the user requirements are typically the same as the manufacturer's specification of functionality and operational limits.

  Conformance of Group B instruments or equipment to user requirements is determined according to the standard operating procedures for the instrument or equipment, and documented during IQ and OQ

## CALIBRATION of QC EQUIPMENT - INSTRUMENTS CATEGORIES

**INSTRUMENT CATEGORIES AND QUALIFICATION**

Examples of instruments in this group are Balances, Melting Point Apparatus, Light microscopes, pH meters, variable pipets, refractometers, thermometers, titrators, and viscometers.

Examples of equipment in this group are Muffle Furnaces, Ovens, Refrigerator-Freezers, Water Baths, Pumps, and Dilutors.

## CALIBRATION of QC EQUIPMENT - INSTRUMENTS CATEGORIES

**INSTRUMENT CATEGORIES AND QUALIFICATION**

Group C includes instruments and computerized analytical systems, where user requirements for functionality, operational, and performance limits are specific for the analytical application. Conformance of Group C instruments to user requirements is determined by specific function tests and performance tests.

Installing these instruments can be a complicated and may require the assistance of specialists.

A full qualification process, should apply to these instruments

## CALIBRATION of QC EQUIPMENT - INSTRUMENTS CATEGORIES

### INSTRUMENT CATEGORIES AND QUALIFICATION

Examples of instruments in this group include the following:

| | |
|---|---|
| • atomic absorption spectrometers | • X-ray fluorescence spectrometers |
| • differential scanning calorimeters | • X-ray powder diffractometers |
| • dissolution apparatus | • densitometers |
| • electron microscopes | • diode-array detectors |
| • flame absorption spectrometers | • elemental analyzers |
| • high-pressure liquid chromatographs | • gas chromatographs |
| • microplate readers | • Mass, IR ,NIR, Raman,UV spectrometers |
| • thermal gravimetric analyzers | • inductively coupled plasmaemission spectrometers |

## CALIBRATION of QC EQUIPMENT - CALIBRATION REQUIREMENTS

Calibration may be required called for the following reasons:

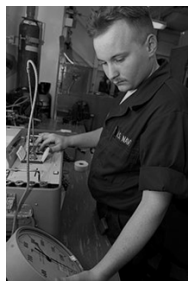
- a new instrument
- after an instrument has been repaired or modified
- when a specified time period has elapsed
- when a specified usage time has elapsed
- before and/or after a critical measurement
- after an event, for example after an instrument has been exposed to a shock, vibration, or physical damage, which might potentially have compromised the integrity of its calibration sudden changes in weather
- whenever observations appear questionable or instrument indications do not match the output of surrogate instruments
- as specified by a requirement, e.g., customer specification, instrument manufacturer recommendation.

## CALIBRATION of QC EQUIPMENT - CALIBRATION METHODOLOGY

**Manual**

**–Example**

Manual Calibration of Pressure Gauge.



(I) Depressurizing the system, and turning the screw, if necessary, to ensure that the needle reads zero,

(ii) fully pressurizing the system and ensuring that the needle reads maximum, within acceptable tolerances,

(iii) replacing the gauge if the error in the calibration process is beyond tolerance.

## CALIBRATION of QC EQUIPMENT - CALIBRATION METHODOLOGY

**Automatic calibration**

**–Example**

Automatic Calibration of Pressure Gauge.

using automatic pressure calibrator, which is a device that consists of a control unit housing the electronics that drive the system, a pressure intensifier used to compress a gas such as Nitrogen, **a pressure transducer used to detect desired levels in a hydraulic accumulator, and accessories such as liquid traps and gauge fitting.**

## CALIBRATION of QC EQUIPMENT - CALIBRATION METHODOLOGY

- Calibration of instruments is done in two ways internal calibration and external calibration
- Internal calibration is done the in-house officials whom have sound knowledge on it.
- External calibration is done according to the instructions of the manufacturer or an authorized Agency.
- Some calibration may require both internal & external services
- In-house calibration data sheet & report format may be used fill the data by external Performer/Reporter
- All Calibration to be as per approved Standard Operating Procedure

## CALIBRATION of QC EQUIPMENT - CALIBRATION METHODOLOGY

**External calibration**

- The Contract agreement copy shall be maintained.
- External service report (or) certificate reference number shall be used for calibration reference wherever required.

**Internal calibration**

- Internal calibration is done the in-house officials whom have sound knowledge on it.

## CALIBRATION of QC EQUIPMENT - CALIBRATION METHODOLOGY

**Process description and documentation**

- The Standard Operating Procedures(SOP) to capture all of the steps needed to perform a successful calibration.
- The recommendations of manufacturer and regulatory requirements should be incorporated in the SOP.
- The Specific Standards to be used should be mentioned in the SOP
- Calibration Data sheet, Calibration report shall be requested and collected from QA prior to start the calibration.

## CALIBRATION of QC EQUIPMENT - CALIBRATION METHODOLOGY

**Process description and documentation**

- The process generally begins with a basic damage check.
- More commonly, the calibration personnel is entrusted with the entire process and preparation of the calibration certificate.
- When the instruments being calibrated are integrated with computers, the integrated computer programs and any calibration corrections are also under control.
- If any reagent solution need to be prepared for calibration that shall be prepared as per authorized procedure and details of preparation shall be entered in relevant documents.

## CALIBRATION of QC EQUIPMENT - CALIBRATION METHODOLOGY

- Unique identification to each instrument may be assigned to standardize the record keeping and keep track of accessories that are integral to a specific calibration condition.
- Calibration data before any routine maintenance may be collected and recorded "as-found" .
- After routine maintenance and deficiencies detected during calibration are addressed, shall be collected and recorded "as-left".

## CALIBRATION of QC EQUIPMENT - CALIBRATION METHODOLOGY

- All Calibration activity shall be recorded in 'INSTRUMENTS CALIBRATION REGISTER .
- Specimen Format

| Date | Instrument/ Equipment Name | Instrument Code | Calibration Reference Number | Date of calibration | Done by (Sign) | Reviewed by (Sign) | Calibration Status | Next Calibration date (to refer Calibration Schedule) | Remarks |
|---|---|---|---|---|---|---|---|---|---|

## CALIBRATION of QC EQUIPMENT - CALIBRATION METHODOLOGY

- On completion of Calibration a labels showing the date of calibration and when the calibration interval dictates when the next one is due is affixed on the instrument
- To prevent unauthorized access to an instrument tamper-proof seals are usually applied after calibration.
- Calibration Report shall be prepared by calibration personnel attaching all data and external reports if any and Approved by Head of Quality Control

## CALIBRATION of QC EQUIPMENT - CALIBRATION METHODOLOGY

**A typical Calibration Label.**

| COMPANY NAME QC CONTROL | | | CALIBRATION REPORT NO |
|---|---|---|---|
| NAME OF THE INSTRUMENT | | INSTRUMENT ID | |
| CALIBRATED ON | | NEXT CALIBRATION DUE | |
| EXTERNAL AGENCY SERVICES UTILISED | | | |
| CALIBRATED BY | | APPROVED BY | |
| | | | |

## CALIBRATION of QC EQUIPMENT - CALIBRATION STANDARDS

- Calibrations should be performed using standards traceable to certified standards .
- Calibration standard may be a Standardized Unit E.g. Standard weight
- A Chemical Substance E.g. Potassium Dichromate, Caffeine
- An Equipment E.g. Master Gauges – For Master equipment used for calibration, the better accuracy shall be considered compare to the instrument accuracy.
- A Material with a Standardized value E.g.. Bursting Strength foil , Polyester film

## CALIBRATION of QC EQUIPMENT - CALIBRATION SCHEDULE

- Annual Program for Calibration of QC instruments/Equipment shall be prepared and followed as per a schedule.
- The Program to capture weekly /monthly Calibration activity of QC instruments
- Calibration details shall be revised during any of the following events, but not limited to.

i. Whenever a new instrument is received and installed in department
ii. Any existing instrument is permanently removed from department.
iii. Whenever the instrument location is changed
iv. Whenever any Break down occur

## CALIBRATION of QC EQUIPMENT - CALIBRATION SCHEDULE

**Specimen format**

| S. No | Instrument Name | Instrument Code | Calibration | | Year: | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | SOP No. | Frequency | | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec |
| | | | | | Due date | | | | | | | | | | | | |
| | | | | | Date of calibration | | | | | | | | | | | | |
| | | | | | Reference Number | | | | | | | | | | | | |
| | | | | | Performed by | | | | | | | | | | | | |

## CALIBRATION of QC EQUIPMENT - CALIBRATION SCHEDULE

**Frequency Generally followed**

| Name Of Instrument | Calibration Frequency | Verification Frequency |
|---|---|---|
| Thermometer | Every Six Months | - |
| Digital Balance | Every Month | Every Day |
| $P^H$ Meter | Every Three Months | Every Day |
| Karl Fisher | Every Time On Usage | |
| Polarimeter | Every Three Months | |
| Friabilator | Every Month | |
| Conductivity Meter | Every 15days | |
| Hardness Tester | Every Year | |
| Disintegration Test Apparatus | Every Month | |
| Dissolution Test Apparatus | Every Three Months | |
| U. V. Spectrophotometer | Every Three Months | |

## CALIBRATION of QC EQUIPMENT - CALIBRATION SCHEDULE

- All internal & external calibration activity shall be completed on schedule period within the Tolerance period mentioned below

| Calibration frequency | Tolerance | Calibration frequency | Tolerance |
|---|---|---|---|
| 1 month & 2 months | ±1 day | 6 months | +15 days |
| 3 months & 4 months | ±2 days | One year | +30 days |

## CALIBRATION of QC EQUIPMENT - CALIBRATION SCHEDULE

- What if the calibration could not be done within the schedule /tolerance Period.
  - Equipment to be moved out from the usage de
  - Label as " OUT OF CALIBRATION" and raise a deviation
  - After recalibration assign revised Calibration Due date shall be Actual calibration date + Calibration frequency

## CALIBRATION of QC EQUIPMENT - SUMMARY

- ALL QC EQUIPMENT GIVING A RESULT OR VALUE TO BE CALIBRATED
- CALIBRATION TO BE DONE BY AUTHORISED INTERNAL /EXTERNAL PERSONNEL
- CALIBRATION TO BE DONE USING TRACEABLE STANDARDS
- CALIBRATION TO BE DONE AS PER SCHEDULE
- ALL CALIBRATION ACTIVITIES TO BE DOCUMENTED

## CALIBRATION of QC EQUIPMENT - CALIBRATION OF BALANCE

- **Following parameters to be checked while performing calibration**
  a.Accuracy b.Precision c. Corner Load Test
- **Accuracy**
  - Accuracy of the balance to be checked by using 5 standard weights.
  - Standard weights to be one by one in the ascending order in the center of the platform and record the observations in the balance calibration record.
  - Acceptance Criteria: Standard Weight ± 2 x Least Count
- **Precision**
  - Precision of the balance to be checked by using standard weight equivalent to 5 % of Max.capacity.
  - Procedure to be repeated for 5 times
  - Same steps to be repeated using standard weight equivalent to 50 % of maximum capacity.
  - Acceptance Criteria : %RSD for both the standard weights NMT 0.5 %

## CALIBRATION of QC EQUIPMENT - CALIBRATION OF BALANCE

- **Corner load test**
  - Standard weight equivalent to 30 % of maximum capacity to be placed in four corners and center of the balance and the readings to be recorded .
  - Acceptance Criteria:Deviation: Standard Weight ± 2 x Least Count % RSD: NMT 0.5 %

- **DAILY CHECK/ VERIFICATION**
  - Daily check shall be done with a minimum of 2 weights in the range daily usage and one weight at 80% of max. capacity of the balance.
  - Electronic balance. shall be calibrated once in 3 months and daily weight check with any two weights covering maximum and minimum in daily usage range.

## CALIBRATION of QC EQUIPMENT - CALIBRATION OF pH METER

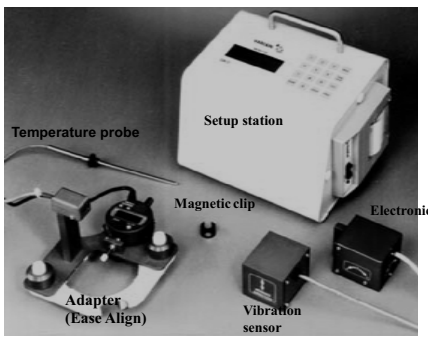
- pH meter to be checked with Buffer solution pH 4.0 to be adjusted to read 4.0 at 20°C
- To be counter checked with 2 other Buffers of pH 7.0 & pH 9.2
- The readings are to be as follows

| | LIMIT |
|---|---|
| Buffer 7.0 | 6.83- 6.93 |
| Buffer 9.2 | 9.18-9.28 |

- The calibration should be carried out daily and it should be recorded.
- The electrode is activated with 0.1 N HCL at the end of every week.

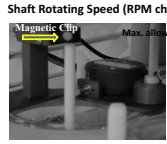
## CALIBRATION of QC EQUIPMENT - CALIBRATION OF DISSOLUTION TEST APPARATUS

- **Physical Parameters**
  - Shaft Rotating Speed
  - Temperature
  - Shaft Alignment
  - Instrument Level
  - Wobble
  - Shaft Centering
  - Vibration

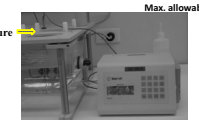



## CALIBRATION of QC EQUIPMENT - CALIBRATION OF DISSOLUTION TEST APPARATUS

Shaft Rotating Speed (RPM check)

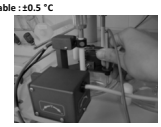



Temperature Test(Bath)

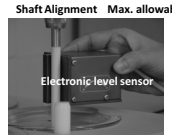


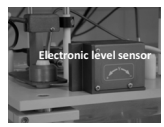

Temperature Test (Vessel)

Max. allowable : ±0.5 °C

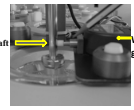


Shaft Alignment Max. allowable :±1.5 °



## CALIBRATION of QC EQUIPMENT - CALIBRATION OF DISSOLUTION TEST APPARATUS





Shaft Centering is dependent on two parameters:


Centering ring

Position of the vessels

Max allowable :±2 mm

## CALIBRATION of QC EQUIPMENT - CALIBRATION OF DISSOLUTION TEST APPARATUS

**Vibration**

**Sources of Vibration**

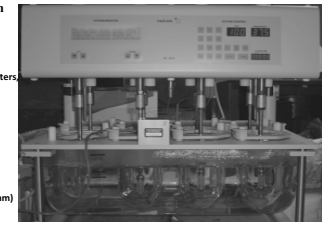
***External:***

ex. centrifuges, double-beam spectrophotometers, pumps, fume hoods, fan, air conditioner etc.

***Internal:***

ex. circulator for the water bath, motor

Max. allowable: Displacement-Z ≤0.1 mils (0.00254 mm)



**4 Parameters**

*Acceleration(g)*
*Frequency (Hz)*
*Velocity (mm/s)*
*Displacement(mm)*

## CALIBRATION of QC EQUIPMENT - CALIBRATION OF DISSOLUTION TEST APPARATUS

- **Random Input Variables Checklist**

| Variable | Maximum allowable | Excess Commonly Seen | Effect of Excess | Methods of Control |
|---|---|---|---|---|
| 1. Eccentricity, Wobble, Tilt | ± 1 mm | 2-5 mm | + 4%-8 | % straighten shafts, use wide shaft guide points |
| 2. Vibration | 0.1 mil | 0.2-0.9 mils | + 5%-10% | eliminate source |
| 3. Shaft Alignment | 1.5° to perpendicular | 2°-7° | +2%-25% | adjust alignment in field |
| 4. Shaft Centering | ± 2 mm (compendium) | ± 2-6 mm | ± 2%-13% | center individual vessels |
| 5. Agitation Rate, Rotating Speed (RPM) | ± 4% | ± 10% | linear | use better, smoother control or use synchronous drive |
| 6. Dissolved gas | deaerated | bubble form | ± 50% | deaerate media |
| 7. Media pH | accuracy | ± 0.05 | ± 10% | check buffers or deaerate, calibrate the pH meter |
| 8. Media contamination | ppm | Ion surfactants | substantial | carefully control media |
| 9. Evaporation | none | 2%-5% | linear | use vessel covers |
| 10.Temperature | ± 0.5 °C | 1 °C-2 °C | linear | monitor individual vessels, allow adequate equilibrium |
| 11. Flow pattern | no interference | turbulence from probes | substantial | remove probes |
| 12. Sampling position | compendium | ± 0.5 cm | little | use care |
| 13. Filters | no sorbing | considerable blockage | significant | check sorbing |
| 14. Detection | use standard | interference | considerable | use standard |
| 15. Sorbing | none | considerable | significant | check materials |

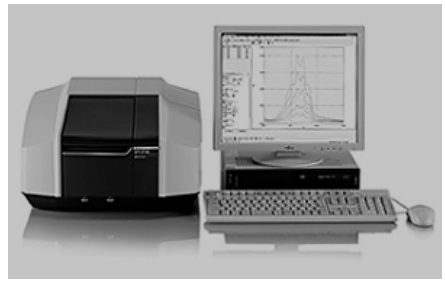
## CALIBRATION of QC EQUIPMENT - CALIBRATION OF DISSOLUTION TEST APPARATUS

- **USP Tablet Calibrators**

| Item | USP Tablet Calibrators | |
|---|---|---|
| | Prednisone Tablets | Salicylic Acid Tablets |
| Type | (Dissolution Calibrator; Disintegrating) | (Dissolution Calibrator; Non disintegrating) |
| Amount | 10 mg/tab | 300 mg/tab |
| Test for Apparatus | I and II | I and II |
| RPM | 50 | 100 |
| Dissolution Medium | Deaerated Water, 500 ml | Deaerated 0.05 M Phosphate Buffer pH 7.4 ± 0.05, 900 ml |
| Time point | 30 minutes | 30 minutes |
| Max λ( nm) | 242 | 296 |
| % alcohol in Std.Solution | ≤ 5% | ≤ 1% |
| Packaging | Plastic Bottle | Blister pack |
| Acceptance values (%la.) Apparatus I Apparatus II | 51-81 26-47 | 23-30 17-25 |

## CALIBRATION of QC EQUIPMENT - CALIBRATION OF UV –VIS SPECTROPHOTOMETER

- **Calibration of UV-Vis Spectrophotometer done on 4 steps**
  - CONTROL OF WAVELENGTH
  - CONTROL OF ABSORBANCE
  - LIMIT OF STRAY LIGHT
  - RESOLUTION POWER



## CALIBRATION of QC EQUIPMENT - CALIBRATION OF UV –VIS SPECTROPHOTOMETER

- **CONTROL OF WAVELENGTH**
  - Holmium oxide filter shall be Scanned in the range of 200 to 700 nm for spectrum keeping Reference cell holder empty
  - The spectrum shall show maximum at the following wavelength

| Maxima at Wavelength (nm) | Limit (nm) |
|---|---|
| 241.15 | 240.15 to 242.15 |
| 287.15 | 286.15 to 288.15 |
| 361.5 | 360.5 to 362.5 |
| 536.3 | 533.3 to 539.3 |

  - Alternatively a 4% solution of Holmium Oxide in 1.4M HCl can be used in place of Holmium oxide filter

## CALIBRATION of QC EQUIPMENT - CALIBRATION OF UV –VIS SPECTROPHOTOMETER

- **CONTROL OF ABSORBANCE**
  - A 0.006% solution of Potassium dichromate in 0.005M $H_2SO_4$ to be scanned using the 0.005 M sulphuric acid solution as blank
  - The A (1% 1cm) value shall be compared with Acceptance criteria in the table below

| Wavelengths (nm) | Limit of A (1% 1cm) |
|---|---|
| 235.0 | 122.9 - 126.2 |
| 257.0 | 142.8 - 145.7 |
| 313.0 | 47.0 - 50.3 |
| 350.0 | 105.6 - 108.2 |

- **LIMIT OF STRAY LIGHT**
  - Absorbance of 2.0% solution of Potassium chloride in water to be measured at 198, 199, 200, 201 nm and 202 nm using water as blank.
  - The absorbance value shall be less than the Acceptance criteria of 2.0
- **RESOLUTION POWER**
  - Spectrum of a 0.02% v/v solution of toluene in hexane shall be recorded in the range of 230 nm to 330 nm .
  - The ratio of absorbance at the maximum at about 269nm to that at the minimum at about 266nm is not less than 1.5.

## CALIBRATION of QC EQUIPMENT - CALIBRATION OF HPLC

- **Calibration of HPLC has 9 parts**
  - Calibration of PUMP
  - Calibration of Column Compartment Oven
  - Base Line Check (Noise & Drift)
  - Detector Lamp Intensity Check
  - Wave Length Accuracy
  - Precession and Linearity of auto injector and detector
  - Gradient accuracy
  - Carryover Test
  - Software calibration.

## CALIBRATION of QC EQUIPMENT - CALIBRATION OF HPLC

- **Calibration of PUMP**
  - The pump to be set at 1.0 ml per minute with degassed Purified water as mobile phase
  - The discharge from the tube through a restriction capillary(after equilibrating for 5 mins) shall be collected for 5 mins, weighed and flow rate is calculated.
  - The procedure is repeated for other flow rates.
  - Acceptance criteria: Flow rate: + 0.1mL

## CALIBRATION of QC EQUIPMENT - CALIBRATION OF HPLC

- **Calibration of Column Compartment Oven**
  - Column to be removed , system to be Purged with Purified water to remove any solvents and previous buffer salts and to be connected to a restricted capillary of dimension 2m x 0.12 mm ID in place of column.
  - With a flow rate of 1.0 mL/min, the sensor of the traceable Digital thermometer to be kept with thermostat in the column oven.
  - Setting the temperature at 30.0°C ,allowing it to attain the set temperature stabilize for 5 mins the temperature displayed by the instrument and the traceable Digital thermometer to be noted.
  - The process to be repeated for 40.0°C, 50.0°C,60.0°C & 70.0°C.
  - Acceptance Criteria: The Displayed temperature on the thermometer should not vary by ± 2.0°C.

## CALIBRATION of QC EQUIPMENT - CALIBRATION OF HPLC

- **Base Line Check (Noise & Drift)**
  - After connecting the restriction capillary, system to be checked for any leakages at all possible points.
  - System to stabilize by passing purified water through the restriction capillary and the detector.
  - Once the base line is the Base line check to be selected by pressing button in the LC set up or through dialog box.
  - After entering the time period for start, end time and Threshold values for the Noise and Drift test 50uV for Noise 5000uV/h for Drift are selected
  - Acceptance Criteria: The Noise & drift values obtained from the test should be within the set Threshold values.
- **Detector Lamp Intensity Check**
  - This is formation will be available in the Detector in Instrument status
  - Acceptance Criteria:Reference energy displayed should not be less than 800 mV at 220 nm.

## CALIBRATION of QC EQUIPMENT - CALIBRATION OF HPLC

- **Wave Length Accuracy**
  - Standard solution : 2.5 mg of caffeine in 100ml of water.
  - Start and end wavelengths for 'Spectrum scan' to be set up as 200 to 300 nm
  - After filling the flow cell with Caffeine solution, scanning to be started
  - The absorbance Maxima in the Spectrum obtained to be compared with Acceptance criteria below

| Standard absorbance maxima | Limit |
|---|---|
| 205nm | 203nm to 207nm |
| 245nm | 243nm to 247nm |
| 273nm | 271nm to 275nm |

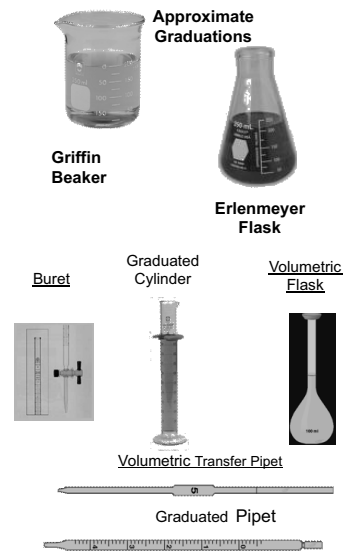
## CALIBRATION of QC EQUIPMENT - CALIBRATION OF HPLC

- **Precession and Linearity of auto injector and detector**
  - Chromatographic conditions:
    - Column : ODS C18 15cm x 4.6mm, 5microns , Mobile phase : Acetonitrile : Purified water (15 : 85 v/v). Flow rate : 1.0mL/min ,Wave length: 273nm Temperature : 360C Run time: 10 minutes
  - Standard solution : 2.5 mg of caffeine in 100ml of mobile phase.
  - Standard solution to be injected in five replicates as 10uL , 20uL ,50uL &100uL and chromatograms to be obtained.
  - Theoretical plates of Caffeine peak should not be less than 3000 and tailing factor should not be more than 2.0 for 20uL injection

## CALIBRATION of QC EQUIPMENT - CALIBRATION OF HPLC

- **Carryover Test**
  - Chromatographic Conditions :
  - Column :ODS C18 15 cm x4.6 mm ID, 5 µm,Flow rate :1.0 mL/min.
  - Detector wavelength : 273 nm, Injection volume : 100 µL Runtime:10 minutes
  - Mobile phase: Acetonitrile : Purified Water (15 : 85 v/v) ,Column oven temp. : 36°C
  - Standard solution: 25 mg of caffeine in100 mL of mobile phase
  - Column to be equilibrated, 100 µL of Standard Solution to be injected and chromatogram to be obtained
  - 3 blanks to be injected and chromatogram to be obtained
  - Any carry over of caffeine in the last blank to be calculated.
  - Acceptance Criteria :Carry over if any should not be more than 0.03% of 100-µL caffeine std peak area.
- **Software calibration.**
  - Perform the validation of the software once in every year and whenever software is updated.

## CALIBRATION of QC EQUIPMENT - CALIBRATION OF VOLUMETRIC GLASS WARE



## CALIBRATION of QC EQUIPMENT - CALIBRATION OF VOLUMETRIC GLASS WARE

- **Calibration Procedure**
  - **Flask & Cylinder**
    - Distilled water to be filled up to the required volume in a tarred glass ware under test
    - From the Weight of the testing container with distilled water Volume of the contents are found.
    - The above to be Repeated 3 times for Flasks and 5 times for Cylinders at least at three different volumes
  - **Pipette & Burette**
    - Pipette/ Burette to be filled with distilled water up to the index mark and delivered to a tarred vessel
    - From the Weight of the vessel with distilled water Volume of the contents are found.
    - The above to be Repeated 3 times for Pipettes and 7 times for Burettes at least at three different volumes
- The temperature of distilled water to be measured to get the volume corresponding for the weight
- Density of water – Table B4 ISO 4787

| Temperature | Density (g/ml) |
|---|---|
| °C | $\rho_w$ |
| 19 | 0.99840 |
| 20 | 0.99820 |
| 21 | 0. 99799 |

## CALIBRATION of QC EQUIPMENT - CALIBRATION OF VOLUMETRIC GLASS WARE

- **VOLUMETRIC FLASKS IS 915:1975**

| Nominal Capacity ml | 5 | 10 | 25 | 50 | 100 | 250 | 500 | 1000 |
|---|---|---|---|---|---|---|---|---|
| Tolerance ± ml | | | | | | | | |
| Class A | 0.02 | 0.02 | 0.03 | 0.04 | 0.06 | 0.1 | 0.15 | 0.2 |
| Class B | 0.04 | 0.04 | 0.06 | 0.08 | 0.15 | 0.2 | 0.3 | 0.8 |

- **ONE MARK PIPETTES IS 1117:1975**

| Nominal Capacity ml | 1 | 2 | 5 | 10 | 20 | 25 | 50 | 100 |
|---|---|---|---|---|---|---|---|---|
| Tolerance ± ml | | | | | | | | |
| Class A | 0.01 | 0.01 | 0.02 | 0.02 | 0.03 | 0.03 | 0.04 | 0.06 |
| Class B | 0.02 | 0.02 | 0.03 | 0.04 | 0.05 | 0.06 | 0.08 | 0.12 |

- **GRADUATED PIPETTES IS 4162:1967**

| Nominal Capacity ml | 1 | 2 | 5 | 10 | 25 |
|---|---|---|---|---|---|
| Subdivision ml | 0.01 | 0.02 | 0.05 | 0.1 | 0.2 |
| Tolerance ± ml | | | | | |
| Class A | 0.006 | 0.01 | 0.03 | 0.05 | 0.1 |
| Class B | 0.02 | 0.06 | 0.10 | 0.15 | 0.15 |

- **v BURETTES IS 4162:1967**

| Nominal Capacity ml | 10 | 25 | 50 | 100 |
|---|---|---|---|---|
| Subdivision ml | 0.05 | 0.05 | 0.1 | 0.1 |
| Tolerance ± ml | | | | |
| Class A | 0.01 | 0.03 | 0.05 | 0.1 |
| Class B | 0.02 | 0.06 | 0.10 | 0.2 |

**CALIBRATION of QC EQUIPMENT -SUMMARY**

- ALL QC EQUIPMENT GIVING A RESULT OR VALUE TO BE CALIBRATTED
- CALIBRATION TO BE DONE BY AUTHORISED INTERNAL /EXTERNAL PERSONNEL
- CALIBRATION TO BE DONE USING TRACEBLE STANDARDS
- CALIBRATION TO BE DONE AS PER SCHEDULE
- ALL CALIBRATION ACTIVITIES TO BE DOCUMENTED

# PHARMACY EDUCATION OF NEXT GENERATION IN TO THE PATIENT

by

**Ms. P. Vidyalakshmi, Vinayaka Mission's College of Pharmacy, Salem**

Note: This article was awarded 1st Prize in the Essay Competition conducted by our Trust

Pharmacy education proud tradition of educating future Pharmacists always ready to meet the needs of the profession. Educators to be forward thinking in advancing our educational programs to meet the changing Pharmacist's role in a diverse variety of health care settings. The AACP commission to implement change provided the academy with the essential missions of Pharmacy practice and education. The curricular outcomes, content and educational process. The responsibility of Pharmacy educators for scholarship, graduate education, fellowships, and post-graduate education and training, and the need for maintaining our commitment to the preparation of graduates capable of providing pharmaceutical care in an evolving health care environment. The mission of Pharmacy education evolved from educating pharmacists with a product focus, involving the safe and effective preparation and dispensing of medications, to educating Pharmacists providing patient centered care and able to integrate and provide services for safe drug preparation and distribution, collaborative drug therapy management, medication therapy management, and medication reconciliation.

Best evidence-based practices and analyzing, synthesizing and applying this information to ensure safe, effective and appropriate use of medications by their patients.

A consistent elements of Pharmacy educational program is the foundation for the pharmaceutical and biomedical sciences. Contemporary pharmacy education has also been strengthened by the growth and enhancement in the clinical, and social and administrative sciences. Our successful future practitioners must have the fundamental knowledge, skills, and attitudes/values in the pharmaceutical, biomedical, clinical, and social and administrative sciences, in conjunction with the practice proficiency gained through experiential learning in our educational programs.

## Profession Education and Practice:

Our focusing health care by improving quality, enhancing information technology, and adding value has been linked to health professions educations. The very nature and structure of health professions education is being refocused on patient centered care, interprofessional teams, evidence based practice, quality improvement, and use of informatics.

## Pre-Professional Pharmacy Educational And Experience:

Pre-professional educational requirements provide the foundation for building the capabilities of professionals. The breadth and depth of preparation, perhaps more than

any other factor, enables or limits the extent to which professional students are able to accept a personal responsibility for their education and consequently their potential as a health provider.

**Interprofessional Education:**

Much attention is being to inter professional education as a strategy to prepare future health care practitioners to achieve the goals of effective, patient-centered, timely, efficient, and equitable health care. Our graduates' repertoire of abilities must include not only the profession of pharmaceutical care, management of resources and or promotion of health and disease prevention, but also how they will fulfill these roles as members of teams of health care professionals. Thus, training pharmacy students to work collaboratively and to effectively communicate with physicians, nurses, and other health care providers.

Patient Counseling:

Patient counseling competence of pharmacists is based on their education, knowledge and skills. Previous studies have indicated that the challenge in pharmacy education is to broaden the role of pharmacists in patient counseling from a traditional approach to an empowerment approach.

**Continuing Professional Development:**

In spite of the increased emphasis on post-graduate training that has been advanced by many professional organizations within pharmacy and by our colleges/schools, only a minority of students are seeking residency training, fellowship and graduate studies. In part, this appears to be influenced by increases in the costs of education, making many students eager to seek employment at full pay to reduce their educational development.

A post-graduate training residency for positions is being hampered by the current shortage of practitioners. However, as the shortage of practicing pharmacists eases over the ensuing decade, employers may emphasize the value of post-graduate education by making it a requirement for entry level or for specific clinical specialist positions. Apart from these external forces, students should be introduced to the value of post-graduate training through exposure to current trainees in our colleges and schools or through collaborations with other health care organizations in our community, this should not be limited to information regarding clinical or academic positions. Nearly all the potential positions for our graduates in the pharmaceutical industry also require skills gained during post-doctoral residencies and fellowships combined with “on the job” training, or through further graduate education. Colleges/schools must take a more active role in providing information on the unique opportunities for our graduates.

**Pharmacist's Roles in the Pharmaceutical Industry:**

Our graduates with a broad scientific knowledge and laboratory skills in optimizing dosage form development and drug delivery and it can be viewed asan entry-level formulator in the pharmaceutical industry.

**Pharmacist's Role in Managed Care Pharmacy:**

The increased emphasis for accessible, high quality and cost-effective health and pharmacy care services combined with a focus on reducing health disparities will require more of our graduates to assume roles in managed care pharmacy. Our graduates have the knowledge and skill sets needed to advance and lead critical areas such drug utilization review and formulary development. Outcomes and practice-based research, integration of health care data and disease.

**Pharmacist's Role in the Environmental Health:**

Role in the evolving “green pharmacy program” or other programs addressing the disposal of medications or medication delivery devices. These programs being developed across the country helps communities to safely dispose or perhaps reutilize expired and unused medications.on the industrial side, safe disposal of waste streams from synthesis facilities and the environmental impact of medicinal in human and veterinary waste have prompted expensive efforts to protect our environment.

**Pharmacist's Patient Care Process:**

The goal of high quality, cost-effective and accessible health care for patients is achieved through team based patient-centered care. Pharmacist's are essential members of the health care team. The profession of pharmacy is continuing its evolution from a principle focus on medication product distribution to expanded clinically-oriented patient care services. As a result of this professional evolution, the importance of , and need for, a consistent process of care in the delivery of patient care services has been increasingly recognized by profession at large.

Pharmacists have unique training and expertise in the appropriate use of medications and provide a wide array of patient care services in many different practice settings. These services reduce adverse drug events, Improve patient safety and optimize medication use and health outcomes. Pharmacists contribute to improving patient's health by providing patient care services as authorized under their scope of practice facilitated by collaborative practice agreements.

# INFORMATION

## M. PHARM & PHARM D SCHOLARSHIPS 2016-17 AWARDED BY TNPSWT

Profile of 1st Rank Projects

### *PHARMACEUTICS*

Name: Ms. Tamal Kusum Das
Project Title: "Design and Development of Valsartan loaded Nano Structured Lipid Carrier for Alleviating Diabetic Neuropathic Pain"
College: J S S College of Pharmacy, Ooty
Guide's Name: Dr. V. Senthil

### *PHARMACEUTICAL CHEMISTRY*

Name: Mr. V. Shivakumar
Project Title: Design, Synthesis, Characterisation and Biological evaluation of some novel heterocyclic derivatives as anti-tubercular agents.
College: Madras Medical College, Chennai
Guide's Name: Dr. A. Jerad Suresh

### *PHARMACEUTICAL ANALYSIS*

Name: Mr. Samrat Debnath
Project Title: Impurity profiling and genotoxicity evaluation of Gemcitabine HCl
College: J S S College of Pharmacy, Ooty
Guide's Name: Dr. M. R. Jeyaprakash

### *PHARMACOLOGY*

Name: Mr. A. Balasachidanandam
Project Title: Development of cucurbitacin derivative through in-silico and in-vitro methods to control prostate cancer cell proliferation
College: PSG College of Pharmacy, Coimbatore
Guide's Name: Dr. M. Ramanathan

## PHARMACOGNOSY

Name: Ms. M. Geethanjali

Project Title: Studies on the leaves of Myristica fragrance Houtt- Effect of its nano-encapsulated volatile oil on in vivo angiogenesis model

College: College of Pharmacy, Madurai Medical College, Madurai

Guide's Name: Prof. Dr. K. Periyanayagam

## PHARMACY PRACTICE

Name: Mr. Titto P Jacob

Project Title: Study on statin induced diabetes and its consequences in LDL cholesterol target attainment in patients at very high cardiovascular risk.

College: College of Pharmacy, SRIPMS, Coimbatore

Guide's Name: Dr. S. Sriram

## PHARM D- PHARMACY PRACTICE

Name: Ms. Debi Ann Abraham, Ms. M. Divya Krupa,
Mr. A. R. Galileo, Ms. S. Janani

Project Title: Effect of cancer treatment on cognitive function and health-related quality of life in patients receiving cancer chemotherapy - A prospective study

College: Sri Ramachandra University, Chennai

Guide's Name: Dr. M. G. Rajanandh

# EVENTS

## Pharma Knowledge and Training Institute (Finishing School)

4th Training on

## Industrial Orientation Training for Production and Quality Management Personnel

The 4th Training programme for the fresh Pharmacy graduates by Pharma Knowledge and Training Institute (Finishing School) under the aegis of Tamilnadu Pharmaceutical Sciences Welfare Trust was held at Trust premises in Spencer Plaza, Anna Salai, Chennai from 23rd January 2017 to 18th March 2017. The trainees are final year B. Pharm students from Vels University. A total of 95 students were trained in this training programme in 3 batches. The students were given training both theoretically and practical on the subject of "Industrial Orientation Training on Production and Quality management Personnel". The duration of the training programme was 4 weeks which includes theory classes and practical training. The following subjects were taught as theory and practical during this training programme.

### Theoretical Training Programme

- Overview of the Pharmaceutical Industry and Job opportunities for the Pharmacy graduates
- Regulatory Requirements of Production and QC under Drugs & Cosmetics Act and Rules, Role of Govt. Drug Testing Laboratories
- Good Manufacturing Practices under Schedule "M" of Drugs & Cosmetics Act in respect of Production, Quality Control, Maintenance of record of Drugs & Pharmaceuticals
- What is Pharmacopoeia, various Pharmacopoeias used world over, how to use pharmacopoeia, monographs, their explanation & General Notices in pharmacopeia and Reference Standards
- What is quality and why it is essential for manufacture of products. Quality Control and its Relationship, with Quality Assurance, Production, R&D and regulatory divisions of Pharma Industry., What are the various divisions of Quality Control
- cGMP's for manufacturing including entry & exit procedures.
- Plant Design & Site Master File
- ICH guidelines for production & Quality Control of Pharmaceuticals

- Documentation and records in Production and QC
- Standard Operating Procedures
- Sampling of Raw Materials, Packing materials, In- process Materials and Finished products
- Basics of production planning & Inventory Control
- Air Systems, Water Systems, their sampling and testing
- Microbiology - An Introduction, Microbiology for non-sterile preparations
- Procedure and Validation of environmental monitoring, Plate exposures, Air Sampling, etc., in manufacturing of Sterile Pharmaceutical products
- General requirements for Tablets, Capsule, Oral liquids & external preparations
- Basic Calculations in Quality Control, Dilutions and Statistical Analysis , Qualitative Analysis, Quantitative Analysis & Elemental
- Selection of Packing Materials like Bottle packing, Strip Packing, Blister Packing etc and selection of different materials according to stability of products Viz: tablets & Capsules, Powders etc.
- Tablets – Part I (Processes involved in the production of Tablets such as size reduction, sieving, granulation, compression, coating etc. ,Various components of a Tablet with examples of different materials used &, In process tests to be carried during production of Tablets)
- Tablets – Part II (types of tablets such as Plain Tablets, Press Coated Tablets, Tablet in Tablet, Film Coated Tablets, Enteric Coated tablets, Delayed Release tablets etc, their advantages , How to control and rectify (in case of failure) weight variation, Disintegration time, Hardness, Friability, Dissolution etc during production , Different types of Coating of Tablets, Materials used for coating & coating process
- Capsules – Part I - Processes involved in the production of Capsules such as size reduction, sieving, granulation, Filling, Cleaning & Polishing etc., Various components of Capsules with examples of different materials used.
- Different sizes of Capsules available in the market, Filling of Capsules: hand filling, Machine Filling High speed filling Machines, In process tests to be carried during production of Capsules, How to control and rectify( in case of failure) weight variation, Disintegration time, Dissolution etc during production of Capsules.
- Reference Standards and Working Standards, Reference / retention samples storage
- Calibration of QC equipments

- Different types of Oral Liquid Dosage Forms such as Liquids, Syrups, Suspensions & Emulsions etc. Facilities required and their methods of manufacture, in process tests to be carried out during their manufacture.
- Ointments, Creams, Emulsions, Gargle solutions, Sanitizers, etc Different types of equipment used for their manufacture, Ingredients used and in-process tests to be carried during their production. Packing of the above products
- Powders for Dry Syrups: Main ingredients with examples of various materials used, equipment used for their manufacture, In process tests to be done, and their packaging , Effervesant Powders their main ingredients their manufacture and packing
- Oral Rehydration Powders(ORS), Equipment used for their manufacture, WHO approved formula, Materials used for formulation of ORS, in process tests to be done and packing of ORS powders
- Dissolution & its Importance, Methods used in Dissolution Testing
- Analytical method validation
- Batch Manufacturing Records, Batch Packing Records and importance of online recording.
- Introduction to Theory of Chromatography & Spectrophotometry
- TLC Gas Chromatography (GC), High Performance Liquid Chromatography (HPLC), a brief introduction
- Stability Testing, Accelerated and Real Time Studies, Packaging Material Stability, Their Testing, Their Importance with Respect to the Product
- Preventive maintenance, Predictive maintenance & Break down maintenance
- Change control, Deviation control and their importance
- Data Integrity of documents in the Pharmaceutical Industry
- Good Laboratory Practices - Schedule L1
- IQ, OQ, PQ and DQ of equipments of Production & QC, Validation, Qualification and calibration.
- Market complaints, CAPA, OOS and OOT etc., what is containment? Essential steps to control contamination, handling of deviation, Risk
- Soft Skill

The following faculties gave lecture on the above subjects

Mr. J. Jayaseelan, Managing Director M/s. Sai Mirra Innopharm Pvt Ltd.

Mr. Sanjay Kumar Dasmohapatra, Vice President – Technical & Operations, M/s. Medopharm

Mr. P.R. Abdul Hameed, Executive Director - Technical, M/s. Medopharm

Mr. S. Sridhar, Vice President – Woks, M/s. Medopharm (Malur Plant).

Mr. K. Saravana Kumar, Corporate – QA Head, M/s. Fourrts (India) Labs Pvt. Ltd.

Mr. D. Satish Kumar – Senior Manager – Production, M/s. Fourrts (India) Labs Pvt. Ltd.

Mr. M. Ramalingam, Head (Plant II), M/s. Fourrts (India) Labs Pvt. Ltd.

Mr. K. M. Sridhar, Head – Quality Control (Plant I), M/s. Fourrts (India) Labs Pvt. Ltd.

Mr. G.T. Arularasu, Head – Quality Control (Plant II), M/s. Fourrts (India) Labs Pvt. Ltd.

Mr. M. Radhakrishnan, Senior Manager – Production, M/s. Fourrts (India) Labs Pvt. Ltd.

Dr. P.Ram Kumar, Head – R & D, M/s. Fourrts (India) Labs Pvt. Ltd.

Mr. Gopinath, Dy. Manager – Production, M/s. Fourrts (India) Labs Pvt. Ltd.

Mr. R. Ramadhas, Asst Manager – AR & D, M/s. Fourrts (India) Labs Pvt. Ltd.

Mr. Mujibur Rahman, Asst Manager – Microbiology, M/s. Fourrts (India) Labs Pvt. Ltd.

Mr. S. Jaya Kumar, Head – Quality, M/s. Apex Laboratories Pvt Ltd.

Mr. S. Murali - GM – Plant Operations, M/s. Apex Laboratories P Ltd.

Mr. D. Srinivasa Rao, GM – Plant Operations, M/s. Apex Laboratories P Ltd.

Mr. P. Raman, GM – Corporate Quality, M/s. Apex Laboratories P Ltd

Mr. V. Arul Selvan - Manager – QC, M/s. Apex Laboratories P Ltd .

Dr. G. Selvaraj, Director of Drugs Control (Retd), Tamilnadu.

Dr. S. Manivannan, Deputy Drugs Controller (I), CDSCO, South Zone, Chennai

Dr. N. Murugesan, Director, CDTL, Chennai.

Mr. R. Kannan, Asst Director of Drugs Control, Tamil Nadu.

Mr. M. Senthil Kumar, Director – Works, M/s. Allianz Biosciences Pvt Ltd.

Mr. S. Ganesan, GM – Works, M/s. Tablets (India) Ltd.

Dr. R. Venkidesh, GM – Quality Control, M/s. Saimirrah Innopharm Pvt. Ltd.,

Mr. M. Murrgan, Head – R & D, M/s. Saimirrah Innopharm Pvt. Ltd.,

Mr. N. Chandar, Pharma Consultant,

Dr. D. Natarajan, Pharma Consultant

Mr. S. Saravanan, IICMS (Indian Institute of Chromatography and Mass Spectrometry), Chennai

Mr. P. Raman, IICMS, Mr. S. L. Vinod Pillai, IICMS, Ms. U. Ram Priya, IICMS

Mr. J. Krishnan, Head – Training, Ripe Consulting Services Pvt. Ltd., Chennai

**Practical Training**

M/s. Fourrts (India) Laboratories Pvt. Ltd., Plant 1 & Plant 2, Chennai, M/s. Apex Laboratories Pvt. Ltd., Alathur, Chennai, M/s. Medopharm, Guduvanchery, Chennai, M/s. Tablets (India) Ltd., T H Road, Chennai, M/s. Sai Mirra Innopharm Pvt. Ltd., Ambattur, Chennai and M/s. The Madras Pharmaceuticals, OMR, Chennai, offered their facilities for practical training to the trainees.

**Evaluation**

All the trainees were evaluated after each of the lecture programme as well as on the final date of completion of the programme on the basis of the evaluation these students were given merit award prizes during the valedictory function.

**Valedictory Function**

The Valedictory function was held at Vels University on 23rd March 2017. Our Trust Chairman Mr. S. V. Veerramnai, inaugurated the function. The Chief guest of the function was Mr. S. V. Vishagan, Executive Director – Apex Laboratories Pvt Ltd. and the guest of honours were Prof. K. Chinnaswamy, President – Tamilnadu Pharmacy Council, Mr. J. Jayseelan, MD M/s, Sai Mirra Innopharm Pvt Ltd., Dr. P. Shanmugasundaram, Director – School of Pharmaceutical Sciences, Vels University. Mr. R. Narayanswamy, Director, PKTI Welcomed the gathering and explained about the 4th training programme. Prizes were awarded to the trainees who have scored highest mark in the evaluation test. Mr. N. Sreenivasen, Secretary, TNPSWT proposed vote of thanks.

## PKTI - 4th Training Programme, Photos of various Lectures & Event




IICMS

## PKTI - 4th Training Programme Valedictory Function & Prize Distribution


## Valedictory Function & Group Photos of Trainees - Vels University, Pharmacy Students

## All India Pharmacy Quiz - 2017

All India Pharmacy Quiz 2017 was conducted on February 25, 2017 by the College of Pharmacy, Madras Medical College, Chennai.

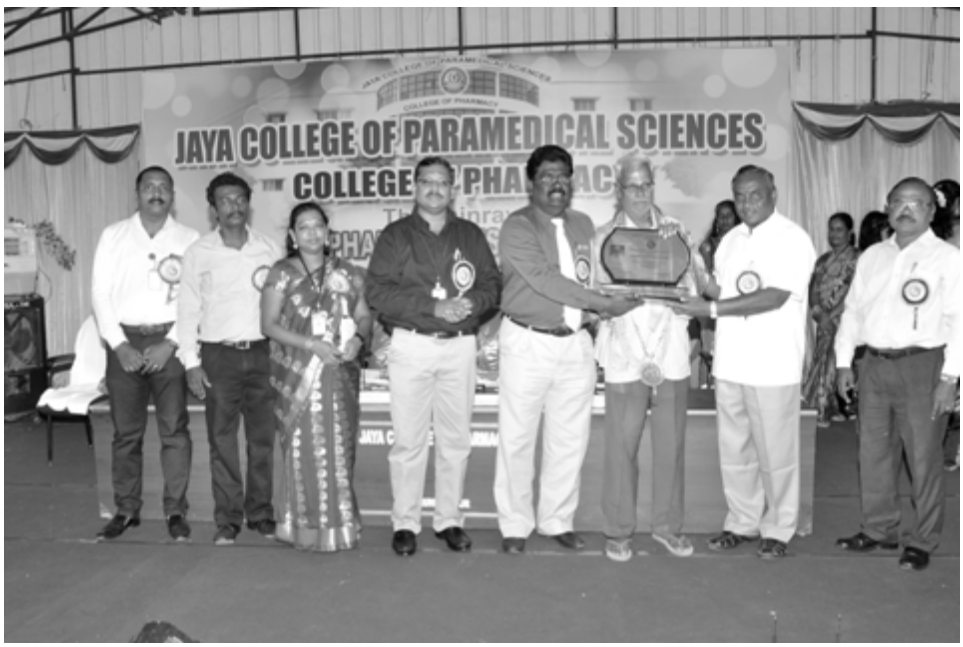
About 543 teams comprising B. Pharm, M. Pharm and Pharm D students from various Pharmacy colleges from Karnataka, Tamilnadu, Andhra Pradesh, Kerala and Maharashtra participated in the quiz programme.

- ***Yash Suniel Nandawani & Aman Rajesh Padamsey*** of AISSMS, College of Pharmacy from Pune, Maharashtra won the first prize of 25,000/-.the prize was sponsored by M/s Delvin Formulations Pvt. Ltd.
- ***Tejaswi. Y & Priyanka.*** *N,* College of Pharmacy, Madras Medical College, Chennai won the second prize of 15,000/- which was sponsored by M/s Apex Laboratories Pvt. Ltd.
- ***Shahana Ahamed. A & Keerthana.M*****,** College of Pharmacy, Madras Medical College, Chennai won the third prize of 10,000/- which was sponsored by M/s Tablets India. The Quiz was co-sponsored by M/s Kniss Laboratories, Fourrts India Pvt. Ltd & Microlabs



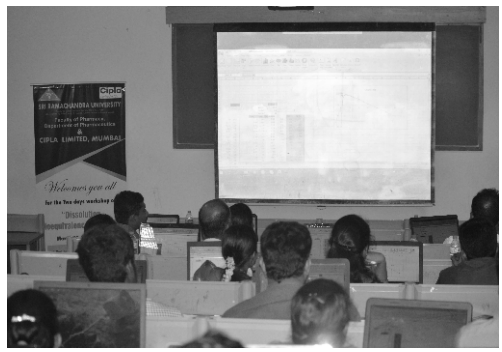
## PHARMA FRESH -2017

Jaya College of Pharmacy celebrated Pharma Fresh – 2017 under the chairmanship of Prof. A. Kanagaraj, Chairman, Jaya Educational Trust. Dr. Stella Robertson has delivered the welcome address to the gathering. Prof. A. Maheswaran, Principal gave a gathering address stating that students imbibe discipline and punctuality along with other curricular activities and emphasized sports also form integral part of academic field. Dr. N. Narayanan gave a fillip felicitation address stating that pedagogical tool of student, success depends on research work and concentration. Prof. A. Kanagaraj, Chairman, Jaya Educational Trust advised the students to be expository thinkers, knowledgeable who can express themselves in many ways. Dr. J. Jayaseelan, Managing Director, Delvin Formulations graced the occasion as chief guest and advised the students to take initiative in finding opportunities to learn to develop the knowledge and skills required to provide optimal drug therapy. An MoU was signed by the college with Delvin formulations, Chennai for the benefit of students regarding industrial visit, research thrust and placement. The faculties of the college were awarded for their achievements. A sport event was also conducted by the college and many students participated the same.



## Workshop on Bioequivalence Study

Sri Ramachandra University, Faculty of Pharmacy, Chennai, conducted a workshop on “Dissolution testing, Bioequivalence studies, Invitro-Invivo Correlation” on 25th & 26th March 2017. Dr. Y. Ashokraj, Dr. Praveen Date, of Cipla Ltd, Mumbai and Dr. R. Rajesh of Apotex Research Pvt. Ltd., Bangalore, gave lecture on Drug development, Dissolution testing and Bioequivalence in correlation with Invitro and Invivo. The research scholars and Post Graduates from various Pharmacy colleges participated in these workshop.




## AGM - Drugs Control Department Retires Officers Association

The Annual General Body meeting of Drugs Control Department Retires Officers Association was held on 9th April 2017, under the Presidentship of Mr. C. V. Ramiah, Retired Director of Drugs Control, Tamilnadu. Prof. Thirunavukarsu, Head of Department, Psychiatry, SRM Medical University, Tamilnadu gave a lecture on stress management as well as current scenario of our life style function. The members of the association elected new office bearers for the year 2017 – 2018. Mr. C. V. Ramiah, as President, Mr. A. Krishna Dev, and Mr. M. Kannan as Vice Presidents, Mr. A. Arunachalam as Secretary and Mr. B. Safi Ahamed as Treasurer. The Association also decided to award medal to the best outgoing student Bachelor of Pharmacy from Madras Medical College & Madurai Medical College in memory of Mr. C. V. Narasiman Ex. Director of Drugs Control of Tamilnadu. The award will be presented to these students during the Pharmacy week celebration from 2017 onwards.


# NOTIFICATION

## MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 4th November, 2016

G.S.R.1041(E).— Whereas a draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945, was published, as required by section 12 read with section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health), number G.S.R. 812(E), dated the 23rd August, 2016, published in the Gazette of India, Extraordinary, Part II, Section 3, sub-section (i), dated the 23rd August, 2016, inviting objections and suggestions from all persons likely to be affected thereby before the expiry of a period of forty five days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas copies of the Gazette were made available to the public on 23.08.2016;

And, whereas, objections and suggestions received from the public on the said rules have been considered by the Central Government;

Now, therefore, in exercise of the powers conferred under section 12 read with section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:-

1. (1)These rules may be called the Drugs and Cosmetics (Seventh Amendment) Rules, 2016.

(2)They shall come into force on the date of their publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945, in Schedule Y, in Appendix III relating to Animal Toxicology (non-clinical toxicity studies), in paragraph 1, in sub- paragraph 1.4 relating to Local Toxicity,-

(A) In Note (i) relating to Dermal toxicity study, for the words and brackets “Daily topical (dermal) application of test substance in its clinical dosage form should be done”, the words and brackets“the initial toxicity study shall be carried out by non-animal alternative tests as given in Organisation for Economic Cooperation and Development Guidelines”, shall be substituted.

(B) In Note (vi) relating to Ocular toxicity studies (for products meant for ocular instillation), after the words “need to include a recovery group.” the words “such initial toxicity studies shall be carried out by non-animal alternative tests as given in Organisation for Economic Cooperation and Development Guidelines.” shall be substituted.

[F.No. X.11014/7/2016-DFQC]
K. L. SHARMA, Jt. Secy.

Note.— The principal rules were published in the Gazette of India vide notification No. F.28-10/45-H (1) dated 21st December 1945 and last amended vide notification number GSR 897(E) dated 21.09.2016.

## MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 28th December, 2016

G.S.R. 1179(E).—The following draft of rules further to amend the Drugs and Cosmetics Rules, 1945, which the Central Government proposes to make, in exercise of the powers conferred by section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), after consultation with the Drugs Technical Advisory Board, is hereby published as required by said sections for the information of all persons likely to be affected thereby, and notice is hereby given that said draft rules will be taken into consideration on or after the expiry of a period of forty-five days from the date on which the copies of the Gazette of India containing these draft rules are made available to the public;

Objections and suggestions which may be received from any person within the period specified above, will be considered by the Central Government.

Objections and suggestions, if any, may be addressed to the Under Secretary (Drugs), Ministry of Health and Family Welfare, Government of India, Room No. 414 'A', D-Wing, Nirman Bhawan, New Delhi-110011.

**Draft rules**

1. (1) These rules may be called the Drugs and Cosmetics (_____Amendment) Rules, 2016.

(2) They shall come into force on date of their final publication in the official Gazette.

2. In the Drugs and Cosmetics Rules, 1945, in rule 64, in sub-rule (2), in the second proviso, for clause (ii), the following clause shall be substituted, namely:-

"(ii) in the charge of a competent person who is a registered pharmacist:

Provided that the person already registered with the state Licensing Authority as competent person for the purposes of grant of license in Form 20B or Form 21 B or both prior to the coming into force of the Drugs and Cosmetics (…….Amendment) Rules, 2016, shall continue to be considered as a competent person for the said purposes.".

[F. No. X -11014/6/2015-DFQC]
K. L. SHARMA, Jt. Secy.

Note: The principal rules were published in the Gazette of India vide notification No. F. 28-10/45-H (1), dated 21st December 1945 and last amended vide notification number G.S.R. 1041(E), dated the 4th November 2016.

## MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 16th January, 2017

G.S.R. 36(E).—The following draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945, which the Central Government proposes to make in exercise of the powers conferred by section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), after consultation with the Drugs Technical Advisory Board, is hereby published for information of all persons likely to be affected thereby, and notice is hereby given that said draft rules will be taken into consideration on or after the expiry of a period of forty five days from the date on which copies of the Gazette of India containing these draft rules are made available to the public.

Objections and suggestions which may be received from any person within the period of specified above will be considered by the Central Government.

Objections and suggestions, if any, may be addressed to the Under Secretary (Drugs), Ministry of Health and Family Welfare, Government of India, Room No. 414 A, D Wing, Nirman Bhavan, New Delhi – 110011 or sent on email at rg.singh72@nic.in .

**Draft rules**

1. Short title and commencement.-(1) These rules may be called Drugs and Cosmetics (_____Amendment) Rules, 2017.

   (2) They shall come into force on the date of their final publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945, in Schedule A, in Form 44, in paragraph 1, relating to 'Particulars of new drug', item (8) and the entries relating thereto shall be omitted.

[F. No. X.-11014/9/2016-DRS]
K. L. SHARMA, Jt. Secy.

Note.- The principal rules were published in the Official Gazette vide notification number F.28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 1041(E), dated the 4th November 2016.

## MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 17th January, 2017

G.S.R. 41(E).— Whereas a draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945, was published, as required by section 12 read with section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare), number G.S.R. 1050 (E), dated the 08th November, 2016, published in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), dated the 08th November, 2016, inviting objections and suggestions from persons likely to be affected thereby before the expiry of a period of forty five days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas copies of the Gazette were made available to the public on 08th November, 2016;

And whereas, objections and suggestions received from the public on the said rules have been considered by the Central Government;

Now, therefore, in exercise of the powers conferred under section 12 read with section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:-

(1) These rules may be called the Drugs and Cosmetics (First Amendment) Rules, 2017.

(2) They shall come into force on the date of their final publication in the Official Gazette.

2.In the Drugs and Cosmetics Rules, 1945, in rule 43-A, for the words “Chennai, Kolkata, Mumbai, Cochin, Nhava Sheva, Kandla, Inland Container Depots at Tuglakabad and Patparganj in Delhi, Tuticorin in Tamil Nadu, Marmugao port in Goa and Visakhapatnam in Andhra Pradesh: in respect of drugs imported by sea into India.”, the following words shall be substituted, namely:- “Chennai, Kolkata, Mumbai, Cochin, Nhava Sheva, Kandla, Inland Container Depots at Tuglakabad and Patparganj in Delhi, Tuticorin in Tamil Nadu, Marmugao port in Goa, Visakhapatnam and Krishnapatnam port in Andhra Pradesh and Hazira port and Inland Container Depot Khohdiyar, Gandhinagar in Gujarat: in respect of drugs imported by sea into India;”

[F. No. X.-11014/1/2015-DFQC]
K. L. SHARMA, Jt. Secy.

Foonote.- The principal rules were published in the Official Gazette vide notification number F.28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 1041(E), dated the 4th November 2016.

## MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 17th January, 2017

G.S.R. 42(E).—The following draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 which the Central Government proposes to make in exercise of the powers conferred by section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), in consultation with the Drugs Technical Advisory Board is hereby published for information of all persons likely to be affected thereby and notice is hereby given that said draft rules will be taken into consideration on or after the expiry of a period of forty-five days from the date on which the copies of the Gazette of India containing these draft rules are made available to the public.

Objections and suggestions which may be received from any person within the period specified above will be considered by the Central Government.

Objections and suggestions, if any, may be addressed to the Under Secretary (Drugs), Ministry of Health and Family Welfare, Government of India, Room No. 414 A, D Wing, Nirman Bhavan, New Delhi – 110011 or send on email rg.singh72@nic.in .

### DRAFT RULES

1. Short title and commencement.-(1) These rules may be called the Drugs and Cosmetics (Amendment)
   Rules, 2017.
(2) They shall come into force on the date of their final publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945, in Schedule H, after serial number 536 and entries relating thereto, the following serial number and entry shall be added, namely:-
   "537. Etizolam".

[F. No. X.-11014/11/2016-DRS]
K. L. SHARMA, Jt. Secy.

Foonote.- The principal rules were published in the Official Gazette vide notification number F.28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 1041(E), dated the 4th November 2016.

## MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 17th January, 2017

GG.S.R. 43(E).—The following draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 which the Central Government proposes to make in exercise of the powers conferred by section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) after consultation with the Drugs Technical Advisory Board is hereby published for information of all persons likely to be affected thereby and notice is hereby given that said draft rules shall be taken into consideration on or after the expiry of a period of forty five days from the date on which the copies of the Gazette of India containing these draft rules are made available to the public.

Objections and suggestions, which may be received from any person within the period specified above, shall be considered by the Central Government.

Objections and suggestions, if any may be addressed to the Under Secretary (Drugs), Ministry of Health and Family Welfare, Government of India, Room No. 414 A, D Wing, Nirman Bhawan, New Delhi – 110011 or sent on email rg.singh72@nic.in.

**Draft rules**

1. Short title and commencement.—(1) These rules may be called Drugs and Cosmetics (_____Amendment) Rules, 2017.
(2) They shall come into force on the date of their final publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945 (hereinafter referred to as the said rules), in rule 24, in sub-rule (1), the words “and by an undertaking in Form 9 duly signed by or on behalf of the manufacturer” shall be omitted;

3. In the said rules, in rule 26, clause (i) and the entries relating thereto shall be omitted;

4. In the said rules, in Schedule A,-
   (a) in Form 8, paragraph 3 shall be omitted;
   (b) in Form 8A, paragraph 3 shall be omitted;
   (c) Form 9 shall be omitted.

[F. No. X.-11014/13/2016-DRS]
K. L. SHARMA, Jt. Secy.

Foonote: The principal rules were published in the Official Gazette vide notification number F. 28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 1041(E), dated the 4th November, 2016.

## MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 17th January, 2017

G.S.R. 44(E).—The following draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945, which the Central Government proposes to make, in exercise of the powers conferred by sections 12 and 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), after consultation with the Drugs Technical Advisory Board, is hereby published as required by sub-section (1) the said section 12 and sub-section (1) of section 33 for information of all persons likely to be affected thereby; and notice is hereby given that the said draft rules will be taken into consideration on or after the expiry of a period of thirty days from the date on which the copies of the Official Gazette containing these draft rules are made available to the public;

Objections and suggestions, if any, may be addressed to the Under Secretary (Drugs), Ministry of Health and Family Welfare, Government of India, Room No.414-A, D Wing, Nirman Bhawan, New Delhi- 110011;

The objections and suggestions which may be received from any person with respect to the said draft rules within the period specified above, will be considered by the Central Government.

### DRAFT RULES

1. (1) These rules may be called the Drugs and Cosmetics (_____Amendment) Rules, 2017.
(2) They shall come into force on the date of their final publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945, in rule 3A, in sub-rule (8), in clause (b), after item (5) and the entries relating thereto, the following shall be inserted, namely:-

"(6) Enzyme and Hormones such as-
(a) Streptokinase (Natural and Recombinant);
(b) Human Chorionic Gonadotropin (hCG);
(c) Human Menopausal Gonadotropin (hMG).

(7) Bacterial vaccine such as-
(a) Bacillus Calmette-Guerin (BCG) vaccine.

(8) Viral vaccines such as-
(a) Live attenuated Measles vaccine;
(b) Live attenuated Rubella vaccine;
(c) Cell culture Rabies vaccine.".

[F. No. A.-11018/2/2016-DFQC]
K. L. SHARMA, Jt. Secy.

Note : The principal rules were published in the Gazette of India vide notification No. F.28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 1041(E), dated 4.11.2016.

## MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 19th January, 2017

G.S.R. 56(E).— Whereas a draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published, as required by section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare), number G.S.R. 1017, dated the 28th October, 2016, in the Gazette of India, Extraordinary, Part II, Section 3, sub-section (i), dated the 28th October, 2016, for inviting objections and suggestions from persons likely to be affected thereby before the expiry of a period of forty five days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And Whereas copies of the said Official Gazette were made available to the public on 28th October, 2016;

And, Whereas, objections and suggestions received from the public on the said rules have been considered by the Central Government;

Now, therefore, in exercise of the powers conferred by section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:-

1. (1) These rules may be called the Drugs and Cosmetics (2nd Amendment) Rules, 2017.
(2) They shall come into force on the date of their publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945 (hereinafter referred to as the said rules), for rule 135A, the following rule shall be substituted, namely,-

"135A. Regulation of import of cosmetics containing mercury. Cosmetics imported into India shall contain mercury in the following proportion, namely;

(a) in cosmetics intended for use only in the area of eye, the level of mercury not exceeding seventy parts per million (0.007 per cent.) of mercury, calculated as the metal, as a preservative;

(b) in other finished cosmetic products, unintentional mercury shall not exceed one part per million (1 ppm).".

3. In the said rules, for rule 145D, the following rule shall be substituted, namely,-

"145D: Regulation of use of mercury compounds in cosmetics. Cosmetics manufactured in the country shall contain mercury in the following proportions, namely,-

(a) in cosmetics intended for use only in the area of eye, the level of mercury not exceeding seventy parts per million (0.007 per cent.) of mercury, calculated as the metal, as a preservative;

(b) in other finished cosmetic products, unintentional mercury shall not exceed one part per million (1 ppm).".

[F.No. X 11035 / 276 /2015-DFQC]
K. L. SHARMA, Jt. Secy.

Foot-note.- The principal rules were published in the Gazette of India vide notification Number F.28-10/45- H (1) dated the 21st December, 1945 and lastly amended vide notification number G.S.R. 41(E) dated the 17th January, 2017.

## MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 31st January, 2017

G.S.R. 76 (E).— Whereas a draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945, was published, as required by section 12 read with section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare), number G.S.R. 312 (E), dated the 16th March, 2016, published in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), dated the 16th March, 2016, inviting objections and suggestions from persons likely to be affected thereby before the expiry of a period of forty five days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas copies of the Gazette were made available to the public on 16th March, 2016;

And whereas, objections and suggestions received from the public on the said rules have been considered by the Central Government;

Now, therefore, in exercise of the powers conferred under section 12 read with section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:-

1. (1) These rules may be called the Drugs and Cosmetics (3rd Amendment) Rules, 2017.
   (2) They shall come into force on the date of their final publication in the Official Gazette.
2. In the Drugs and Cosmetics Rules, 1945, in Schedule K, for serial numbers 35 and 35 and the entries relating there to, the following serial numbers and entries shall be substituted, namely:-

| Class of Drugs | Extent and Conditions of Exemption |
|---|---|
| "35. Homeopathic hair oils having active ingredients up to 3X potency only. | The provisions of Chapter IV of the Act and the rules made thereunder which require them to be regulated with a sale license subject to the condition that such products have been manufactured under a valid manufacturing license and sold in the original sealed packing of the licensed manufacturers. |
| 36. Custom made devices. | All provisions of Chapter IV of the Act and the rules made thereunder, subject to the condition that the device being specifically made in accordance with a duly qualified medical practitioner's written prescription under his responsibility, in accordance with specific design, characteristics and the same is intended for the sole use of a particular patient and the label contain the words 'custom made device'.<br>**Explanation.-** Mass produced devices, which only need adoption to meet the specific requirement of a medical practitioner or any other professional user, shall not be considered as custom made device. |
| 37. Zinc sulphate tablets and oral solutions having 10 mg and 20 mg of elemental zinc. | The provisions of Chapter IV of the Act and rules thereunder which require them to be covered by a sale licence, subject to the condition that such a product has been manufactured under a valid drug manufacturing licence.". |

[F. No. X 11014/5/2012-DFQC]
K. L. SHARMA, Jt. Secy.

Note.- The principal rules were published in the Gazette of India vide notification No. F.28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 56(E), dated the 19th January, 2017.

## MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 1st February, 2017

G.S.R. 80(E).—The following draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 which the Central Government proposes to make in exercise of the powers conferred by section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) after consultation with the Drugs Technical Advisory Board is hereby published for information of all persons likely to be affected thereby and notice is hereby given that said draft rules shall be taken into consideration on or after the expiry of a period of forty five days from the date on which the copies of the Gazette of India containing these draft rules are made available to the public.

Objections and suggestions which may be received from any person within the period specified above shall be considered by the Central Government.

Objections and suggestions, if any, may be addressed to the Under Secretary (Drugs), Ministry of Health and Family Welfare, Government of India, Room No. 414 A, D Wing, Nirman Bhawan, New Delhi – 110011 or sent on email rg.singh72@nic.in.

**Draft rules**

1. (1) These rules may be called Drugs and Cosmetics (_____Amendment) Rules, 2017.
(2) They shall come into force on the date of their final publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945 (hereinafter referred to as the said rules), in rule 67C, the following proviso shall be inserted, namely:-
"Provided that no licence shall be required for exhibiting the drugs for promotional activities in any fair.".

3. In the said rules, in rule 67F, in sub-rule (1), for the words "who is in the opinion of the licensing authority competent to deal in Homeopathic medicines:" the words "who is holding,–
(a) degree in Homoeopathy from a recognised University; or

(b) degree in pharmacy from a recognised University; or

(c) Bachelor's degree from a recognised University with one year experience of dealing in Homoeopathic medicines in the premises of a registered Homoeopathic Medical Practitioner or premises holding licence in Form 20C or Form 20D:"
shall be substituted.

4. In the said rules, in rule 67G, for clause (2), the following clause shall be substituted, namely:-
"(2) In the case of licence in Form 20C the Homeopathic medicines shall be sold,-
(i) under the supervision of a person having qualifications referred to in sub-rule (1) of rule 67F; and
(ii) in manufacturer's sealed packing only except dispensing of medicines in globules, water or milk sugar or as per prescription of a Homoeopathic Medical Practitioner.".

5. In the said rules, in rule 85E, after sub-rule (2), following sub-rule shall be inserted, namely:-
"(2A) Certificate of Good Manufacturing Practice.- The certificate of Good Manufacturing Practice to manufacturers, who comply with the requirements of Good Manufacturing Practices of Homeopathy drugs, as specified in Schedule M-I, shall be issued upto the date of validity of licence.".

6. In the said rules, in Schedule K, for serial number 31 and the entries relating thereto, the following serial number and enteries relating thereto shall be substituted, namely:-

| Class of Drugs | Extent and Conditions of Exemption |
|---|---|
| "31. Homoeopathic medicines | The provisions of Chapter IV of the Act and the rules made thereunder which relates to sale licence in Form 20-C, subject to the following conditions: -<br><br>(i) These medicines shall be sold in the original sealed small quantity packings of the licensed manufacturers;<br><br>(ii) Medicines shall be stocked and sold by retail dealers of medicines licensed under rule 61;<br><br>(iii) Medicines shall be stored separately from other allopathic drugs;<br><br>(iv) Medicines shall be purchased from a manufacturer or a dealer licensed under these rules;<br><br>(v) Purchase and sale records of medicines shall be maintained by the dealer for a minimum period of three years; and<br><br>(vi) Medicines shall be labelled in generic or pharmacopoeial names." |

7. In the said rules, in Schedule M-I,-

(i) in paragraph 1 relating to 'General requirements', in sub-paragraph 1.1, for the words "or outside" wherever they occur, shall be omitted;

(ii) in paragraph 2 relating to 'Plant and Equipment', in sub-paragraph 2.1, for the word "origins" wherever it occurs, the word "types" shall be substituted;

(iii) in paragraph 3 relating to 'Requirement of Equipment and Facilities',-

(A) in sub-paragraph 3.1,-

(a) in items (v), (vi) and (ix), for the words and figures "stainless steel of grade 304" wherever they occur, the words and figures "stainless steel of grade not below 304" shall be substituted;

(b) for the words and figures "shall be separate and shall be 55 square meters for each for basic installations", the words and figures "shall not be less than 55 square meters for basic installations" shall be substituted;

(B) in sub-paragraph 3.3, in the Notes, in Note (b), after the words, "neutral glass", the words "or stainless steel" shall be inserted;

(C) in sub-paragraph 3.4, after the words, "shall be provided", the words "as per the requirements of manufacturing process" shall be inserted;

(D) in sub-paragraph 3.6, after the words "shall be provided", the words "as per the requirements of manufacturing process" shall be inserted;

(iv) in paragraph 4 relating to 'Quality Control Division', in sub-paragraph 4.3, for item (ii), the following item shall be substituted, namely:-

"(ii) Compound microscope;";

(v) in paragraph 5 relating to 'Raw Materials', in sub-paragraph 5.1,

(A) in clause (a),-

(I) for item (iv), the following item shall be substituted, namely:-

"(iv) the materials shall conform to the pharmacopoeial standards;"

(II) in item (v), the words "and should not be more than six months old" wherever they occur, shall be omitted;

(B) in clause (b):-

(I) for item (i), the following item shall be substituted, namely:-

"(i) the raw materials of plant origin shall be as per pharmacopoeia";

(II) for item (vi), the following item shall be substituted, namely:-

"(vi) fresh herbs shall be stored in open mesh bags and materials in closed containers";

(III) for item (vii), the following item shall be substituted, namely:-

"(vii) each consignment of the material shall be accompanied by a statement of the supplier's name; name of the plant with description of the part supplied; the Pharmacopoeial reference, place of collection, date of packaging and weight";

(vi) in paragraph 6, sub-paragraph 6.4 shall be omitted;

(vii) in paragraph 9, relating to 'Expiry Date', after the word "manufacture", the words "except Homoeopathic dilutions and back potencies, if preserved under hygienic conditions." shall be inserted.

[F. No. X-11014/1/2017-DRS]
K. L. SHARMA, Jt. Secy.

Note : The principal rules were published in the Gazette of India vide notification No. F-28-10/45-H (1) dated 21st December 1945 and last amended vide notification number G.S.R. 56(E) dated 19th January, 2017.

## MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 2nd February, 2017

G.S.R.101(E).—The following draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 which the Central Government proposes to make in exercise of the powers conferred by section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) after consultation with the Drugs Technical Advisory Board is hereby published for information of all persons likely to be affected thereby and notice is hereby given that the said draft rules shall be taken into consideration on or after the expiry of a period of forty-five days from the date on which the copies of the Gazette of India containing these draft rules are made available to the public.

Objections and suggestions, which may be received from any person within the period specified above, shall be considered by the Central Government.

Objections and suggestions, if any may be addressed to the Under Secretary (Drugs), Ministry of Health and Family Welfare, Government of India, Room No. 414 A, D Wing, Nirman Bhawan, New Delhi – 110011 or sent on email drugsdiv-mohfw@gov.in .

**Draft rules**

1. (1) These rules may be called Drugs and Cosmetics (_____Amendment) Rules, 2017.
(2) They shall come into force on the date of their final publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945, (hereinafter referred to as the said rules) in rule 122 P, after item (xiii), the following items shall be inserted, namely:-
"(xiv) The whole human blood and blood components may be transferred, under prescribed storage conditions, to another blood bank which have facilities to store and monitor blood distribution.
(xv) The recipient blood bank shall not further transfer units obtained from another blood bank except to another blood storage centre or a patient."

3. In the said rules, in Schedule F, in Part XII B under the heading "II. BLOOD DONATION CAMPS", after item (c), the following items shall be inserted, namely:-
"(d) a licensed blood bank run by registered voluntary or charitable organization recognised by State or Union territory Blood Transfusion Council; or (e) a private hospital blood bank."

4. In Schedule K to the said rules, in item 5(B), under the column relating to extent and conditions of exemption, condition (2) shall be omitted.

[F. No. X.11035/290/2015-DFQC]
K. L. SHARMA, Jt. Secy.

Note.- The principal rules were published in the Gazette of India vide notification No. F. 28-10/45-H (1) dated 21st December 1945 and last amended vide notification number GSR 76(E) dated 31st January, 2017.

MINISTRY OF HEALTH AND FAMILY WELFARE
(Department of Health and Family Welfare)

NOTIFICATION
New Delhi, the 2nd February, 2017

G.S.R. 102(E).—The following draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 which the Central Government proposes to make in exercise of the powers conferred by section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), after consultation with the Drugs Technical Advisory Board, is hereby published for information of all persons likely to be affected thereby and notice is hereby given that said draft rules will be taken into consideration on or after the expiry of a period of forty-five days from the date on which copies of the Gazette of India containing these draft rules are made available to the public.

Objections and suggestions which may be received from any person within the period specified above will be considered by the Central Government.

Objections and suggestions, if any, may be addressed to the Under Secretary (Drugs), Ministry of Health and Family Welfare, Government of India, Room No. 414 A, D Wing, Nirman Bhavan, New Delhi – 110011 or sent on email drugsdiv-mohfw@gov.in

Draft rules

1. (1) These rules may be called the Drugs and Cosmetics (_____Amendment) Rules, 2017.
(2) They shall come into force on the date of their final publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945 (hereinafter referred to as the said rules), in rule 2, after clause (a), following shall be inserted, namely,-

(aa) "biopharmaceutical classification system" means a system used to classify drugs on the basis of solubility and permeability, classified as category I- high solubility and high permeability, category II- low solubility and high permeability, category III- high solubility and low permeability, and category IV- low solubility and low permeability.";

3. In the said rules, in rule 74, after clause (p), the following clause shall be inserted, namely.-
"(q) the applicant shall submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.".

4. In the said rules, in rule 74B, after clause (7), the following clause shall be inserted, namely.-
"(8) the applicant shall submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.".

5. In the said rules, in rule 76, after clause (9), the following clause shall be inserted, namely.-
"(10) the applicant shall submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.".

6. In the said rules, in rule 78, after clause (q), the following clause shall be inserted, namely.-
"(r) the applicant shall submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.".

7. In the said rules, in rule 78A, after clause (8), the following clause shall be inserted, namely.-
"(9) the applicant shall submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.".

[F. No. X.11014/12/2016-DRS]
K. L. SHARMA, Jt Secy.

Note : Principal rules were published in the Official Gazette vide notification number F.28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 76(E) dated the 31st January, 2017.

MINISTRY OF HEALTH AND FAMILY WELFARE
(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 2nd February, 2017

G.S.R. 103(E).—Whereas a draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required by section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare) number G.S.R. 667 (E), dated the 5th July, 2016, published in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), dated the 5th July, 2016, inviting objections and suggestions from persons likely to be affected thereby before the expiry of a period of forty five days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas copies of the Gazette were made available to the public on 5th July, 2016;

And whereas objections and suggestions received from the public on the said rules have been considered by the Central Government;

Now, therefore, in exercise of the powers conferred under section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:-

1. (1) These rules may be called the Drugs and Cosmetics (4th Amendment) Rules, 2017.
(2) They shall come into force on the date of their publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945 (hereinafter referred to as the said rules), after rule 36, the following rule shall be inserted, namely:-
"36A Import of drugs by charitable hospital free of cost.—(1) Small quantity of drugs received in donation by a charitable hospital for the purpose of treatment of the patients in the said hospital may be imported provided the drugs are given or administered to the patients free of cost.
(2) The drugs shall not be prohibited for import and permitted to be marketed in the country with residual shelf life of one year or more."

3. In the said rules, in rule 45, in sub-rule (1), after the words "in accordance with these rules", the following words and the proviso shall be inserted, namely:-

"within a period of sixty days of the receipt of the sample:

Provided that where it is not possible to test or analyse the sample within the specified period, the Government Analyst shall seek extension of time from the Government giving specific reasons for delay in such testing or analysis.";

4. In the said rules, in rule 91, for the words "one year from the date of issue", the words "three years from the date of issue" shall be substituted.

5. In the said rules, rule 124A shall be omitted.

6. In the said rules, in Schedule A,
(a) in Form 11, in paragraph 3, for the words, "one year", the words "three years" shall be substituted;

(b) in Form 29, in paragraph 3, for the words "one year", the words "three years" shall be substituted.

[F. No. X.-11035/288/2015-DFQC]
K. L. SHARMA, Jt. Secy.

Note: The principal rules were published in the Official Gazette vide notification number F. 28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 76(E) dated the 31st January, 2017.

MINISTRY OF HEALTH AND FAMILY WELFARE
(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 17th February, 2017

G.S.R. 144(E).—Whereas the Central Government was satisfied that the drugs 'Oseltamivir Phosphate' and 'Zanamivir' were essential to meet the requirements of emergency arising due to epidemic and in public interest, and it was necessary and expedient to regulate and restrict the manufacture, sale and distribution of the said drugs and preparations based thereon for preventing their misuse;

And Whereas the Central Government in exercise of the powers conferred by section 26B of the Drugs and Cosmetics Act, 1940 (23 of 1940), vide notification published in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), number G.S.R. 677(E), dated the 15th September, 2009, directed that no person shall manufacture for sale or distribution, or sell or stock, or exhibit or offer for sale, or distribute any preparation containing the drug 'Oseltamivir Phosphate' or 'Zanamivir' except in the manner specified in the said notification;

And Whereas, the Drugs Technical Advisory Board considered the issue of restriction of sale of the drugs 'Oseltamivir Phosphate' and 'Zanamivir' similar to the drugs referred to in the Schedule X of the Drugs and Cosmetics Rules, 1945 on 15th November, 2016 and recommended that the notification G.S.R. 677(E), dated the 15th September, 2009 shall be withdrawn and the said drugs be permitted for sale similar to the drugs referred to in the Schedule H1 of the said rules;

Now, therefore, in exercise of the powers conferred by section 26B of the Drugs and Cosmetics Act, 1940 (23 of 1940) and on the basis of the recommendations of the Drugs Technical Advisory Board, the Central Government hereby and in supersession of the notification of the Government of India, Ministry of Health and Family Welfare (Department of Health) published in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), vide number G.S.R. 677(E) dated the 15th September, 2009 except as respects things done or omitted to be done before such supersession directs that no person shall manufacture for sale or for distribution or sale or stock or exhibit or offer for sale or distribute any preparation containing the drug 'Oseltamivir Phosphate' or 'Zanamivir' except in the following manner, namely:-

(a) no person shall himself or by any other person on his behalf manufacture for sale or for distribution without the prior approval in writing from the Drugs Controller General (India).

(b) the conditions specified in the Drugs and Cosmetics Rules, 1945 in respect of the drugs specified under Schedule H1 to that rules shall apply to the drugs 'Oseltamivir Phosphate' and 'Zanamivir' or any preparation based thereon. Provided that the Drugs Controller General (India) may allow export of the drug 'Oseltamivir Phosphate' and 'Zanamivir' or any preparation based thereon for reasons to be recorded in writing and in consultation with the Central Government.

(c) every manufacturer of the drug 'Oseltamivir Phosphate' and 'Zanamivir' or any preparation based thereon shall submit to the Drugs Controller General (India) a monthly statement, containing therein the quantity of such drugs supplied by them to distributors, stockists, dealers by the end of every month.

(d) every distributor, stockist and dealer holding stocks of 'Oseltamivir Phosphate' and 'Zanamivir' or any preparation based thereon shall submit to the concerned licensing authority in the State or Union territory, as the case may be, a monthly statement, containing therein the quantity of such drugs available with them, by the end of every month.

2. This notification shall come into force on the date of its publication in the Official Gazette.

[F.No. X.11014/10/2016-DRS]
K. L. SHARMA, Jt. Secy.

Note: The principal notification was published in the Official Gazette, Extraordinary, Part II, Section 3, Sub-section (I) vide notification number G.S.R. 677(E) dated the 15th September, 2009.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 17th February, 2017

G.S.R. 145(E).—Whereas the Central Government had in exercise of the powers conferred by section 26A of the Drugs and Cosmetics Act, 1940 (23 of 1940), suspended the manufacture for sale, sale and distribution of letrozole for induction of ovulation in anovulatory infertility vide the notification of the Government of India in the Ministry of Health and Family Welfare, Department of Health and Family Welfare, published in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), vide number G.S.R. 752(E), dated the 12th October, 2011, after taking note of the fact that the use of the drug letrozole for induction of ovulation in anovulatory infertility was likely to involve risk to human beings;

And whereas, the Indian Council for Medical Research in the Central Government conducted a systematic review and meta analysis including studies in India in respect of the drug letrozole for induction of ovulation in anovulatory infertility and whereas, the expert committee of the Indian Council for Medical Research recommended that suspension of manufacture and sale of the said drug may be revoked;

And whereas, the Drugs Technical Advisory Board has now examined the issue of suspension of manufacture and sale of the said drug on 3rd January, 2017 in its Seventy-fifth meeting and recommended that the suspension of manufacture, sale and distribution of the said drug may be revoked and the drug be allowed for induction of ovulation in anovulatory infertility;

Now, therefore, the Central Government in exercise of the powers conferred by section 26A of the said Act, hereby rescinds the notification of the Government of India in the Ministry of Health and Family Welfare, Department of Health and Family Welfare, published in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (I) vide G.S.R. 752(E), dated the 12th October, 2011 with immediate effect, except as respects things done or omitted to be done before such rescission.

[F. No. X.11014/4/2017-DR]

K. L. SHARMA, Jt. Secy.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 15th March, 2017

G.S.R. 250(E).—Whereas a draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required by section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare) number G.S.R. 44(E), dated the 17th January, 2017, published in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), dated the 17th January, 2017, inviting objections and suggestions from persons likely to be affected thereby before the expiry of a period of thirty days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas copies of the Gazette were made available to the public on 17th January, 2017; And whereas objections and suggestions received from the public on the said rules have been considered by the Central Government;

Now, therefore, in exercise of the powers conferred under section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:—

1. (1) These rules may be called the Drugs and Cosmetics (5th Amendment) Rules, 2017.
(2) They shall come into force on the date of their publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945, in rule 3A, in sub-rule (8), in clause (b), after item (5) and the entries relating thereto, the following shall be inserted, namely:-

"(6) Enzyme and Hormones such as-

(a) Streptokinase (Natural and Recombinant);
(b) Human Chorionic Gonadotropin (hCG);
(c) Human Menopausal Gonadotropin (hMG).

(7) Bacterial vaccine such as-

(a) Bacillus Calmette-Guerin (BCG) vaccine.

(8) Viral vaccines such as-

(a) Live attenuated Measles vaccine;
(b) Live attenuated Rubella vaccine;
(c) Cell culture Rabies vaccine"

[F. No. A.11018/2/2016-DFQC]
K. L. SHARMA, Jt. Secy.

Note : The principal rules were published in the Official Gazette vide notification number F.28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 103 (E) dated the 02nd February, 2017.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 30th March, 2017

G.S.R.302(E).—The following draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 which the Central Government proposes to make in exercise of the powers conferred by section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), after consultation with the Drugs Technical Advisory Board, is hereby published for information of all persons likely to be affected thereby and notice is hereby given that said draft rules will be taken into consideration on or after the expiry of a period of forty-five days from the date on which copies of the Gazette of India containing these draft rules are made available to the public.

Objections and suggestions which may be received from any person within the period specified above will be considered by the Central Government.

Objections and suggestions, if any, may be addressed to the Under Secretary (Drugs), Ministry of Health and Family Welfare, Government of India, Room No. 414 A, D Wing, Nirman Bhawan, New Delhi – 110011 or sent on email drugsdiv-mohfw@nic.in.

**Draft rules**

1. These rules may be called the Drugs and Cosmetics (_____Amendment) Rules, 2017.

2. In the Drugs and Cosmetics Rules, 1945 (hereinafter referred to as the said rules), in rule 96, in sub-rule (1), in clause (i), in sub-clause (A), for the portion beginning with the words “For this purpose” and ending with the words “name and shall be”, the words “For this purpose, the proper name of the drug or fixed dose combination drug other than fixed dose combinations of vitamin and other fixed dose combinations containing three or more drugs, shall be printed or written in a conspicuous manner which shall be in the same font but at least two font size larger than the brand name or the trade name, if any, and in other cases the brand name or the trade name, if any, shall be written in brackets below or after the proper name and shall be” shall be substituted.

[F. No. X.11014/5/2017-DRS]
K. L. SHARMA, Jt. Secy.

Note : The principal rules were published in the Gazette of India vide notification No. F.28-10/45-H (1) dated 21st December 1945 and last amended vide notification number G.S.R. (E) dated.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 30th March, 2017

G.S.R. 303(E).— Whereas the draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required by sections 12 and 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), dated the 17th January, 2017 vide notification of the Government of India in the Ministry of Health and Family Welfare, number G.S.R. 42(E), dated the 17th January, 2017 for inviting objections and suggestions from all persons likely to be affected thereby before the expiry of a period of forty-five days from the date on which copies of the Official Gazette containing the said notification was made available to the public;

And Whereas the copies of the said Gazette were made available to the public on 17th January, 2017;

And, Whereas, objections and suggestions received from the public on the said rules have been considered by the Central Government.

Now, therefore, in exercise of the powers conferred by sections 12 and 33 of the said Act, the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945,namely:-

1. (1) These rules may be called Drugs and Cosmetics (Sixth Amendment) Rules, 2017.
(2) They shall come into force on the date of their publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945, in Schedule H, after serial number 536 and entries relating thereto, the following serial number and entry shall be added, namely:-
"537. Etizolam".

[F.No. X 11014/ 11/2016-DRS]
K. L. SHARMA, Jt. Secy.

Foot-note.- The principal rules were published in the Gazette of India vide notification Number F.28-10/45-H (1) dated the 21st December, 1945 and lastly amended vide notification number G.S.R. 102(E) dated the 15th March, 2017.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 31st March, 2017

G.S.R. 319(E).—The following draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945, which the Central Government proposes to make, in exercise of the powers conferred by sections 12 and 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), in consultation with the Drugs Technical Advisory Board, is hereby published as required under the provisions of the said sections 12 and 33, for information of all persons likely to be affected thereby; and notice is hereby given that said draft rules will be taken into consideration on or after the expiry of a period of fortyfive days from the date on which the copies of the Official Gazette containing these draft rules are made available to the public;

Objections and suggestions, if any, may be addressed to the Under Secretary (Drugs), Ministry of Health and Family Welfare, Government of India, Room No. 414 A, D Wing, Nirman Bhavan, New Delhi.—110011 or e-mailed at drugsdiv-mohfw@nic.in;

Objections and suggestions which may be received from any person within the aforesaid period will be considered by the Central Government.

And Whereas the copies of the said Gazette were made available to the public on 17th January, 2017;

And, Whereas, objections and suggestions received from the public on the said rules have been considered by the Central Government.

**DRAFT RULES**

1. These rules may be called Drugs and Cosmetics (_____Amendment) Rules, 2017.

2. In the Drugs and Cosmetics Rules, 1945 (hereinafter referred to as the said rules), in rule 59,—
   (a) in sub-rule (2), the words "or renewal" shall be omitted.
   (b) sub-rule (4) and the proviso thereto shall be omitted.

3. In the said rules, in rule 62B, in sub-rule (2), in the proviso, the words "or renew" shall be omitted.

4. In the said rules, in rule 62C,—
   (a) in sub-rule (1), the words "or renewal", shall be omitted;
   (b) the proviso thereto shall be omitted.

5. In the said rules, for rule 63, the following rule shall be substituted, namely:—
   "63. Duration of licence.—(1) A licence issued in Form 20, 20A, 20B, 20BB, 20F, 20G, 21, 21A, 21B and 21BB shall remain valid, if licencee deposits a licence retention fee referred to in sub-rule (2) before the expiry of a period of every succeeding five years from the date of its issue, unless, it is suspended or cancelled by the licensing authority.

   (2) The licence retention fee referred to in sub-rule (1) shall be equivalent to the respective fee required for the grant of such licence.

   (3) If the licencee fails to pay licence retention fee on or before the due date as referred to in sub-rule (1), he shall be liable to pay licence retention fee along with a late fee calculated at the rate of two per cent. of the licence fee for every month or part thereof up to six months, and in the event of non-payment of such fee, the licence shall be deemed to have been cancelled.".

6. In the said rules, rules 63A and 63B shall be omitted.

7. In the said rules, in rule 64,—
(a) the words "or renewed" wherever they occur shall be omitted;
(b) in sub-rule (2),—
(i) the words "or renewing" shall be omitted;
(ii) in first proviso, the words "or renew" shall be omitted.

8. In the said rules, in rule 65, the words "or renewal" at both the places where they occur shall be omitted.

9. In the said rules, after rule 65A, the following new rule shall be inserted, namely:—
"65B. Inspection for verification of compliance.—The licensing authority shall cause inspection, by the Inspector appointed under the Act, of each premises licensed under this Part, to verify the compliance with the conditions of licence and the provisions of the Act and these rules at least once in a year.".

10. In the said rules, in rule 68A,—
(a) in the marginal heading, the words "or Renewal" shall be omitted;
(b) the words "or renewed" at both the places where they occur shall be omitted;
(c) the words "or renewal" where they occur shall be omitted;
(d) in sub-rule (2), clause (iii) shall be omitted;
(e) the words "or renew" at both places where they occur shall be omitted.

11. In the said rules, in rule 69,—
(a) in sub-rule (1), the words "or renewal" shall be omitted;
(b) in sub-rule (2), the words "or for the purpose of renewal of the licence" wherever they occur shall be omitted;
(c) sub-rule (3) shall be omitted.

12. In the said rules, in rule 69A, in sub-rule (1),—
(a) the words "or renewal" shall be omitted;
(b) the proviso thereto shall be omitted.

13. In the said rules, in rule 71,—
(a) in the marginal heading, the words "or renewal" shall be omitted;
(b) the words "or renewed" shall be omitted.

14. In the said rules, in rule 71A,—
(a) in the marginal heading, the words "or renewal" shall be omitted;
(b) the words "or renewed" shall be omitted.

15. In the said rules, in rule 71B,—
(a) in the marginal heading, the words "or renewal" shall be omitted;
(b) the words "or renewed" shall be omitted.

16. In the said rules, for rule 72, the following rule shall be substituted, namely:—
**"72. Duration of licence.—**
(1) A licence issued in Form 25, Form 25B, Form 25F, Form 28, Form 28B and Form 28D shall remain valid if the licencee deposits a licence retention fee referred to in sub-rule (2) before the expiry of a period of every succeeding five years from the date of its issue, unless, it is suspended or cancelled by the licensing authority.

(2) The licence retention fee referred to in sub-rule (1) shall be equivalent to the respective fee required for the grant of such licence.

(3) If the licencee fails to pay licence retention fee on or before the due date as referred to in sub-rule (1), he shall be liable to pay licence retention fee along with a late fee calculated at the rate of two per cent. of the licence fee for every month or part thereof up to six months, and in the event of non-payment of such fee, the licence shall be deemed to have been cancelled.".

17. In the said rules, the rules 73 and 73A shall be omitted.

18. In the said rules, for rule 73AA, the following rule shall be substituted, namely:—

**"73AA. Duration of loan licence.-**

(1) A licence issued in Form 25A, Form 28A and Form 28DA shall remain valid if licencee deposits a licence retention fee referred to in sub-rule (2) before the expiry of a period of every succeeding five years from the date of its issue, unless, it is suspended or cancelled by the licensing authority.

(2) The licence retention fee referred to in sub-rule (1) shall be equivalent to the respective fee required for the grant of such licence.

(3) If the licencee fails to pay licence retention fee on or before the due date as referred to in sub-rule (1), he shall be liable to pay licence retention fee along with a late fee calculated at the rate of two per cent. of the licence fee for every month or part thereof up to six months, and in the event of non-payment of such fee, the licence shall be deemed to have been cancelled.".

19. In the said rules, after rule 73AA, the following new rule shall be inserted, namely:—

**"73AB. Inspection for grant of licence and verification of compliance.-**

(1) Before the grant of licence under Form 25, Form 25A, Form 25B, Form 25F, Form 28, Form 28A, Form 28B, Form 28D and Form 28DA, the premises shall be inspected jointly by Inspectors appointed by the Central Government and the State Government under this Act.

(2) The premises licensed under sub-rule (1) shall be inspected jointly by Inspector appointed by the Central Government and State Government to verify the compliance with the conditions of licence and the provisions of the Act and these rules at least once in a year.".

20. In the said rules, the rules 73B shall be omitted.

21. In the said rules, in rule 75,—

(a) in sub-rule (1),—

(i) the words "or renewal" and "or for the purpose of renewal of licences" shall be omitted;

(ii) the proviso thereto shall be omitted;

(b) in sub-rule (2),—

(i) the words "or renewal" and "or for the purpose of renewal of licences" shall be omitted;

(ii) the second proviso thereto shall be omitted;

(c) in sub-rule (3),—

(i) the words "or renewal" and "or for the purpose of renewal of licences" shall be omitted;

(ii) the proviso thereto shall be omitted.

22. In the said rules, in rule 75A,—

(a) in sub-rule (1),—

(i) the words "or renewal" and "or for the purpose of renewal of licences" shall be omitted;

(ii) the proviso thereto shall be omitted;

(b) in sub-rule (1A),—

(i) the words "or renewal" and "or for the purpose of renewal of licences" shall be omitted;

(ii) the proviso thereto shall be omitted;

23. In the said rules, in rule 76,—
(a) in the marginal heading, the words “or renewal” shall be omitted;
(b) in the opening portion, the words “or renewed” shall be omitted.

24. In the said rules, in rule 76A, in the marginal heading, the words “or renewal” shall be omitted.

25. In the said rules, rule 77 shall be omitted.

26. In the said rules, in rule 79,—
(a) in the marginal heading, the words “or renewal” shall be omitted;
(b) the words “or renewed” shall be omitted.

27. In the said rules, the rules 83, 83A and 83AA shall be omitted;

28. In the said rules, in rule 84A,—
(a) in the marginal heading, the words “or renewed” shall be omitted;
(b) the words “or renew” shall be omitted.

29. In the said rules, after rule 84B, the following new rule shall be inserted, namely:—
**“84C. Inspection for verification of compliance.**—The Central Licence Approving Authority or the licensing authority, as the case may be, shall cause inspection of each establishment licensed under this Part jointly by the Inspectors appointed by the Central Government and the State Government under the Act, to verify the compliance with the conditions of licence and the provisions of the Act and these rules at least once in a year.”.

30. In the said rules, in rule 85, in sub-rule (2), the words “or renewed” shall be omitted.

31. In the said rules, in rule 138,—
(a) in sub-rule (1), the words “or renewal” and “or for the purpose of renewal of licence” shall be omitted;
(b) sub-rule (2) shall be omitted.

32. In the said rules, in rule 138A,—
(a) in sub-rule (1), the words “or renewal” shall be omitted;
(b) sub-rule (2) shall be omitted.

33. In the said rules, in rule 139,—
(a) in the marginal heading, the words “or renewal” shall be omitted;
(b) in the opening portion, the words “or renewed” shall be omitted.

34. In the said rules, in rule 139AA,—
(a) in the marginal heading, the words “or renewal” shall be omitted;
(b) the words “or renewed” shall be omitted.

35. In the said rules, in rule 139AC,—
(a) in sub-rule (1), the words “or renew” shall be omitted;
(b) the sub-rule (2), the words “or renewed” shall be omitted.

36. In the said rules, in rule 139AE, the words “or renew” shall be omitted.

37. In the said rules, for rule 140, the following rule shall be substituted, namely:—
**“140. Duration of licence**.—(1) A licence issued under Form 32, Form 32A and Form 33 shall remain valid if the licencee deposits a licence retention fee referred to in sub-rule (2) before the expiry of period of every succeeding five years from the date of its issue, unless, it is suspended or cancelled by the licensing authority.

(2) The licence retention fee referred to in sub-rule (1) shall be equivalent to the respective fee required for the grant of such licence.

(3) If the licence holder fails to pay licence retention fee on or before the due date as referred to in sub-rule (1), he shall be liable to pay licence retention fee along with a late fee calculated at the rate of two per cent. of the licence fee for every month or part thereof up to six months, and in the event of non-payment of such fee, the licence shall be deemed to have been cancelled.".

38. In the said rules, rules 141, 141A and 141AA shall be omitted.

39. In the said rules, after rule 143, the following new rule shall be inserted, namely:—

**"143A. Inspection for grant of licence and verification of compliance:—**

(1) Before the grant of licence under Form 32, Form 32A and Form 33, the premises shall be inspected jointly by Inspectors appointed by the Central Government and the State Government under the Act.

(2) The premises licensed under sub-rule (1) shall be inspected jointly by Inspectors appointed by the Central Government and the State Government to verify the compliance with the conditions of licence and the provisions of the Act and these rules at least once in a year.".

40. In the said rules, in Schedule A,—

(a) in Form 20, Form 20A, Form 20B, Form 20BB, Form 21, Form 21A, Form 21B, Form 21BB, Form 25B and Form 32, for paragraph 2, the following paragraph shall respectively be substituted, namely:—

"2. The licence unless sooner suspended or cancelled, shall remain valid perpetually. However, the compliance with the conditions of licence and the provisions of the Drugs and Cosmetics Act, 1940 (23 of 1940) and the Drugs and Cosmetics Rules, 1945 shall be assessed at least once in a year.";

(b) in Form 20F, Form 20G, Form 25, Form 28DA and Form 32A, for paragraph 3, the following paragraph shall respectively be substituted, namely:—

"3. The licence unless sooner suspended or cancelled shall remain valid perpetually. However, the compliance with the conditions of licence and the provisions of the Drugs and Cosmetics Act, 1940 (23 of 1940) and the Drugs and Cosmetics Rules, 1945 shall be assessed at least once in a year.";

(c) in Form 25A, Form 28 and Form 28B, for paragraph 4, the following paragraph shall respectively be substituted, namely:—

"4. The licence, unless sooner suspended or cancelled, shall remain valid perpetually. However, the compliance with the conditions of licence and the provisions of the Drugs and Cosmetics Act, 1940 (23 of 1940) and the Drugs and Cosmetics Rules, 1945 shall be assessed at least once in a year.";

(d) in Form 25F and Form 28D, for paragraph 5, the following paragraph shall respectively be substituted, namely:—

"5. The licence, unless sooner suspended or cancelled, shall remain valid perpetually. However, the compliance with the conditions of licence and the provisions of the Drugs and Cosmetics Act, 1940 (23 of 1940) and the Drugs and Cosmetics Rules, 1945 shall be assessed at least once in a year.";

(e) in Form 28A, for paragraph 3A, the following paragraph shall be substituted, namely:—

"3A. The licence, unless sooner suspended or cancelled, shall remain valid perpetually. However, the compliance with the conditions of licence and the provisions of the Drugs and Cosmetics Act, 1940 (23 of 1940) and the Drugs and Cosmetics Rules, 1945 shall be assessed at least once in a year.";

(f) in Form 37, for paragraph 3, the following paragraph shall be substituted, namely:—

"3. The approval, unless sooner suspended or cancelled, shall remain valid perpetually. However, the compliance with the conditions of approval and the provisions of the Drugs and Cosmetics Act, 1940 (23 of 1940) and the Drugs and Cosmetics Rules, 1945 shall be assessed at least once in a year.";

(g) in Form 19, Form 19A, Form 19AA and Form 19C, in the heading, the words "OR RENEWAL" shall respectively be omitted;

(h) Form 21C, Form 21CC, Form 26, Form 26A, Form 26B, Form 26F, Form 26H, Form 33 and Form 33A shall be omitted;

(i) in Form 24, Form 24A, Form 24B, Form 24C, Form 24F, Form 27, Form 27A, Form 27B, Form 27D, Form 27DA, Form 31 and Form 31A,—

(a) In the heading, the words "OR RENEWAL" shall respectively be omitted;

(b) in paragraph 1, for the words "grant/renewal", the words "grant" shall respectively be substituted;

(j) in Form 25, Form 25A, Form 25B, Form 25F, Form 28, Form 28A, Form 28B, Form 28D, Form 28DA, Form 32 and Form 32A, in condition 1, the words, "and any certificate of renewal in force" shall be omitted.

[F. No. X. 11014/6/2017-DRC]
K. L. SHARMA, Jt. Secy.

Foot note: The principal rules were published in the Official Gazette vide notification No. F.28-10/45-H (1) dated 21st December, 1945 and last amended vide notification number G.S.R. (E) dated

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 3rd April, 2017

G.S.R. 327(E).—Whereas the draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required by sections 12 and 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), dated the 2nd February, 2017 vide notification of the Government of India in the Ministry of Health and Family Welfare, number G.S.R. 102(E), dated the 2nd February, 2017 for inviting objections and suggestions from all persons likely to be affected thereby before the expiry of a period of forty-five days from the date on which copies of the Official Gazette containing the said notification was made available to the public;

And whereas the copies of the said Gazette were made available to the public on 2nd February, 2017;

And, whereas, objections and suggestions received from the public on the said rules have been considered by the Central Government.

Now, therefore, in exercise of the powers conferred by sections 12 and 33 of the said Act, the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:-

1. (1) These rules may be called Drugs and Cosmetics (Ninth Amendment) Rules, 2017.
(2) They shall come into force on the date of their publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945 (hereinafter referred to as the said rules), in rule 2, after clause (a), following shall be inserted, namely,-

(aa) "biopharmaceutical classification system" means a system used to classify drugs on the basis of solubilityand permeability, classified as category I- high solubility and high permeability, category II- low solubility and high permeability, category III- high solubility and low permeability, and category IV- low solubility and low permeability.";

3. In the said rules, in rule 74, after clause (p), the following clause shall inserted, namely.-

"(q) the applicant shall submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.".

4. In the said rules, in rule 74B, after clause (7), the following clause shall inserted, namely.-

"(8) the applicant shall submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.".

5. In the said rules, in rule 76, after clause (9), the following clause shall inserted, namely.-

"(10) the applicant shall submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.".

6. In the said rules, in rule 78, after clause (q), the following clause shall inserted, namely.-

"(r) the applicant shall submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.".

7. In the said rules, in rule 78A, after clause (8), the following clause shall inserted, namely.-

"(9) the applicant shall submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.".

[F. No. X.11014/12/2016-DRS]
K. L. SHARMA, Jt. Secy.

Foot note: Principal rules were published in the Official Gazette vide notification number F.28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 303 (E) dated the 30th March, 2017.

## A short note of Gazette Notification No. GSR 78 (E) dated 31.01.2017 New Medical Devices Regulatory requirements

Ministry of Health and Family welfare wide Gazette Notification No. GSR 78 (E) dated 31st January 2017 notified Medical Devices Rule 2017. This Rule is effective from 1st January 2018. Both manufacturing and loan license are allowed in the new Rule. Medical Devises have been classified as Class A – low risk, Class B – Low moderate risk, Class C – Moderate high risk and Class D – high risk. Manufacture of Class A and Class B devices are entrusted to state drugs controller of the respective state, where as class C & Class D rest with Drugs Controller General of India(DCGI). All classes of Medical Devices are controlled through an import registration method by DCGI. A notified body is being registered by DCGI for the purpose of inspection of manufacturing units of the Medical Devices.

The import registration fees as well as manufacturing licensing fees have been enhanced and the validity of the license increased to 5 years. The renewal of manufacturing as well as import licenses are discontinued in this new Rule. However in case of retention of license by the license it can be done by paying the retention fees before expiry of the license. The environmental classification like Class 1,00,000, Class 10,000 and class 1,000 are prescribed for manufacture of Medical Devices through proper Air Handling System (AHU). All the diagnostics kits / Reagents are also covered under this new Rule.

Readers may go through the link http://cdsco.nic.in/forms/list.aspx?lid=2057&Id=31 (January 312017GSR 78(E)) for getting the details of the new Rule.

**CDSCO/IT/2017- (7)**
**Directorate General of Health Services**
**Central Drugs Standard Control Organization**
**O/o Drugs Controller General (India)**

FDA Bhawan, Kotla Road
New Delhi:110002
Dated: 03.04.2017

**NOTICE**

**Sub: Creation of databases of drug manufacturing facilities and approved drug formulations on SUGAM portal-regarding**

CDSCO as part of its comprehensive e-Governance program has launched the online portal "SUGAM" for filing, tracking and processing of applications for the various services rendered by CDSCO. The portal is being developed in phases.

In the latest phase, modules for the creation of databases of drug manufacturing facilities, approved drug formulations and retail and wholesale licenses in the country have been developed under the portal SUGAM. In regard to the database of the drug manufacturing facilities and approved drug formulations the data is to be uploaded by the respective manufacturer and subsequently authenticated by the Concerned State Drugs Controller.

All pharma drug manufacturers, not yet registered in SUGAM, are hereby requested to register their firm under SUGAM portal at https://cdscoonline.gov.in. The registration page can be accessed from the "Register Data with State FDA" section of the homepage of SUGAM. This section is available as you scroll down the home page. Once the web form is filled up and submitted online, the details will be verified by the respective State Drugs Controller and your account will be activated by him. After the account is activated you have to submit the data as per the procedure provided. A user manual with detailed steps is provided for ease of operation. Please note that the firm has to be registered only once on SUGAM even if a firm is holding manufacturing facilities in more than one State. No separate registration is required on SUGAM for each additional site. However, the data regarding the facilities located in various States can be submitted from single account.

The existing users of SUGAM can fill their manufacturing facility details from their user profile.

For any queries in this regard please contact your State Drugs Controller or you may write to us at *it-helpdesk@cdsco.nic.in* or to Sh. R Chandrasekhar, DDC(I), e-Governance Cell at *ranga.cs@cdsco.nic.in*

Yours faithfully,

**(Dr G. N Singh)**
**Drugs Controller General (India)**

To,

All Drug Manufacturers/Associations
Copy to:

1. All State Drugs Controllers
2. PPS to JS(R)

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 3rd April, 2017

G.S.R. 328(E).— Whereas the draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required by sections 12 and 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), dated the 2nd February, 2017 vide notification of the Government of India in the Ministry of Health and Family Welfare, number G.S.R. 101(E), dated the 2nd February, 2017 for inviting objections and suggestions from all persons likely to be affected thereby before the expiry of a period of forty-five days from the date on which copies of the Official Gazette containing the said notification was made available to the public;

And Whereas the copies of the said Gazette were made available to the public on 2nd February, 2017;

And, Whereas, objections and suggestions received from the public on the said rules have been considered by the Central Government.

Now, therefore, in exercise of the powers conferred by sections 12 and 33 of the said Act, the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945,namely:-

1. (1) These rules may be called Drugs and Cosmetics (Sixth Amendment) Rules, 2017.
(2) They shall come into force on the date of their publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945, (hereinafter referred to as the said rules) in rule 122 P, after item (xiii), the following items shall be inserted, namely:-
"(xiv) The whole human blood and blood components may be transferred, under prescribed storage conditions, to another blood bank which have facilities to store and monitor blood distribution.
(xv) The recipient blood banks shall not further transfer units obtained from another blood bank except to another blood storage centre or a patient.

3. In the said rules, in Schedule F, in Part XII B under the heading "II. BLOOD DONATION CAMPS", after item (c), the following items shall be inserted, namely:-
"(d) a licensed blood bank run by registered voluntary or charitable organization recognised by State or Union territory Blood Transfusion Council; or
(e) a private hospital blood bank."

4. In Schedule K to the said rules, in item 5(B), under the column relating to extent and conditions of exemption, condition (2) shall be omitted.

[F. No. X.11035/290/2015-DFQC]
K. L. SHARMA, Jt. Secy.

Note.- The principal rules were published in the Gazette of India vide notificationNo. F. 28-10/45-H (1) dated 21st December 1945 and last amended vide notification number G.S.R. 303 (E) dated 30th March, 2017.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 3rd April, 2017

G.S.R. 329(E).—Whereas the draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required by sections 12 and 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), dated the 16th January, 2017 vide notification of the Government of India in the Ministry of Health and Family Welfare, number G.S.R. 36(E), dated the 16th January, 2017 for inviting objections and suggestions from all persons likely to be affected thereby before the expiry of a period of forty-five days from the date on which copies of the Official Gazette containing the said notification was made available to the public;

And whereas the copies of the said Gazette were made available to the public on 16th January, 2017;

And, whereas, objections and suggestions received from the public on the said rules have been considered by the Central Government.

Now, therefore, in exercise of the powers conferred by sections 12 and 33 of the said Act, the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:-

1. (1) These rules may be called Drugs and Cosmetics (Seventh Amendment) Rules, 2017.
(2) They shall come into force on the date of their publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945, in Schedule A, in Form 44, under paragraph 1, relating to "Particulars of new drug" item (8) and the entries relating thereto shall be omitted.

[F. No. X. 11014/9/2016-DRS]
K.L. SHARMA, Jt. Secy.

Foot note.- The principal rules were published in the Official Gazette vide notification number F.28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 303(E), dated the 30th March, 2017.

## Now, Diabetes Drug to Help Treat TB

A drug widely used to treat type-2 diabetes, metformin, will now be prescribed with a cocktail of antibiotics for patients with tuberculosis as part of the clinical study in select cities by the end of the year, IndianCouncil of Medical Research (ICMR) Director Soumya Swaminathan has said.

Research suggests that metformin, which controls glucose levels, works as a protective agent against TB regardless of whether someone has diabetes or not. “The drug reduces inflammation, enhances immune response and the efficacy of conventional TB drugs. Some research has even shown that it improves control of TB infection and decreases disease severity. We want to see if this will work as adjunctive therapy for improving the effective treatment of TB in our population”, she said.

Doctors say the relationship between TB and diabetes isn't new. As of now, patients testing positive for diabetes at government facilities are referred to undergo examination for TB. TB patients are also asked to check their blood glucose levels. In 2016, a guideline was framed by the central TB division after studies showed people with diabetes had 2-3 times higher risk of contracting TB. TB patients are also asked to check their blood glucose levels.

A study by Dr Vijay Viswanathan, chief diabetologist at Chennai-based M V Hospital for Diabetes and University of Massachusetts Medical School found that 54.1% of the 209 patients surveyed with pulmonary tuberculosis were diabetic, while 21% were pre-diabetic. “According to data, every fourth person has latent TB, which surfaces when the immune system is weak”, said Dr Viswanathan. “Diabetes increases the risk of progression to active TB disease in people infected with Mycobacterium tuberculosis, the bacteria that causes TB. Conversely, TB has an effect on diabetes. It can not only worsen blood sugar control but also complicate clinical management of diabetes. The TB-diabetes combination is as bad as TB and HIV”, he said.

Now, scientists say, adding metformin, even if the patient's sugar levels are normal, may not just prevent or delay diabetes, but also improve outcomes of TB treatment. So, a select group of people will receive the drug during the five-day antibiotics treatment.

Last year, the World Health Organization increased its estimate of the number of new TB patients in India to 2.8 million in 2015 compared to 2.2 million in 2014. India, now, is home to more than a quarter of the global TB population.

A bacterial disease commonly affecting the lungs, TB can be cured using a cocktail of antibiotics for six months. These drugs are available for free in India which, however, hasn't been able to drastically bring down infection rates due to lack of awareness and access to treatment.

The Indian Revised National Tuberculosis Control Programme uses thrice-weekly treatment with standard drug doses.

Recently, scientists trying to find out reasons for poor outcomes studied 1,912 adult TB patients receiving anti-TB treatment in Chennai and found the concentration of Rifampicin, Isoniazid and Pyrazinamide in the blood inadequate in a majority of the population. Rifampicin was inadequate in more than 90% of the population. "We have now increased the treatment to five days a week. We are hoping it will make treatment effective and reduce risks of drug resistance. It has rolled out in five states. By the end of the year, it will be the standard for people across the country, Dr Swaminathan said.

**Source:** *The Times of India, 13th February 2017*

## Potent Malaria Vaccine on the Anvil

A malaria vaccine that mimics a mosquito bite yielded encouraging results in human trials, its makers said on Thursday, raising hopes for thwarting a parasite that kills a child every two minutes.

The candidate drug, called PfSPZ, provided up to 100% protection for 10 weeks in a trial in Germany, although a trial in real life conditions in Mali gave a lower level of defence, they reported in two separate studies. "We are extremely encouraged by these findings," said Stephen Hoffman of vaccine developer Sanaria, a company based in Maryland.

But he stressed a lot of work lay ahead, and a registered vaccine may take another two years to reach the market.

**Sporozoite parasite**

PfSPZ uses a live, immature form of the malaria parasite, called a sporozoite, to stimulate an immune reaction in humans.

In one trial, a version of PfSPZ required fewer shots and a lower dose of live malaria parasites than tested to date, researchers reported in the science journal Nature .

For another form of the vaccine, sporozoites are exposed to radiation to weaken them before being injected into the human bloodstream. A previous trial with the irradiated version saw 44 trial volunteers given five shots, each with up to 1,35,000 sporozoites, or three doses with up to 1.8 million sporozoites in total. The highest dose conferred up to 100% immunity, a 2013 report said.

For the German trial, volunteers were given only three injections over eight weeks or 10 days, with sporozoite doses ranging from 3,200 to 51,200 per shot.

All nine volunteers in the high-dose group enjoyed malaria protection 10 weeks after the last dose, compared to six out of nine in the medium and three out of nine in the low-dose groups, said Dr. Hoffman.

"The ability to complete an immunisation regime in 10 days will facilitate the use of PfSPZ-CVac in mass vaccination programmes to eliminate the malaria parasite and to prevent malaria in travellers," he added.

The reason that fewer sporozoites were required was that they were not irradiated before injection. Instead, the vaccine was administered in conjunction with an anti-malarial drug, chloroquine, to stop the parasite causing disease once inside the human body.

PfSPZ is being developed against the Plasmodium falciparum mosquito-borne parasite, by far the deadliest type. Further trials are to follow in Mali, Ghana, the U.S. and Gabon.

A second report, published in The Lancet Infectious Diseases , said 44 people given five doses of PfSPZ in Mali had a lower rate than non-innoculated peers after six months. Of the control group given a placebo or dummy injection, 93% contracted malaria, said the team. In the vaccinated group, “only” 66% were infected. That's the highest level of protection ever seen with a malaria vaccine... in a real setting,” Dr. Hoffman said.

According to the World Health Organization (WHO), there were 212 million malaria cases in the world in 2015 and 4,29,000 deaths. More than 90% of deaths occur in Africa.

**Aiming for efficiency**

Another vaccine called RTS,S, developed by GlaxoSmithKline, is being tested in children — the most affected population.It is considered the most advanced candidate, but results last year from a Kenyan trial showed it was only about four per cent effective after seven years.

The developers of PfSPZ are aiming for efficiency of about 80-90% protection lasting for six months to a year, Dr. Hoffman said. “We hope we'll be there this year, maybe next year. We're closing in on it,” he said.

Source: *The Hindu, 17th February 2017*

## Hosps Can't Charge Margin on Stents'

**'Clean –Up of Medical System Has Begun'**

Four days after capping the price of cardiac stents, much to the chagrin of manufacturers and distributors, the Centre on Saturday (Feb 18) turned its attention to the role of hospitals in inflating angioplasty bills. Leaving no room for confusion, it said hospitals can't charge any margin from manufacturers and retailers for stents.

National Pharmaceutical Pricing Authority (NPPA) sources told that no margin was envisaged for hospitals in pricing of stents as hospitals are not retailers of the particular product. “They need to earn income from (cardiac) procedures and compete with other hospitals on cost and quality of procedure, not medical devices used in the procedure, “said sources.

Many hospital chains started reworking their 'angioplasty packages' after prices of drug-eluting stents were capped at Rs 29,600 plus taxes. A circular sent by one of the biggest hospital chains to its doctors states the cost of a simple angioplasty was reworked to Rs 1.75 lakh. The hospital previously charged Rs 1.35 lakh for this package.

Another mega hospital chain sent a circular stating its central purchase unit has only cleared three second-generation stents for use of its paying patients. Another chain of hospitals has cleared only four mid-range stents for its "cash/walk-in/TPA" patients and three India-make stents for government panel patients.

In fact, the 'disappearance' of cardiac stents from hospitals and companies' reluctance to relabel them with revised MRPs had much to do with margins, as there was no clarity on

mark-ups for hospitals and distributors. Margins are at the centre of the controversy over stents, marked up almost 900% from their landing cost; as bulk of this inflated fee would allegedly be pocketed by hospitals.

On Saturday, the government made it clear hospitals are "zero margin" entities. "Since the hospital is not the retailer of stents and has not taken a licence for retailing the medical device, they can't demand any margin," sources said.

NPPA chairman Bhupendra Sing told TOI. “The NPPA has not considered hospitals as retailers while arriving at the price caps for stents”. The Association of Indian Medical Device Industry's coordinator Rajiv Nath,who was present at the NPPA meeting on Saturday afternoon said,” This is the beginning of the clean-up of the healthcare system. After sometime you may find many stents being sold for even less than the capped MRP.”

**Source:** *The Times of India, 19th February 2017*

## Private Hospitals Reuse Disposables, Make you Pay for them

Disposables like catheters, guide wires and balloons used in every angioplasty are reused and billed repeatedly in many private hospitals.

Adding to the risk of infection, you could be paying for something that has already been paid for. And the hospital may be making a profit of Rs 20,000 to Rs 30,000 on every procedure with simple reuse and rebilling, say industry sources.

The practice is so rampant that the health ministry has issued an office memorandum warning against reuse of disposable surgical items, particularly in cardiology, when they are meant for one-time use.

"The items after one procedure are sterilised and reused and (patients) are charged full amount of these items," stated the memo dated December 21, 2016. The matter had been "viewed by this ministry seriously", it said, and clarified that "reuse of disposable items, particularly in cardiology and other specialties, is not permitted in healthcare organisations empanelled under CGHS (Central Government Health Scheme)".

It goes on to warn of "suitable action including withdrawal of CGHS empanelment" against defaulters. It is silent on action against big corporate hospitals that are not empanelled under CGHS.

"Most private hospitals, especially hospitals chains, insist that cardiologists reuse these items. While reusing these items a couple of times might be justified in some cases where you want to help bring down costs for a patient, in most of these hospitals, not only do they reuse four or five times, patients are also billed afresh for each of these items, helping the hospitals make a profit of Rs 20,000 to Rs 30,000 on each procedure or patient," explained a cardiologist who has worked in several leading private hospitals.

All disposable items have clear instructions on the packaging saying they should be used only once and cannot be resterilised. Some cardiologists in private hospitals admitted that reuse was common but said it was not a problem if the items were properly resterilised. Companies, they said,

insisted on single use to sell more of their products.

Cath lab technicians and dealers who sell disposables and stents to hospitals also confirmed that such reuse was common. Hospitals like AIIMS and PGI hardly ever reuse these items as there is no pressure to cut corners to make profit.

"In the US, solid catheters or catheters without holes can be resterilised and reused but only once or twice. But reuse of catheter with holes like a guide catheter used in angioplasty is not allowed as it is difficult to clean the insides where blood residue might remain. This is to prevent any chance of HIV and Hepatitis B infection. Also, resterilising affects the quality of the item as it hardens the plastic, making it less flexible," explained a senior AIIMS cardiologist.

Chain hospitals are the worst offenders, according to a cardiologist who has worked in one such institution. "If doctors in one hospital in the chain reuse an item five or six times, that is lauded as a great example of cost saving. It is pushed as standard operating procedure across the entire chain, putting enormous pressure on doctors who try to resist such unethical overuse of a disposable item," explained the cardiologist.

"Reuse is bad and doing so without the patient's consent is criminal," said another cardiologist. "And charging for reused items is fraud of the highest order being done in most elite hospitals to push up profits. It is easy to investigate and expose this. The government can get the number of angioplasties done in a hospital and ask for proof of purchase of the disposables for the last two years. There is a formula for how many disposables are needed for each angioplasty. They will find that far fewer disposables have been purchased than the required number, which will show clear reuse. Such hospitals should be prosecuted," he said.

**Source:** *The Times of India, 19th February 2017*

## Pill Cuts Cancer Risk For 30 Years

Women who have taken contraceptive pills get protection from some types of cancer for as long as 30 years, a new study claims. The results of the “world's longest study” into the effects of the pill showed that women who had ever used it were less likely to have colorectal, endometrial or ovarian cancer than those who never had. The results of the study conducted by the University of Aberdeen in the UK, showed that using the pill during reproductive years did not produce new cancer risks later in life, when more cancer occur. The findings relate to 46,000 women, followed for up to 44 years. “Because the study has been going (on) for such a long time we are able to look at the very long-term effects, if there are any, associated with the pill, “ said Dr Lisa Iversen of the University of Aberdeen, “The protective benefits from using the pill during their reproductive years are lasting for at least 30 years after women have stopped using the pill

**Source:** *The Times of India, 23rd March 2017*

## 14 More Medical Devices May See Price Regulation

After cardiac stents, around 14 more medical devices that are rampantly sold at inflated rates in hospitals, could see a price regulation in the coming months. The list includes orthopedic implants, intraocular lenses and artificial heart valves to consumables such as syringes, needles and catheters.

The National Pharmaceutical Pricing Authority (NPPA) has begun scrutiny of such devices, even asking makers to log in every detail about their manufacture and cost. NPPA chairman Bhupendra Singh told TOI, "We are collecting data on these devices on a war-footing. It will give us a fair idea about the volume of consumption, cost of manufacturing and price at which they are supplied to a patient. Exorbitant pricing in the health system will be dealt with strongly."

In terms of steep retail markups, orthopedic implants probably come closest to cardiac stents. A selected imported hip and knee implants easily see profit margins in the range of 500-1,000 percent, industry insiders said. Indian implants too are sold at margins of 200-500 percent, though surgeons often prefer imported types. The cost of intraocular lenses also varies widely depending on the hospital and the operating surgeon. Consumables, on the other hand, are not just sold at arbitrary MRPs, but also billed in bulk to add to the patient's bill.

Currently, only 14 devices are classified as 'drugs' under Section 3 of the Drugs and Cosmetics Act, but none feature in the list of essential medicines. Cardiac stents therefore had to be included in the National List of Essential Medicines (NELM) before their prices could be capped. If a drug is not in the NELM, the NPPA can merely ensure that their MRP is not increased by more than 10 percent annually.

"It is therefore important for us to see the extent of profiteering in other devices and seek the union health ministry's help to add them to the list of essential medicines before their prices can be capped. In our online platform IPDMS (Integrated Pharmaceutical Database Management System), a tab has been created for information on medical devices and not just stents," said Singh.

Singh said the NPPA is undeterred by the medical industry's hue and cry that innovation and research will be throttled by price regulation. "We did an elaborate study before cracking the whip on stents. When an original manufacturer sells a product, the cost of innovation, packaging and everything else is built into it. The importer spends nothing on R&D or packaging. The money is only spent on marketing, paying commissions and distorting the system. With price-capping, affordability will increase," Singh said.

**Source:** *The Times of India, 21st February 2017*

## Healthcare, Patient Groups Oppose Hep-C Drug Patents

Healthcare aid and patient groups have come together in patent courts to flight against" abusive strategies" of Big Pharma to ensure access to affordable treatment in hepatitis C. The initiative for Medicines, Access & Knowledge (I-MAK) – together with the Delhi Network of Positive People (DNP+) and international medical humanitarian organization Medecins Sans Frantiers (MSF) – on Tuesday filed two patent challenges on daclatasvir, one on velpatasvir and a furher challenge on sofosbuvir. The patent challenges could remove barriers to production and distribution of affordable generic versions of direct-acting antiviral (DAA) medicines, including Gilead's sofobuvir and velpatasvir, and Bristol Myers Squibb's daclatasvir. Sofosbuvir (brand name Sovaldi) is Gileads' blockbuster drug for hepatitis patent challenge. The Indian Patent Office granted a patent on the drug last year with the decision challenged by patient groups.

In the present challenge, the two cases oppose crystalline forms of sofosbuvir and daclatasvir and should be rejected for not being in compliance with Indian law, a statement from MSF said. Indian law, a statement from MSF said Indian law recognizes that crystalline forms of known medicines are not inventions and should not be awarded patients. This was confirmed by Supreme Court on April 1, 2013, which refused a patent on Novartis cancer drug Gleevee by holding that a crystalline form of a known pharmaceutically active compound cannot be regarded as involving an inventive step.

**Source:** *The Times of India, 21st Feb 2017*

## Pollution Reduces Antibiotics Effectiveness

Air pollution may increase the potential of bacteria to cause respiratory infections by reducing the effectiveness of antibiotics, scientists have found in a first.

The study by researchers at the University of Leicester has important implications for the treatment of infectious diseases, which abound in areas with high levels of air pollution. A major component of air pollution is black carbon. The research showed that this pollutant changed the way in which bacteria grew and formed communities, which could affect how they survived on the lining of our respiratory tracts and how well they were able to hide from, and combat, our immune systems.

"Our research could initiate an entirely now understanding of how air pollution affects human health. It will lead to enhancement of research to understand how air pollution leads to severe respiratory problems and perturbs the environmental cycles essential for life, " said professor Julie Morrissey.

The research focused on two humans pathogens, Staphylococcus aureus and Streptococcus pneumoniae.

The team found that black carbon altered the antibiotic tolerance of Staphylococcus aureus communities and increased the resistance of communities of Streptococcus pneumoniame to penicillin, the front line treatment of bacterial pneumonia. It was also found that black carbon caused Streptococcus pneumoniae to spread from the nose to the lower respiratory tract, which is a key step in development of disease.

**Source:** *The Times of India, 4th March 2017*

## More Accountability: Price Control on Stents is a Blunt Instrument, more Nuanced Regulation is needed

Following an order last week by drug price regulator NPPA to cap the price of coronary stents there are reports that some manufacturers have withdrawn premium stents. A single shot reduction in maximum selling price by over 75% in case of some products has led to shortages. The new price regulations were preceded by numerous instances of profiteering and extensive discussions between NPPA and industry. But laudable as NPPA's intention was, unintended consequences of price fixing should not come as a surprise. In the days to come, there will be more evidence of it.

NPPA's research ahead of the price fixing order concluded that there are huge mark ups at every step of the supply chain. The root cause is, according to NPPA, "information asymmetry between doctors and patients". This is precisely why it is difficult to be upbeat about the price order. Some of the biggest mark ups come at hospitals and there is no guarantee the current price control order will discourage hospitals from marking up related costs to offset the price control order of a coronary stent. In addition, there could be negative fallouts such as a shortage of premium stents.

The new system will be more flexible and pThe use of coronary stents has increased on the heels of a jump in cardiac interventions, which exceeded two lakh in 2013. But a stent's final price charged is highly influenced by a few hospitals which perform the bulk of angioplasties in India. Unless hospitals are made more accountable the current price control order may not help much. In this context, we need to keep in mind that accountability in India is so low that according to some estimates up to 30% of angioplasties are unnecessary. While NPPA's motive is unexceptionable, price control on stents may not be an adequate solution.

**Source:** *The Times of India, 21st Feb 2017*

## Ashwagandha, A Good Sleep-Inducer: Study

**Scientists find tests on mice promising**

Having trouble falling asleep? Try Ashwagandha (Withania somnifera), suggest scientists, including one of Indian origin, who have found that an active component in the leaves of the ayurvedic herb significantly induces sleep.

Researchers, including those from University of Tsukuba in Japan, investigated the effect of various components of Ashwaganda on sleep in mice.

They found that the water extract of Ashwaganda leaf rich in triethylene glycol (TEG) promoted non-rapid eye movement (NREM) sleep significantly and changed rapid eye movement (REM) sleep slightly, while the alcoholic extract containing active withanolides showed no effect on sleep. The sleep induced by TEG was similar to normal sleep.

Commercially available TEG also increased the amount of NREM sleep. Researchers concluded that TEG is the active component that induces physiologically sound sleep. The findings of the study could revolutionise the natural plant-based therapies for insomnia and sleep related disorders, said Mahesh K Kaushik of University of Tsukuba.

Ashwagandha is a central herb in Ayurveda, the traditional home medicine native to India.

Its Latin name somnifera, means sleep-inducing, it has been recommended for sound sleep through centuries, researchers said.

**Source:** *The Hindu, 2nd April 2017*

## WHO Names 12 Drug-Resistant Superbugs; Most are Present in India

The World Health Organisation (WHO) has published its first ever list of antibiotic-resistant 'priotity pathogens' -a catalogue of 12 families of bacteria that pose the greatest threat to human health. This is bad news for India as most if these 12 superbugs are present in the country.

The list was drawn up to promote research and development of new antibiotics, the global health agency said, adding that the move was part of efforts to address the problem of growing global resistance to antimicrobial medicines. "Antibiotic resistance is growing and we are fast running out of treatment options. If we leave it to market forces alone, the new antibiotics we urgently need are not going to be developed in time," said Dr Marie-Paule Kieny , WHO's assistant director-general for health systems and innovation.

TOI had reported the case of an elderly American woman who died in the US recently after having contracted an infection while being treated for a thigh bone fracture in India two years ago.

Tests showed no drug or combination of drugs available in the US would have cured the infection. CDC Atlanta, which houses one of world's most advanced laboratories, conducted tests on the woman's wound specimen later and confirmed the presence of New Delhi MetalloBeta-Lactamase (NDM) -a superbug that makes bacteria resistant to antibiotics.

Experts in Delhi's top super-speciality hospitals, including AIIMS, say such instances are becoming common due to antibiotic resistance – the consequence of among other things, the misuse of high- end antibiotics for treatment of common health conditions. AIIMS trauma centre doctors said at least eight patients had been identified with colistin-resistant Klebsiella pneumonia at their hospital recently.

There are four common ways in which superbugs attack -ventilator-associated pneumonia, surgical site infection, central line associated blood stream infection and catheter-associated urinary tract infection. If hospitals ensure proper care to avoid such infections, many lives can be saved," said Dr Purva Mathur, a senior microbiologist at the hospital.

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**Source:** *The Times of India, 2nd March 2017*

## Penicillin Mould Created by Fleming Sells for Rs 97.5 Lakh

**Microbes preserved in a glass case that features the doctor's writing on the back**

How much is an old, dried out piece of mould worth? Apparently more than £11,875 (Rs. 97.5 lakh) if it was created by the doctor who discovered penicillin.

The nearly 90-year-old swatch of mould has a rather extraordinary history. It came from the laboratory of Dr. Alexander Fleming whose revolutionary discovery brought the world its first antibiotic, credited with saving millions of lives worldwide.

The patchy bit of mould from his niece's collection was auctioned in London on Wednesday. The buyer was not identified. The mould is preserved in a round glass case and features an inscription by Fleming on the back, describing it as "the mould that first made penicillin."

That, however, may be a stretch. The Scottish-born doctor likely made at least dozens of such mould mementos, derived from his original sample of the fungus.

Fleming "sent these samples out to dignitaries and to people in the scientific world, almost as a kind of holy relic," said Matthew Haley, director of books and manuscripts at the auction house Bonham's.

Miracle drug.

Before the discovery, infections like pneumonia and rheumatic fever were almost death sentences.

"When it first became available, penicillin was called a miracle drug," said Kevin Brown, archivist at the Alexander Fleming Laboratory Museum . "Its discovery began a new, life-saving era in medicine."

In some ways, the discovery was accidental. Fleming found mould growing in an experiment when he returned to his cramped lab after a stay at his country house.

One petri dish was full of bacteria except for an area where mould was growing. He later realized the mould — a rare strain of penicillin — was killing off the bacteria around it. He suggested that it might be used as an antiseptic in wounds, and published an account of this work in 1929.

"Fleming noticed something that other people would have missed and saw the potential of penicillin to treat patients," said Mr. Brown.

However, Fleming couldn't find a way of extracting enough of the penicillin to be of therapeutic use without it becoming ineffective. Scientists at Oxford University further developed penicillin, and production was ramped up so that enough of the antibiotic would be available for the Allied invasion in 1944. Fleming and Oxford scientists Ernst Boris Chain and Howard Walter Florey were awarded the Nobel Prize in medicine in 1945.

Brown noted that not everybody was thrilled to receive the preserved mould medallions and that some got multiple copies, including Queen Elizabeth's husband, Prince Philip. "Every time he met Fleming, he got another one of these things," Mr. Brown said.

**Source:** *The Hindu, 3rd March 2017*

## U.S. Nixed India's Plea on Reforms in Medicine

**At WHO meet, New Delhi proposed discussion on 'Access to Medicines' report by UN panel**

A month after the 140th World Health Organisation's (WHO) Executive Board meeting, a Freedom of Information Act (FOIA) response has revealed that the United States government had opposed including agenda items proposed by India, which aimed at reforming medical innovation that currently pump up drug prices to unaffordable levels.

The Indian government — along with 11 South East Asian countries — had proposed a discussion on an 'Access to Medicines' report by the United Nations High Level Panel that had recommended reforms in the funding of biomedical research and development.

However, the set of documents released by Knowledge Ecology International (KEI), a not for profit organisation that gives technical advice to governments, reveals that both the United States and the WHO opposed including the proposal by India.

**Email exchange**

An email exchange dated September 28, 2016, between Dr. Thomas Frieden, CDC Director and Vice-Chairman of the WHO EB, and Ambassador Jimmy Kolker, Assistant Secretary for Global Affairs at the U.S. Department of Health and Human Services, sets out the position of the U.S. government, stating that, "Access to medicines (oppose proposal by India): The USG should be on the record opposing this proposal from India that seeks to take forward recommendations from in the U.N. Secretary General's High Level Panel on Access to Medicines report, which was released in September. We have serious concerns about the narrow mandate of the Panel and its recommendations . "

The 11 member-states — Bangladesh, Bhutan, South Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, and Timor-Leste — as well as Brazil, Iran, and South Africa supported the inclusion of the agenda item.

The delays by WHO to place the UN HLP recommendations on the agenda of the WHO's EB and subsequently at the World Health Assembly have drawn widespread criticism from Asian civil society organisations.

"The U.N. report says there is a need for an RD treaty and it recommended reforms in the area of biomedical R&D. The U.S. government has a policy of blocking all reforms that would lead to funding the R&D system in a way that it prioritises diseases that kill million of people in the developing world. The U.S. government is not just a member-state of WHO but also a big donor. This is consistent with the U.S. policy to pressure countries like India to have more IP barriers while blocking all attempts at reforms," said Leena Menghaney, lawyer and access campaigner.

**Policy incoherence**

The U.N. Access to Medicines report had recommended solutions for remedying the policy incoherence between justifiable rights of inventors, trade rules and global public health targets. The report recommended that "governments and the private sector must refrain from explicit or implicit threats, tactics or strategies that undermine the right of WTO Members to use TRIPS flexibilities."

On March 1, India delivered a statement during WTO TRIPS Council discussions on the Access to Medicines report, urging member-states to discuss the report's recommendations.

**Source:** *The Hindu, 4th March 2017*

## Stents, Other Med Devices Have to Declare MRP's

Medical devices such as stents, heart valves and orthopaedic implants will soon have to declare the maximum retail price (MRP) and consumers will no longer have to remain in the dark on their exact costs.

The consumer affairs ministry has come out with this draft proposal following recommendation from the department of pharmaceuticals.

Sources in the consumer affairs ministry said earlier all medical devices were covered under the Legal Metrology (Packaged) Commodities Rules. But, in 1995 some of them were declared as drugs and so, they stopped mentioning MRP. "A sub-committee set up to propose changes in the rules recommended bringing them back under MRP regime. All items covered under these rules will need to mention the place of origin and assembling," said an official.

He added non-application of MRP led to a crisis where consumers were charged arbitrarily by hospitals for medical devices.

The amendments in rules will also make it mandatory for all packaged items sold online or through e-commerce sites to mention MRP to end any ambiguity whether online firms are actually giving the huge discounts that they claim in their advertisements.

The changes will be notified by this month end. Moreover, every packaged product for human consumption will have to mention the date specifying "best before" (date of minimum durability) or "use by" (expiry date) for consumer information.

Meanwhile, an online survey conducted by an online citizens' platform Local Circles found 66% consumers had paid higher than MRP for water bottles in hotels and restaurants. Out of 8197 citizens who participated, only 8% said the bottle had a regular MRP and they were billed for MRP only.

**Source:** *The Times of India, 7th March 2017*

## Combination Therapy Helps Scientists Tackle Drug-Resistant Superbugs

Researchers have found an “effective” combination therapy to treat the world's worst infectious diseases -the superbugs resistant to all known antibiotics.

The researchers said the advance had the potential to change medical practices for the treatment of drug-resistant infections.

“We looked for compounds that would mess with these bacteria, and I think we are nailing it,“ said Eric Brown, a professor at McMaster University in Canada.

The team focused on Gram-negative bacteria, which are resistant to all antibiotics, including last-resort drugs, and lead to pneumonia, wound, or surgical site and bloodstream infec tions, as well as meningitis in healthcare settings.

Gram-negative bacteria have an intrinsically impenetrable outer shell that is a barrier to many otherwise effective antibiotics, and this makes these infections deadly , particularly in hospital settings.

Researchers tested a collection of 1,440 off-patent drugs in search of one that might compromise that barrier. “These pathogens are really hard nuts to crack, but we found a molecule that shreds that shell and allows antibiotics to enter and be effective,“ said Brown.

The scientists discovered the antiprotozoal drug pentamidine disrupts the cell surface of even the most resistant Gram-negative bacteria. The anti-fungal medication was particularly potent when used with antibiotics against multidrug resistant bacteria. Pentamidine, when used with other antibiotics, was found to be particularly effective against two of the three pathogens identified by WHO as being a “critical priority” for development of new antibiotics.

Those were Acinetobacter baumannii and the enterobacteriaceae. The discovery was found to be effective in the lab and in mice, but more work is needed to offset potential side effects.

**Drug `cures 1/3rd of cancer patients'**

A private firm has developed an experimental cancer drug that has produced “extraordinary“ results, with a third of very ill lymphoma patients showing no signs of the disease after a single treatment. However, Kite Pharma cautioned that its version of CAR-T cell therapy may have also killed two of the 101people in the study. The patients had non-Hodgkin lymphoma and all other treatments had failed. The treatment uses gene therapy to prompt blood cells to attack cancer. In total 82% of the patients saw their tumours shrink by half or more at some point in the study. Independent expert Dr Roy Herbst of Yale Cancer Centre said the treatment was “extremely encouraging“ but added that further studies were needed.

**Source:** *The Times of India, 8th March 2017*

## Diabetic Drug Pricing Cartelisation Issue Reaches CCI, Health Ministry

Allegations of cartelisation of anti-diabetes drug Vildagliptin, which are being investigated by the National Pharmaceutical Pricing Authority, have now reached the Competition Commission of India and the health ministry. The whistleblower who alerted the drug pricing regulator has written to the CCI and the health secretary about the issue. In a letter dated March 18, the whistleblower has detailed how Swiss drugmaker Novartis, US-based Abbott and domestic companies Emcure and USV Pharma colluded to keep prices of their brands of Vildagliptin at artificial and similar levels, going against fair trade practices. The regulator had been informed about the cartelisation allegations in a letter dated February 27, ET reported earlier. At that time, Novartis denied the allegations and NPPA Chairman Bhupendra Singh told ET that it would “look into this issue.” ET has viewed a copy of the letter to the CCI, the monopoly watchdog, and the health secretary. CCI didn't immediately respond to an email from ET asking if it had initiated action. Health secretary CK Mishra told ET the ministry had received the letter and that the issue “relates to the Department of Pharmaceuticals,” which is part of the Ministry of Chemicals & Fertilizers. Novartis did not respond to an email query by ET seeking comment on the latest letter and USV could not be reached for comment. ET has learnt that Novartis has sought internal legal opinion on this issue. An Abbott spokesperson said it has not received any communication on this matter from the authorities. Vildagliptin, sold under the brand

Galvus, is a proprietary drug of Novartis that comes under a new class of medicines DPP 4 inhibitors, which are considered more effective in controlling blood glucose levels in patients with type 2 diabetes.

Novartis licensed the drug to Abbott, which sells it as Zomelis, USV, which branded it Jalra and Emcure, which offers it as Vysov.

The various brands of Vildagliptin recorded sales of Rs 822 crore in the Rs 10,000 crore anti-diabetic drug market last year.

The whistleblower contended in his letter to the NPPA that Novartis controls the pricing structure that is followed by the license holders and the drug prices are matched to the lowest decimal. Though there is no written communication, these companies also synchronise every price change, it was alleged. According to trade data that ET viewed, the combination of Novartis' Galvus and metformin costs Rs 258 for 10 tablets of 500 mg each, as do the combination of Jalra by USV and Vysov by Emcure. Abbott's Zomelis costs Rs 235.

"How can such corporates, having global presence, fleece Indians for several years fearlessly, without getting noticed? I request CCI to investigate the matter and impose the heaviest possible penalty to set an example in the corporate landscape world over," the whistleblower said in the letters to the health secretary and CCI chairman. Price cartelisation is prohibited under the Competition Act, 2002.

**Source:** *The Economic Times, 24th March 2017*

## Govt Eases Rules For HIV, Hep B & C Combo Drugs

With an aim to make new combination drugs for HIV and Hepatitis B & C available to patients at the earliest, the government has decided to waive some of the regulatory processes to fast-track approvals.

India's top drug regulator has said in a new order that companies manufacturing combination drugs for HIV and Hepatitis B & C can seek early approval with a WHO recommendation even if internationally the medicines are not approved as a combination but only individually. However, the drugs have to be relevant for India.

"Many of these combination products, recommended in WHO guidelines for concomitant use, may not have been approved internationally in combination but may have been approved individually. However, given the risk-benefit and recommendations by WHO the requirement of generated data may be waived based on the fact that the product has been recommended for concomitant use by WHO," the notice by G N Singh, the Drugs Controller General of India (DCGI) said.

The move is expected to benefit many of the over 21 lakh people estimated to be living with HIV in India. Moreover, viral hepatitis has also been recognised as a serious public health problem in India by the World Health Organisation (WHO) with a total of over 52 million people infected with chronic hepatitis in the country. Out of this, 40 million people in India are chronically infected with Hepatitis B and 6 to 12 million people are chronically infected with Hepatitis C, latest assessment by the UN agency shows.

The regulator has also allowed leeway to manufacturers for conducting clinical trials or bio-equivalence studies in India. While these studies are conducted to test new drugs on local patients, they take a long time and hence often delays launches in the country.

The new norms issued by the regulator allows companies to apply for such studies and product approvals simultaneously, whereas usually companies have to submit data from trials before seeking product approvals.

In fact, in some cases the regulator has also suggested waiving off clinical trials for urgent use.

"Clinical trial waiver for such products recommended by WHO for concomitant use may be given, as being falling under the category of extreme urgency and under the provisions of the Drugs and Cosmetics Rules," it said.

Though India has demonstrated a 57% reduction in overall annual number of new HIV cases, it continues to have the third highest number of people living with HIV in the world. Similarly, chronic Hepatitis is placing a huge disease, social and economic burden on affected families as well as the health system. The condition can be self-limiting or can progress to liver fibrosis (scarring), cirrhosis or liver cancer.

Early approvals in India are also likely to benefit people around the world as India is a major supplier of generic medicines, mainly anti-retroviral.

**Source:** *The Times of India, 23rd March 2017*

## Health Spending to be 2.5% of GDP

The government will pursue ambitious targets like reducing Under-Five Mortality to 23 by 2025 and Maternal Mortality Ratio from current levels to 100 by 2020, and Infant Mortality Rate to 28 by 2019. It also seeks to reduce neonatal mortality to 16 and stillbirth rate to "single digit" by 2025.

In September 2016, the Supreme Court had directed the Centre to finalise the crucial health policy guaranteeing " assured health services to all". The policy has come after a gap of 15 years to address the current and emerging challenges necessitated by the changing socio- economic, technological and epidemiological landscape.

As a crucial component, the NHP2017 proposes raising public health expenditure to 2.5% of the GDP in a time bound manner.

The policy advocates a progressively incremental assurance-based approach but activists maintain that without a legal consequence, guaranteeing health is an empty assurance.

"Previous drafts of this policy proposed to make this a fundamental rights, failure to provide health would have legal consequences. Removing that section just makes this an empty promise. Such assurances have been made umpteen times by different governments since 1980s. Further, while the policy promises to increase health spending to 2.5% of the GDP, it does not square up with the past three budgets of this government. Money for all critical programmes has either stagnated or gone down in real terms," said Dr Amit Sengupta, Convenor of the India Chapter of People's Health Movement, a non-govermental organistion advocating universal health care.

The policy envisages a time-bound Implementation Framework with clear deliverables and milestones to achieve the policy goals. Under this policy, the government will be looking at ambitious targets like reducing Under Five Mortality (U5MR) to 23 by 2025 and MMR from current levels to 100 by 2020.

**Source:** *The Hindu, 17th March 2017*

## Need Stents? Skip A Beat No More

**The ceiling on prices of stents comes as a boon for patients. The onus is now on them to hold hospitals to account**

On February 9, when 31-year-old Mumbai resident Augustine Chettiar underwent an angioplasty, a top-of-the-line drug-eluting stent called Alpine by Abbott cost him 1.2 lakh. He required two stents — tiny mesh-like devices that release measured doses of medication in the blocked artery — for two of his blockages. But during the procedure, a complication forced the doctor to use both stents in one single artery. Mr. Chettiar was advised to get the second blockage fixed after a few weeks.

On February 14, the National Pharmaceutical Pricing Authority (NPPA) announced a Ceiling on the prices of stents. The bare metal stent was capped at 7,260 while all drug-eluting stents were capped at 29,600.

When Mr. Chettiar went for his second angioplasty on March 3, a high-end drug-eluting stent called Xpedition from Abbott cost him merely 29,600. And to top it, he also received a clear bill that marked out the stent price.

**Hospitals under the scanner**

Hospitals across the country are closely being watched by the NPPA and the State Food and Drug Administration authorities on their pattern of billing after the capping of stent prices.

The NPPA has directed all hospitals to issue detailed bills to the patients, specifically and separately mentioning the cost of the coronary stents, along with the brand name of the manufacturer, importer, batch number and other details. Those who fail to comply stand to be pulled up by drug controllers.

"When we got the hospital bill after the second angioplasty, it was simple and understandable. More importantly, the price of the overall procedure reduced drastically," says Mr. Chettiar's wife Angela. "My husband had an insurance of 5 lakh. But the first procedure at Holy Spirit Hospital in Andheri cost us 4.5 lakh, of which 2.24 lakh was merely for the two stents. Fortunately, his company got the insurance firm to pass the additional amount for the second procedure that he underwent at Surana Hospital. It cost us merely 1.5 lakh," she adds.

While lakhs of patients have benefitted from the government's decision, the NPPA continues to receive complaints from across the country of overcharging and lack of clarity in the bill.

"Most of the complainants have got a refund from the hospitals. There are some others for whom we have asked for copies of the bill for

better clarity," says NPPA Chairman Bhupendra Singh, adding that they have asked the State drug controllers to re-audit all angioplasty cases from February 14, of hospitals that have complaints against them. A month since the price ceiling was introduced, the NPPA has received 37 cases of which five are fresh complaints.

**Don't miss the fine print**

Activists say that patients need to come forward and complain against any kind of non-compliance. "The government has set up a system in place. So it is now up to the patients and relatives to ensure that the bill they get is itemised," says health activist Dr. Abhay Shukla.

The new rule has drained out a major chunk of revenue for hospitals and thus there are chances of them trying to recover the money by inflating other costs. "The ideal way to compare is to get a bill of a patient who has undergone the procedure before February 14 and check if the hospital is overcharging in other aspects of the bill," suggests Dr. Shukla.

Hospital owners, however, see a new era of trust and greater volumes that will offset potential losses. "People who needed more stents and underwent cardiac surgeries can now afford angioplasties. The number of angioplasties will definitely see a rise now," says Dr. Prince Surana, medical director of the Surana Group of Hospitals in Mumbai.

**Source:** *The Hindu, 19th March 2017*

## Clincial Benefit Yes, Cost-Benefit No?

**Medical practitioners are upbeat about the advantages of using cholesterol-lowering drug Repatha, but investors are not impressed**

The first rigorous test of an expensive new drug that radically lowers cholesterol levels has found that it significantly reduces the chance that a high-risk patient would have a heart attack or stroke. These were men and women who had exhausted all other options

The results of the study, which cost about $1 billion and was paid for by Amgen, maker of the drug, were published on Friday in The New England Journal of Medicine and presented at the annual meeting of the American College of Cardiology.

The drug, Repatha, is called a PCSK9 inhibitor and can make cholesterol tumble to levels almost never seen naturally in adults, or even in people taking cholesterol-lowering statins. The Amgen drug and a similar one, sold by Sanofi and Regeneron, were approved by the U.S. Food and Drug Administration in 2015 with the hope — and expectation — that they would lower the risk of heart attacks and strokes, and not just reduce levels of LDL cholesterol, the dangerous kind.

That hope has now been realised for the Amgen drug.

"This is like the era of the statins coming in," says Dr. Eugene Braunwald, a cardiologist at Harvard Medical School, who was founding chairman of the research group that conducted the study, but was not an investigator on it. Like statins, which were introduced in the 1980s, the new class of drugs has the potential to improve the health and longevity of millions of Americans with heart disease, the nation's leading killer, accounting for 1 in 4 deaths.

"It's a new ball game," he says.

**Issue of cost**

But cost will be an issue. Statins are available as cheap generics. The new drugs have a list price of $14,523 a year. "The next big challenge is financial: how to pay for it," says Dr. David Maron, director of preventive cardiology at Stanford, who also was not involved in the study.

Insurance companies have been reluctant to pay for the drug without evidence it protected high-risk patients from heart attacks and strokes. Kristine Grow, a spokeswoman for the insurers' organisation, America's Health Insurance Plans, says insurers would consider the new data.

Investors greeted the trial results with initial disappointment and appeared to assume that insurers would continue to restrict access to the drug, in part because it did not show a benefit in overall death rates from cardiovascular causes.

Dr. Harlan Krumholz, a Yale cardiologist, agrees that given the expense of the drug, the results raise questions about what it is worth and who should get it. But he called the study "a solid outcomes trial" and said "we should celebrate" that it showed the drug is capable of reducing risk.

The problem, he said, was that expectations were running so high. "There was a lot of hubris about how pushing LDL down to 30 would eliminate heart disease," he says. Of course, it did not. About 10% of patients taking the drug had a heart attack or stroke, or died of heart disease during the trial.

The study involved 27,564 men and women. About 80% had already had a heart attack, and the rest had had a stroke or had pain in their legs and feet from narrowed arteries. They were taking optimal doses of inexpensive, cholesterol-lowering statins, which gave them an average LDL of 92, well within the range — an LDL of under 100 — that has been advised for high-risk patients.

All continued with their statins, but half were assigned to inject themselves with Repatha, also known as evolocumab, and the rest were assigned a placebo. Those taking the new drug reached an average LDL of 30. A quarter of participants got to an LDL of 19 or lower. Amgen estimates that about 11 million Americans are eligible to take the drug. They include people like those in the study and people who have a genetic condition, familial hypercholesterolemia, that results in intractably high LDL levels and a grave risk of a heart attack.

**Source:** *The Hindu, 19th March 2017*

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