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25 Years

Pharma Web

Newsletter of Tamilnadu Pharmaceutical Sciences Welfare Trust

Jul. - Aug. - Sep. 2018

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Tamilnadu Pharmaceutical Sciences Welfare Trust

Pharma Web

Newsletter of Tamilnadu Pharmaceutical Sciences Welfare Trust

ISSUE : 39 Jul. - Aug. - Sep. 2018

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EDITORIAL

Dear Readers,

We are happy to publish the 39th issue of Pharma Web Newsletter for Jul – Sep 2018.

We are happy to inform that our IPA (TN) Branch is getting Best branch award this year. Mr. J. Jayaseelan and Mr. T. Sathish, trustees of trust are also getting Fellowship award this year. The awards are distributed during IPCA conference, Delhi.

We regret to inform you one of our founder Trustee Dr. K. A. Narendra Nath passed away a few weeks ago. Our condolences to his family.

There is a delay for the release of this 39th issue is being issued. It is due to preoccupation of our trust staff and myself in conducting the 7th Industrial training programme for the fresh pharmacy graduates. We regret for the same.

In this News letter the following articles are published:

- **Failure Investigation in Pharmaceutical Industry** by **Shri. Gandhish Kamat,** Executive Vice President & Global Quality Head, Dr. Reddy's Laboratories Ltd., Hyderabad
- **Extractable / Leachables studies – Impact on Pharmaceutical Packaging** by **Shri. Shivkumar Vishwanathan,** Vice President – Marketing, CVS Cibatech Pvt. Ltd., Mumbai

Gazette Notifications pertaining to the Pharma profession under Drugs & Cosmetics Act & Rules.

The PKTI also conducted 7th Industrial Orientation Training Programme for fresh Pharmacy graduates during the month of September 2018. The highlights of this programme will be published in this issue.

The Newsletter also contain various events like Pharmacist Day Celebration, programmes of IPA TN Branch etc.,

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

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ARTICLES

FAILURE INVESTIGATION IN PHARMACEUTICAL INDUSTRY

by
Shri. Gandhish Kamat
Executive Vice President & Global Quality Head, Dr. Reddy's Laboratories Ltd., Hyderabad

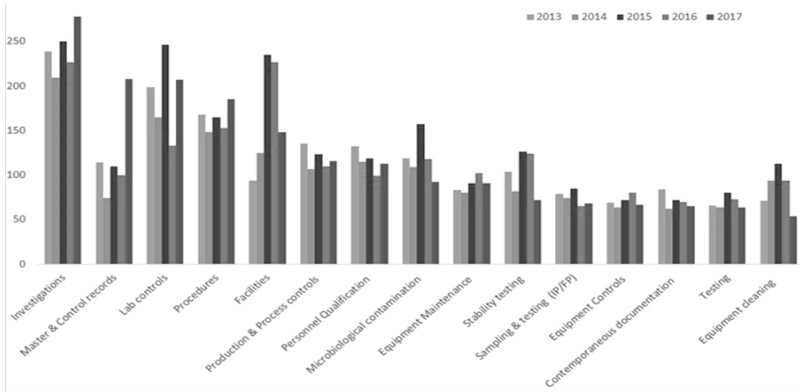
Nobody in Pharmaceutical industry likes non-conformities or failures, because they result in extra work; delays in manufacturing, shipment, product launches, sometimes recalls, regulatory scrutiny so on and so forth.However, we do not live in a perfect world and failures are part of life.

Failure investigation begins with understanding what a “Failure”.

Failure refers to the state or condition of not meeting a desirable objective. It also can be defined as opposite of compliance. Failure is a term that encompasses failure of product (at any stage), utility and quality system. It also includes market complaints and deviations.

Investigations are necessary to identify the root cause of the failures and take corrective actions to prevent recurrence and further loss to the company. Investigations can also help us in identifying any potential failures and take preventive actions to avoid their occurrence in proactive manner. Investigations also help in continuous improvement as the CAPAs taken help in improving the process robustness and process capability.Last but not the least the Investigation of failures is required by all GMP regulations.

All the GMP regulations require every failure to be thoroughly investigated to identify the root cause and take CAPA. Investigation is required irrespective of whether the material is rejected or approved. The motive behind this is toensure that manufacturers know their process well and the failures get reduced over a period of time thereby avoiding any interruptions in drug supplies and also avoiding any potential impact on the consumers if the failures go undetected. Let us be aware that the testing is always based on sampling and there is always some probability that defective unit does not get picked up in sampling. Review of FDA 483 observations issued from 2013 to 2017 show that highest number of observations are related to inadequate investigations.



Why do we have failures?

In Pharmaceutical industry every process is validated. Building, utilities, equipment, manufacturing processes, cleaning procedures, computer systems, even personnel in some cases are qualified. Validation in simple terms is the exercise carried out to prove that the equipment, process etc. are capable of consistently producing desired results. Deducing from these statements we should have no failures.

The main reason for the failures is current approach towards process development and its qualification. In spite of the fact that new validation guideline became effective from 2011, many manufacturers still consider successful execution of three consecutive batches as validation and lack full understanding of the product and process. For instance –

- All the variability's in CMAs are not identified and their impact on the process and product quality are not understood.
- All critical process parameters are not identified based on scientific evaluation and are not adequately controlled.
- The control strategies are not based on scientific risk assessment. That means not based on the study of the impact of variability in the inputs or process parameters on the final product quality.
- Operating ranges are mentioned for various process parameters rather than properly defining the process. This allows the operators flexibility of varying the conditions within the limits as per his fancy or gut feel rather than based on scientific rationale. This can result in large number of permutations of different parameters making each batch unique and varying from others. Also most of the time procedure to handle exceptions are not defined in the process and again it is left to operator's judgement. All these result in high operator dependence and hence process is prone to human errors. That is why most investigations end up in identifying human error as the cause and re-training as CAPA.

Why our investigations fail to reach root cause?

The reasons for not reaching the root cause are –

- Urge for quick solutions based on trials or based on past experiences rather than systematic approach and use of appropriate statistical tools for data analysis
- Lack of understanding about product and the process – Many times knowledge about product & process is available in R&D but is not passed to manufacturing sites as part of tech transfer. Development report provides useful information about what conditions can result in certain type of failures and what control measures are built in process to avoid such failures. Knowledge of such information can help in carrying out focused investigation.

- Lack of understanding about manufacturing equipment – Many times equipment qualification activities remain as document generation activity rather than the improving the understanding of the equipment.
- Lack of availability of relevant information. Many time we end up measuring what is possible to be measured rather than what is required to be measured for adequate control.
- Many failures are due to combined effect of multiple factors and univariate analysis fail to detect such causes.
- Reluctance to accept unfavorable data. We can't blame the test method or the lab only when there is failure while we merrily accept the passing results produced by same lab using same method.

Six sigma approach to problem solving in investigation

- Six sigma adopts a systematic method of problem solving and we can adopt the same for the failure investigations. The Six sigma approach involves five phases namely Define, Measure, Analyze, Improve and Control.
- In the define phase, the problem is defined in specific& measurable way. The target is defined in terms of certain level of improvement from the baseline by certain time frame.
- Measure phase involves measurement of defect rates and associated parameters in the current process.
- Analyze phase involves processing data to measure process capability and also understand relationships between the defect rates and process parameters.
- Improve phase involves taking corrective actions to eliminate the causes for defects.
- Control Phase involves monitoring process performance so that the defects do not recur.

Use statistical tools in investigation

Some of the statistical tools which can be used in the investigation are brain storming, 5 whys, fault tree analysis, process flow diagrams, cause and effect diagram, FMEA, histograms, Pareto chart, scatter diagram, reference analysis etc. This is not an exhaustive list. There are other tools which can also be used. We must remember that these are the means and not the end. As any mechanic or carpenter does not use every tool in his box for every job, we also need to be selective in deciding which tool will help us in reaching the root cause for each investigation. It requires learning and regular use to master these tools.

After the problem is defined the first step of investigation is doing Brain storming to identify all the possible causes. Why analysis is also a good tool to identify probable causes.

Next step is to identify what data is to be collected for investigations. This can be done using Cause and Effect diagram or C&E matrix or FMEA. Use of these tools helps in reducing the efforts in data collection by systematic evaluation of various causes and their relation to effect.

Once the data is collected, it needs to be analyzed to draw meaningful conclusions. For this purpose tools like Histogram, Pareto analysis, Scatter plots, Regression analysis can be used. Based on the analysis of the data we can identify whether there is any assignable cause.

If any assignable cause is identified, finalize the CAPA and implement the changes. Once the changes are implemented further data should be collected to see whether the CAPA has been effective.

If analysis of data does not lead to identification of the root cause further investigation from analyzing current process is required. Additional experiments may be required to collect more data.

If the data analysis or experimentation is still not able to reach to root cause the problem could be due to low process capability or process design. In such cases we have to go to DOE to freshly work on process improvement.

If the Implemented CAPA is satisfactory we continue monitoring the process using tools like Process control charts.

Brain storming is good tool for generating lot of ideas. The exercise requires involvement of people from different functions with different expertise. Crux is generating as much ideas without eliminating.

Five Whys is technique, where you keep asking why till you get to the root cause. Generally the root cause is reached by 5th why but that number is not sacrosanct.

The process flow diagram helps in understanding the process, by identifying critical steps, critical parameters, control measures defined in the process etc. Thus, it helps in identifying the data to be collected for analysis and sometime may even help in identifying probable causes.

Fault tree analysis is a graphical representation of the major faults, the causes for the faults, and potential counter measures. It helps in identifying areas of concern for new product design or for improvement of existing products. It helps identify root cause of failure as well as establishing the corrective actions. Thus this tool can be used for both designing a robust process as well as in investigation of failure.

Cause and Effect diagram is also called as fish bone diagram due to its appearance. It was developed by Karaou Ishikawa. This diagram is used to explore the potential causes under 6 Ms which can result in undesirable effect or failure. The 6 Ms which are explored are Man, Machine, Material, Methods, Measurement and Milieu (which is the French term for environment).

Various factors which are investigated under each of the 6 Ms are listed below –

Man - • Skill, knowledge, competency and attitude • Adequacy of supervision & support • Clarity about job role • Experience, training • Shift in which the activity was done • Conducive work environment? • Availability of tools / equipment	**Machine** - • Age of equipment or machine • Maintenance history • Was machine operating correctly? • Machine capability • Operating parameters • Recent changes	**Materials –** • Whether there has been any change in Source of material • Whether the manufacturer has made change in his process • Age of material v/s stability • Test results at incoming stage / re-test • Material packing • Storage condition • Correctness of Quantity • Quality trends
Method –(Manufacturing procedure.) • Adequacy of process design • Identification of Critical Process parameters • Adequacy of control parameters • Robustness of the process • Process capability • Recent changes if any • Deviations in execution • Trend analysis of process parameters • Safety mechanisms & challenges	**Measurement** - • Inadequate method • Improper execution • Analyst training, • Instrument maintenance / calibration • Standards / reagents used	**Milieu (Environment)** • Deviations from environmental condition which could have resulted in the undesirable effect. - Temperature / RH - Pressure differential Viable / non-viable particle counts

Failure mode effect analysis (FMEA) is a scientific method of risk assessment. It analyzes each step with respect to its impact on the quality, probability of occurrence & detectability. This assessment helps in filtering the probable causes and also helps in identifying the data to be collected for investigation.

Various statistical tools are available for analysis of data. Type of data should determine the tool to be used. Some of the tools which can be used for data analysis are –

- **Histogram-** depicts frequency distribution against the class intervals. It helps in understanding the process center, the spread and type of the distribution. From the histogram we can estimate the process capability &probability of the results going out of limits.

- **Pareto analysis-** frequency is plotted against the defect or cause type which are arranged in decreasing order as bar chart. Cumulative % frequency is plotted as line graph with separate axis in such a way that total number of defects match with 100%. This helps in prioritizing the defects and the causes.

- **Scatter plots** - are plot of outcome against the impacting parameter. It shows the correlation between two independent variables.

- **Regression analysis** - While scatter plot shows correlation in graphical manner in qualitative way, regression analysis gives quantitative estimation of the correlation between two variables.

Control charts are useful in process monitoring and also in trend analysis. There are two types of data. One is attribute type or discrete data like number of defectives in certain sample size and other is variable type or continuous data like Assay of batch.

Different types of control charts are available for monitoring attribute and variable type of data.

- **Control charts for variable data** - X-bar chart, Sigma chart, R-Chart, Run chart.
- **Control charts for attributes -** C charts, P charts, nP charts.

Control charts indicate central line, warning and control limits. Warning and Control limits are dynamically calculated based on the data and can be used for monitoring and control of the process.

Control charts can also be used to see the effectiveness of the CAPA.

Data review -

Lot of data is normally available in Pharmaceutical companies which is helpful in investigations.The data to be reviewed depends upon the type of failures and is identified by using various tools described earlier like FMEA and C&E diagram. Given below is the list of data which may have to be reviewed for various types of investigations and how they can help in investigation.

- **Process flow –** Helps in understanding the process & its critical control points and identifying probable causes.
- **Development report –** It helps in better understanding of the product and process design and what factors can result in the type of defect under investigation and what control measures are built in the design to prevent those failures. Based on this what area to focus can be decided.
- **Forced degradation study & degradation profile –** This helps in understanding pathway of formation of different impurities.
- **Past history –** Helps in understanding likelihood of occurrence, investigation findings and CAPAs taken in the past. This can avoid duplication of work.
- **Material usage / left over stock reconciliation –** Helps in verifying if right quantities of different ingredients have been added in the batch.
- **Critical process parameters & controls –** Helps in checking if there were any deviations from the process
- **Trends of process parameters, process timing, hold time** - helps in understanding if there is any difference in the failing batch as compared to other batches
- **Yields –** Helps in identifying weighing errors or process losses.
- **Machine logs –** Helps in identifying possibility of any cross contaminations or mix-ups.
- **Distribution records –** Tells if anything went wrong during transit. Helpful in market complaint investigation or impact assessment.
- **Quality trends, Process capability –** Tells about robustness of the process and can help in establishing correlation with process parameters.
- **Stability data (exhibit & commercial batches) –** Helps in understanding the degradation profile and also comparing trends of current batches with earlier batches.
- **Method validation & transfer data –** Helps in finding out any method related issues.
- **Equipment / Utility qualification documents -**Helps in understanding equipment capabilities, critical machine parameters, adequacy of controls, shift in performance etc.

Given below are some examples of the data which is generally required to be reviewed for different type of failures. The list is just indicative and actual data required will have to be determined based on FMEA or C&E diagram.

Assay failures-

- Correctness of Formulation
- Label claim, Salt correction factor, Water molecules and its correction factor, Batch size etc.
- Correctness of quantities of ingredients
- Weights of the raw materials, reconciliation of left over quantities in the warehouse, yields at different stages etc.
- Validity of the standards used, Comparison of the response with earlier runs, changes in the working standard, results of the other batches analyzed using same working standard.
- Loss / gain of material during processing
- Whether yield is higher or lower than normal, whether water content results are out of trend etc. Sometimes physical verification of quantities of the material may provide useful clues.
- Possibility of segregation in the blend or in the sample.
- Adequacy of the Sampling technique used
- Review of Sample solution preparation method to see if it is prone for any errors.

Failure in impurities -

- Development report to understand the pathway of formation of the impurity in question, its structure, control measures built in the design to control that impurity etc.
- Forced degradation study to understand how the impurity is formed if the same is not explained in the development report. This helps in knowing the pathway in case of unidentified impurities.
- Manufacturing conditions – Review of manufacturing conditions in light of the degradation pathway can tell whether some condition during manufacturing could have resulted in higher level of impurity. For instance higher drying time could be reason for higher level of thermal or oxidative impurity.
- Solution stability data can tell us whether delay in testing or abnormal condition during testing could be responsible for failure

- Past trend helps in understanding whether there is any process capability issue
- Review of stability data of the earlier batches indicate whether the batch is behaving similar or showing different trend.
- Possibility of contamination needs to be explored in manufacturing as well as testing in case of unexpected unknown impurity by checking of the instrument logs and activities carried out in the proximity.

Failures in dissolution –

- Verification of dissolution medium preparation record to verify usage of right materials, proper degassing, and verification of actual pH.
- Review of CMAs of critical components like drug release polymers, binders, disintegrants etc.
- Review of critical process parameters and their comparison with trends of other batches. Review of following parameters may be helpful:
    - Granulation parameters like power or current at the end point of granulation, PSD, BD / TD of the granules etc.
    - Drying parameters such as Inlet & outlet temperatures, drying time, LOD etc.
    - Mixing time especially to see if there is possibility of over lubrication
    - Compression machine parameters like speed, force feeder RPM, compaction force, thickness, hardness, DT
    - Coating parameters like air flow, inlet temperature, bed temperature, exhaust temperature, RPM, spray rate, distance of spray gun, left over solution, weight gain etc.
    - Capsule filling parameters like tamping setting, machine principle etc.

Corrective and Preventive actions (CAPA)

The terms corrective action and preventive action are often misunderstood. General perception is any action taken to salvage the situation is corrective action where as any action taken to prevent recurrence is preventive action. These are incorrect definitions.

Corrective action is an action taken to eliminate the cause of a detected non-conformity or other undesirable situation to prevent recurrence of the non-conformity.So to take a corrective action, we must first identify the root cause of the non-conformity or at least probable cause.

Preventive action is an action to eliminate other undesirable situation which are likely to occur to prevent occurrence of potential non-conformity.

21 CFR 820.100 lists out 3 types of actions –

1. **Correction –** which means correcting the non-conforming product & other quality problems.
2. **Corrective action –** action taken for preventing recurrence of nonconforming product and other quality problems.
3. **Preventive action –** actions taken for eliminating cause of potential non-conforming product and other quality problems.

Investigation report -

The investigation must be documented in the form of investigation report.Writing investigation report is as important as investigation itself. The investigation report should be self explanatory with all information presented in logical sequence so that reader do not have to ask questions.

Investigation report should typically include following sections –

- **Problem definition -** Document complete results / observations along with the specification limits. Include the extent of the problem. If there are multiple batches involved or certain period is involved mention it clearly in the problem definition. In case of market complaints it is important to capture exact technical description of the problem instead of reproducing the verbatim description given by complainant.
- Summary of analytical results / observations – Include original test results, repeat analysis results, results of experimental testing if any, results of related samples like control samples, other batches analyzed together etc., observation of the complaint samples and discussions and conclusions based on analysis of all these results
- Summary of data reviewed – As mentioned earlier, investigation involves review of lot of data. It is important to capture the summary of all the data reviewed. The data may be presented in tabular form or in graphical form so as to interpret it easily. Many statistical tools like Pareto, Histogram, regression charts, control charts etc while good in data analysis can also be used for presentation of the data in logical manner. Presentation of data should be followed by discussion on summary of findings, scientific rationale for the findings based on the product knowledge and conclusions. More data collection may be required if collected data is not leading to definite conclusion or indicate involvement of some other parameter not reviewed earlier. This should be documented in the conclusion and the additional data can be added in the addendum to the report.

- Summary of experiments - Sometimes investigation involve carrying out some experiments to confirm hypothesis or probable causes. In such case the investigation report should clearly explain the Scientific rational for the experiment, its purpose, description of the experiment and the method of evaluation or measurement. Based on the findings of the experiments following should be included in the report –
    - Summary of the results
    - Conclusions based on the evaluation of the results and scientific rationale
    - Need for additional experimentation if conclusion not reached. (In such case addendum to report should be prepared to include results and conclusions of additional experiments)
- Final Conclusion– Summary of investigation findings, root cause or probable cause identified, impact assessment should be summarized in final conclusion along with scientific rationale.
- Impact assessment – Investigation often involves evaluation impact of the problem on the batches involved, product distributed in the market, other products etc. Summary of this assessment with action plan should be captured in this section. These action may include batch rejection, salvage the batches if possible or actions like recall for the safety of the consumers
- Corrective and Preventive action – This section of the report should include listing of Corrective actions identified to eliminate the root causes or probable causes and Preventive actions identified to eliminate any potential non-conformities along with the target completion dates. Incase evaluation of effectiveness is required, the method for same should also be documented.

Summary - Investigation of failures is critical in Pharmaceutical both from improvement and regulatory perspective. The Pharma personnel making the investigations must possess certain skills like domain knowledge, Investigation skills, analytical ability, knowledge of statistical skills and technical writing skills.

EXTRACTABLE / LEACHABLES STUDIES – IMPACT ON PHARMACEUTICAL PACKAGING

by

Shri. Mr. Shivkumar Vishwanathan

Vice President – Marketing, CVS Cibatech Pvt. Ltd., Mumbai

I. Introduction:

A pharmaceutical company was surprised to find Benzophenone (a suspected carcinogen) appearing as an impurity during stability testing (6 month accelerated sample) of an ophthalmic product. Further investigation revealed benzophenone leaching from the adhesive used to fix the label on the outer surface of the ophthalmic bottle.

In another case, large levels (> 100 ppm) of a phthalate was found in a lipophilic drug product used for oral application which was found to have migrated from the adhesive used in multi-layer laminate used to pack the formulation.

In an extractable study conducted on a blister pack, a powerful sensitizer was discovered which had originated from the glue. As the product was pulmonary product this was a great risk to patient safety and the package had to be modified.

These examples show that impurities leaching out from packaging materials is indeed a serious concern. Pharma companies need to have a robust risk assessment strategy in place to detect these impurities as early as possible so that there is no risk to the patient.

Extractable/Leachable (E/L) studies are Qualitative and Quantitative investigations which ensure that a pharmaceutical packaging or contact material is safe with regard to chemical components and which does not negatively influence the drug product packed inside.

- **Extractables:** Those substances that are present in the material, component, system that can be extracted from that material by a solvent under exaggerated conditions.
- **Leachables:** Those substances that are present in the drug product due to its contact with a material, component, system etc.

	Patient Safety	Container
Extractables	Possible Impact	Test Material
Leachables	Actual Impact	Test Product

Fig 1: Extractable v/s Leachable

Amongst the various functions that packaging is supposed to perform – compatibility with the product is one of them. For Pharmaceutical products which typically have a shelf-life from 1 year to 3 years, this is particularly an important and sensitive aspect. No primary packaging material can claim to be totally inert and some interaction with the drug product (formulation) is to be expected. Back in the late 90s regulators were increasingly concerned about patients having adverse effects and even fatalities that were suspected due to impurities leaching from the packaging material into the drug product. These were initially for Orally Inhaled and Nasal Drug Products (OINDP) and the Product Quality Research Institute (PQRI) was tasked with developing guidelines. Over the past 15 years several guidelines covering wide variety of packaging materials and devices have been published and the packaging and pharmaceutical community is required to demonstrate the compatibility of packaging material for any new drug product which are especially going to be sold in the regulated market.

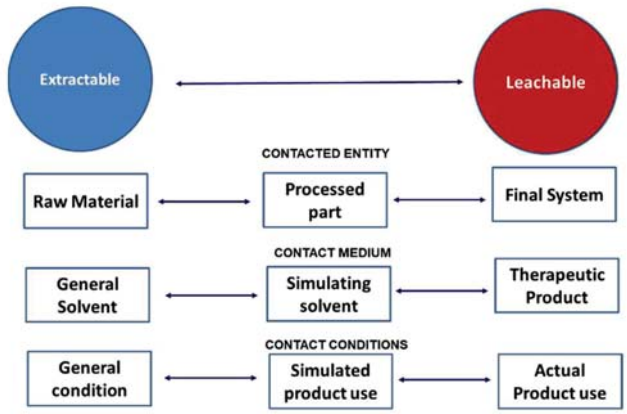


Fig 2: Relationship between extractable and leachable.

II) Regulatory landscape

There are several guidelines that deal with E/L. This presents a huge challenge to the industry on performing the study and interpreting the results. However the one that is widely accepted is the PQRI guideline and science based study design with co-relation between extractable and leachables and coverage of all potential extractable type will usually be sufficient. It is important to bear in mind that despite whatever extractable data is available the regulatory agency is always interested to see the results of study in the drug product i.e. for potential leachables.

Degree of concern associated with the route of administration	Likelihood of packaging component-dosage form interaction		
	High	Medium	Low
Highest	Inhalation Aerosols and Sprays	Injections and Injectable Suspensions; Inhalation Solutions	Sterile powders and powders for injection, inhalation powders
High	Transdermal Ointments and Patches	Ophthalmic Solutions and Suspensions; Nasal Aerosols and Sprays	-
Low	Topical Solutions and Suspensions, topical and lingual aerosols, oral solutions, and suspensions	-	Oral tablets and oral (hard and soft Gelatin) capsules; Topical powders, oral powders

Fig 3: Modified FDA/CDER/CBER Risk-Based Approach for Leachables
SOURCE: USP <1664> "ASSESSMENT OF DRUG PRODUCT LEACHABLES ASSOCIATED WITH PHARMACEUTICAL PACKAGING/DELIVERY SYSTEMS"

Fig 2 shows the relative risk of various dosage forms related to extractables/leachables. Inhalation products, injectable represent the highest risk and E/L data will be required to prove compatibility whereas on the other end solid orals have the lowest risk and may not require detailed E/L studies.

III) How to perform E/L Study?

An E/L study is a risk assessment. Knowledge about the packaging materials, the chemistry, the conversion process and drug product are critical in making the right assessment.

With a wide variety of materials, devices, drug products, what are the factors to be considered in coming with the correct assessment and study design?

An E/L Study should answer these three fundamental questions

1. What: What are the compounds that can leach from the packaging material? (Identification)

2. How Much: What is the quantity in which these compounds are leaching? (Quantification)

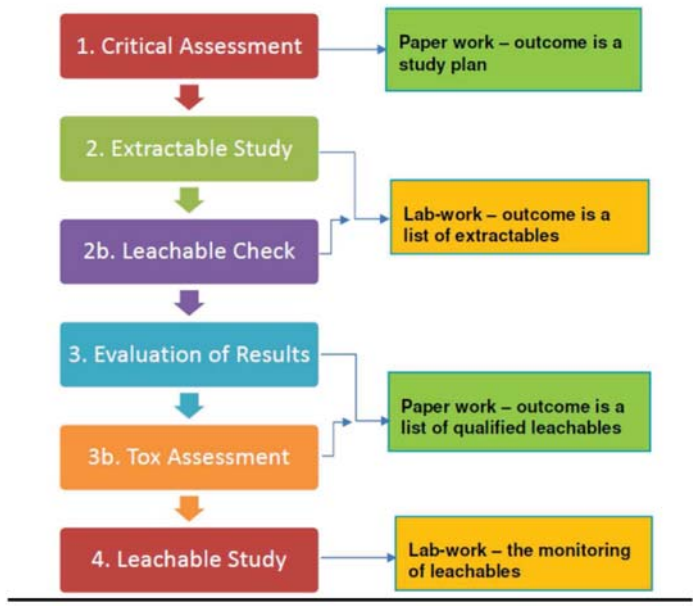
3. Why: Why are these compounds leaching?

Questions 1 and 2 are generally answered as a part of any E/L study, but rarely is the 'Why' aspect looked into, as this requires material and packaging expertise which usually the pharmaceutical companies lack.

The packaging suppliers can play an important part in characterising the materials used which can be of value to the pharma company. But finally it is the responsibility of the pharma company to test the stability samples of the drug product to prove there are no leachables that can cause a patient safety concern.

IV) Steps in an EL Study

An E&L investigation is not one single study, it is at least divided in 4 subsequent major steps:



The thresholds for interpreting the results of E/L studies are:

- 1.5 µg/day is Safety Concern Threshold (SCT) – If leachable exposure is below this value no further action is required irrespective of the toxicological nature of compound.
- 5 µg/day for sensitizer and irritants – If compound is not a sensitizer/irritant then leachable exposure up to this limit is acceptable.
- 150 µg/day for General toxicity (QT) – For compounds more 5 µg/day apply the general rules of toxicological and perform the risk assessment accordingly.

V) Challenges in performing E/L Study

The E/L study is not a limit test nor has a defined standard to evaluate the results. When we start an E/L study we are not even sure of what compounds to expect. So it is a risk assessment, knowledge and creativity of the analysts is very important.

A few common issues that the pharma industry encounters in doing E/L studies are:-

1. Expertise – Far too often Pharmaceutical companies look at E/L as a merely analytical issue and the packaging team is not sufficiently involved which creates problems later on. A combination of packaging knowledge, material science and drug product is essential for a successful E/L assessment.

2. Supply Chain – Pharma customers expect their packaging vendors to supply extractable data which although in theory is good, but practically is a challenge for vendors as more often than not they are not aware about the drug product that will be packed. Also a typical packaging supply chain may involve inputs from several vendors and as such this limits the ability of the convertor to give accurate and reliable information. However packaging manufacturers are generating quality Extractable data which could prove very valuable to pharma companies as they can directly proceed to the leachable assessment.

3. Guidelines – There is no standard way or a one size fits all approach for E/L. The dosage form, route of administration, the daily dose, nature of primary and secondary packaging, etc have to be taken in to consideration which is precisely why there are several guidelines that have to be adapted to the current situation. However this creates confusion in designing a good analytical strategy and interpretation of results.

4. When to do the study – Pharma companies tend to underestimate the importance of E/L and leave it too late in the development process. Any surprises in the E/L study then leaves very little time to take any corrective action. Ideally, once the packaging material specifications are fixed or the device has been finalised an extractable study can be done and the risk of E/L assessed.

VI) The Analytical Tool Box for a good E/L characterization

In the extractables study a standard set of analytical methods, which includes TDGC/MS, GC/MS of derivatives, HS-GC/MS, LC/MS and ICP-OES, allows the comprehensive identification and quantification of extractable compounds from container/ closure systems.

The criteria for these methods are that they are on the one hand exhaustive and comprehensive in the sense that all potentially extractable analytes from polymeric materials of a container/ closure system can be covered qualitatively and (semi)-quantitatively. On the other hand this set of methods should be generic in the sense that the methods are applicable for extractables studies on various different polymeric materials of container/ closure systems.

(a) Thermodesorption-GC/MS (TDS-GC/MS)

A very useful first experiment in an extractables study is the application of TDS-GC/MS on the raw polymeric materials of a container/ closure system.

With thermoplastic materials the TDS-GC/MS chromatogram can be very complex, because many saturated and unsaturated hydrocarbons are thermally stripped from the polymeric matrix. Still, a detailed analysis of these chromatograms can strongly aid in the later identification of and search for analytes in the extracts of the material. Therefore, analytes found in extracts of polymers by GC/MS are often a subset of analytes that are found by TDS-GC/MS of the raw polymeric material.

A good example for these similarities is illustrated in figure 5, where the TDS -GC/MS chromatograms (ion traces of the most prominent fragment of one of the extractables - Bisphenol A, the compound that is labelled with an asterisk in figure 4 of the raw polymeric material and extracts thereof are overlaid:

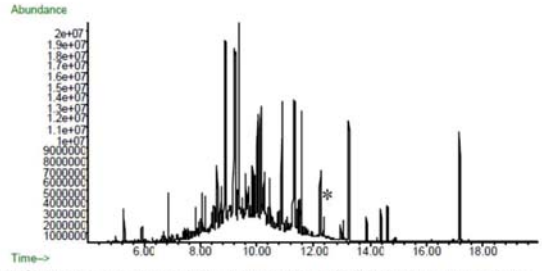


Fig 4: **TDS-GC/MS chromatograms of polymeric part of a catheter system**

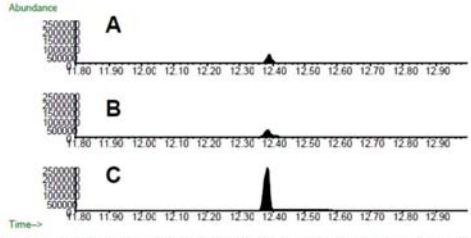


Fig 5: **TDS-GC/MS chromatograms (ion trace) of A: raw polymeric material, B: ethanolic extract, C: aqueous extract after workup**

The limitation of TDS-GC/MS is that it can only be applied for the identification and quantification of unipolar and (semi-)volatile compounds, whereas strongly polar and/ or high molecular weight compounds demand for different methods.

(b) Headspace-GC/MS (HS-GC/MS)

Volatile extractables are analytically accessible with the aid of HS-GC/MS. The application of this method is best exemplified by studying a case, where printing inks where used on the polymeric container/ closure system to indicate the date of filling, shelf life of the pharmaceutical product etc. One of the ingredients of the ink formulation was cyclohexanone, and this particular compound could easily be detected and later onquantified on a ~1 ppm level (in relation to the amount of extracted polymer) in the aqueous extracts of the container/ closure system, as illustrated in figure 6:

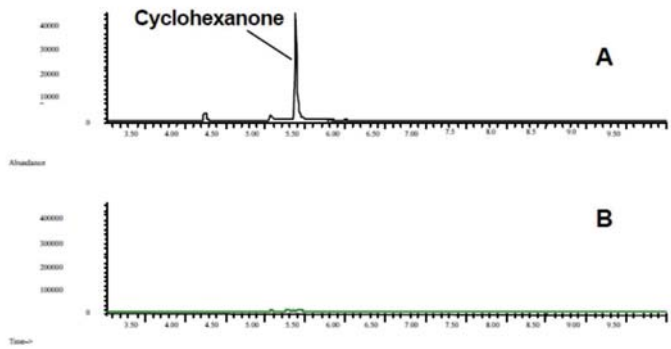


Figure 6: Overlay of HS-GC/MS chromatograms of aqueous extracts of a printed (A) and an unprinted (B) polymeric container/ closure system.

© LC/MS

The application of all GC/MS methods is limited to (semi)-volatile analytes. The analysis of polar and/ or high molecular weight extractables demands for the application of liquid chromatography coupled to the powerful tool of mass spectrometry.

(d) ICP OES or ICP- MS

Often inorganic additives and pigments are compounded into polymeric materials. The analysis of this class of chemicals demands for methods that can sensitively detect metals, and ICP -OES or ICP -MS are best suited for this.

(e) Analytical Methods for Leachable Studies

In contrast to extractables studies leachables studies are performed under cGMP with drug product formulations that usually come out of stability testing. The methods that are used (and validated) for leachables testing underlie certain criteria: on the one hand they have to be very specific, because the leachable compound has to be extracted from or detected in the often very complex drug formulation. On the other hand the applied method should be very sensitive, because the specifications of the potentially leachable compounds within the drug formulation are usually very low. Additionally, as these methods will later on be applied in the routine quality control of the drug product, they should be as simple as possible.

Methods for the analysis of extractables require the complete qualitative and quantitative coverage of compounds with a broad spectrum of chemical structures and properties. After an extractable study the analyst should be confident that no other compounds than the detected ones can potentially leach from the container/ closure system into the pharmaceutical formulation. Once this confidence is established specific methods for the quantification of the potentially leachable analytes in the drug formulation are developed and validated - and these methods obviously strongly depend on the type of analyte and on the matrix.

VII) Key Messages and Summary.

- Limited direct regulation covering E/L.
- Science led risk based approach is a key to which dosage forms are likely to require
- E/L testing and how much testing is to be done.
- A formal risk assessment is useful in determining where to aim the E/L testing.
- Thresholds for safety assessment are key in determining the limits to apply to E/L testing.
- Variety of analytical tools required for comprehensive coverage of potential extractables.
- Control strategies and life cycle management are closely linked to supplier relationships which are important to identify and detect potential leachables as early as possible.

It is mandatory for Pharmaceutical companies to demonstrate compatibility of the device/packaging with the drug product by submitting E/L data to the regulatory agencies. Hence it is advisable to give due importance to E/L during the drug development and packaging selection process and involve all stakeholders as early as possible.

Also E/L can also be used as a tool for packaging development by developing or improving packaging materials and devices which have lower leachability and hence better compatibility.

References

1. Leachable Risk Assessment: A Structured approach to meet regulatory expectations – Smithers Rapra/GSK.
2. Safety Thresholds and Best practices for Extractables and Leachables in Orally Inhaled and Nasal Drug Products – PQRI
3. Leachables and Extractables Working Group Initiatives for Parenteral and Ophthalmic Drug Products (PODP) – PQRI
4. Leachables and Extractables Handbook: Safety Evaluation, Qualification, and Best Practices Applied to Inhalation Drug Products – Douglas Ball, Daniel Norwood.
5. Analytical Methods for Extractables and Leachables Studies: Case Studies - Dr. Michael Jahn, Dr. Armin Hauk, Ciba Expert Services.

NOTIFICATION

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 22nd October, 2018

G.S.R.1051(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 thirty 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 emailed at drugsdiv-mohfw@gov.in.

DRAFT RULES

1. (1) These rules may be called the Drugs and Cosmetics (…… Amendment) Rules, 2018.

   (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 word “Tuticorin” the words “Tuticorin and Kamrajar Port”; and for the word “Gandhinagar” the words “Gandhinagar and Mundra Port” respectively shall be substituted.

[F. No. X.11014/25/2018-DR]
SUNIL SHARMA, Jt. Secy.

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 5th October, 2018

G.S.R. 1000(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 shall be taken into consideration on or after the expiry of a period of fifteen 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. 414A, D Wing, Nirman Bhavan, New Delhi – 110011 or emailed at drugsdiv-mohfw@gov.in.

DRAFT RULES

1. (1) These rules may be called the Drugs and Cosmetics (……Amendment) Rules, 2018.
(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 to be referred as said rules), in rule 24,-
a. in sub-rule (1),-
(i) for the words “one thousand rupees”, the words “ten thousand rupees” shall be substituted;
(ii) in the Proviso, for the words “one hundred rupees”, the words “one thousand rupees” shall be substituted;
b. in sub-rule (3), for the words “two hundred and fifty rupees shall be paid”, the words “one thousand five hundred rupees shall be paid for making amendment in the licence or” shall be substituted.

3. In the said rules, in rule 24A,-
a. in sub-rule (3),-
(i) in clause (i), for the words and letters “one thousand and five hundred US dollars”, the words and letters “ten thousand US dollars” shall be substituted;
(ii) in clause (ii), for the words and letters “one thousand US dollars” wherever they occur, the words and letters “five thousand US dollars” shall be substituted;

b. in sub-rule (5), for the words and letters “five thousand US dollars”, the words and letters “twenty five thousand US dollars” shall be substituted;

c. in sub-rule (7), for the words and letters “three hundred US dollars or its equivalent in Indian rupees shall be paid”, the words and letters “one thousand eight hundred US dollars or its equivalent in Indian rupees shall be paid for making amendment in the registration certificate or” shall be substituted.

4. In the said rules, in rule 34, in sub-rule (3), for the words “one hundred rupees for a single drug and an additional fee of fifty rupees”, the words “five thousand rupees for a single drug and an additional fee of two thousand rupees” shall be substituted.

5. In the said rules, in rule 34A, in sub-rule (3), for the words “one hundred rupees for a single drug and an additional fee of fifty rupees”, the words “six hundred rupees for a single drug and an additional fee of three hundred rupees” shall be substituted.

6. In the said rules, in rule 122A, in sub-rule (1), in clause (b),-

(i) for the words “fifty thousand rupees”, the words “two lakh fifty thousand rupees” shall be substituted;

(ii) in the first Proviso and in the second Proviso, for the words “fifteen thousand rupees”, at both the places where they occur, the words “one lakh rupees” shall be substituted.

7. In the said rules, in rule 122D, in sub-rule (1), for the words “fifteen thousand rupees”, the words “one lakh rupees” shall be substituted.

8. In the said rules, in rule 129A,-

a. in sub-rule (1), for the words and letters, “two hundred and fifty US dollars or its equivalent toIndian rupees for each brand of cosmetic”, the words and letters “two thousand US dollars or its equivalent to Indian rupees for each brand of cosmetic and a fee of fifty US dollars for each variant” shall be substituted;

b. in sub-rule (5), for the words and letters “one hundred US dollars”, the words and letters “five hundred US dollars” shall be substituted.

[F. No. X.11014/32/2018-DR]
SUDHIR KUMAR, 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

TARIFF FOR ADVERTISEMENTS

The members of the Tamilnadu Pharmaceutical Science Welfare Trust desire to accept and publish important advertisements in Pharma Web, from Pharma and allied industries, Pharmacy colleges, etc. The following are the tariff :

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MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

CORRIGENDUM

New Delhi, the 25th September, 2018

S.O. 4972(E).— In 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 (ii), vide number S.O. 4707(E) dated the 7th September, 2018 (English version), in line number 3 for the figures '4607' read '4707'.–

[F.No. X.11035/53/2014-DFQC(PT. II)]
SUDHIR KUMAR, Jt. Secy.

CORRIGENDUM

New Delhi, the 25th September, 2018

S.O. 4973(E).—In 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 (ii), vide number S.O. 4489(E) dated the 7th September, 2018 (English version), in line number 5 for the word 'Chloramphenicol' read 'Clotrimazole'.–

[F.No. X.11035/53/2014- DFQC(PT. II)]
SUDHIR KUMAR. Jt. Secy.

CORRIGENDUM

New Delhi, the 25th September, 2018

S.O. 4974(E).—In 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 (ii), vide number S.O. 4667(E) dated the 7th September, 2018 (English version), in line number 6 for the word 'Dimethieone' read 'Dimethicone'.–

[F.No. X.11035/53/2014- DFQC(PT. II)]
SUDHIR KUMAR, Jt. Secy.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 28th August, 2018

G.S.R. 817(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 emailed at drugsdiv-mohfw@gov.in.

Draft Rules

1. (1) These rules may be called the Drugs and Cosmetics (_____Amendment) Rules, 2018.
(2) It shall come in to force after their final publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945 (hereinafter to be referred as said rules) after rule 67H and before Part VII the following PART VIB shall be inserted, namely,-

"PART VIB
SALE OF DRUGS BY E-PHARMACY

67-I. Definitions.- In this PART unless the context otherwise requires,-

(a) "e-pharmacy" means business of distribution or sale, stock, exhibit or offer for sale of drugs through web portal or any other electronic mode;
(b) "e-pharmacy portal" means a web or electronic portal or any other electronic mode established and maintained by the e-pharmacy registration holder to conduct business of e-pharmacy;
(c) "Central Licensing Authority" for the purposes of this PART, the Central Licensing Authority means licensing authority appointed by the Central Government under clause (b) of rule 21 of the Drugs and Cosmetics Rules, 1945;
(d) "prescription" means an instruction from a Registered Medical Practitioner to a patient, written by hand or in any electronic mode duly signed, to dispense a drug and quantity of drug to a patient;
(e) "sale by way of e-pharmacy" means a sale whether to a hospital, or dispensary, or a medical, educational or research institute or to any other person through e-pharmacy by way of retail sale;"
(f) The words and expressions used herein and not defined in this PART but defined in the Drugs andCosmetics Act, 1940 and rules made thereunder shall have the same meaning assigned to them in thatAct or rules, respectively.

67J.Registration of - e-pharmacy- (1) With effect from the commencement of PART VIB of these rules, no person shall distribute or sell, stock, exhibit or offer for sale of drugs through e-pharmacy portal unless registered under rule 67N.

(2) The e-pharmacy registration holder shall receive the orders for retail sale through e-pharmacy portal.

(3) e-pharmacy registration holder shall arrange or provide the drugs, as per the prescription received from the customer, within the period specified by the e-pharmacy registration holder at the time of placement of the order through e-pharmacy portal.

(4) The e-pharmacy registration holder shall have a facility for customer support and grievance redressal of all stakeholders which shall run not less than twelve hours for all seven days of a week:

Provided, that the facility for customer support shall have registered pharmacist in place to answer the queries of customers through such customer helpline.

67K. Disclosure of information generated through e-pharmacy portal. - (1) The information received by the e-pharmacy registration holder from the customer by way of prescription or in any other manner shall not be disclosed by the e-pharmacy registration holder for any other purposes nor shall same be disclosed to any other person.

(2) The e-pharmacy registration holder shall be duty bound to provide such information to the Central Government or the State Government, as the case may be, as and when required for public health purposes.

(3) The e-pharmacy portal shall be established in India through which they are conducting the business of epharmacy and shall keep the data generated localised:

Provided, that in no case the data generated or mirrored through e-pharmacy portal shall be sent or stored, by any means, outside the India.

67L. Application for registration of e-pharmacy. - (1) Any person who intends to conduct business of epharmacy shall apply for the grant of registration to the Central Licensing Authority in Form 18AA through the online portal of the Central Government.

(2) The information furnished above shall be supported by the duly notarised affidavit from the applicant.

(3) Any application for the grant of e-pharmacy registration of e-pharmacy made in Form 18AA to the Central Licensing Authority shall be accompanied with a fee of fifty thousand rupees and the information and documents as specified in Form 18AA.

67M. Conditions of registration of e-pharmacy. -

(1) An e-pharmacy registration holder shall comply with provisions of Information Technology Act, 2000 (21 of 2000) and rules made thereunder.

(2) The details of patient shall be kept confidential and shall not be disclosed to any person other than the Central Government or the State Government concerned, as the case may be.

(3) The supply of any drug shall be made against a cash or credit memo generated through the epharmacy portal and such memos shall be maintained by the e-pharmacy registration holder as record which shall contain the following particulars: -

(i) name, address and sale licence number of the licencee who is dispensing the drugs mentioned in prescription uploaded on the e-pharmacy portal;

(ii) serial number and date of the cash/credit memo; and

(iii) the name of the drug, quantity, batch number or lot number, date of expiry and name of the manufacturer;

(iv) name and address of e-pharmacy registration holder with Registration Number along with signature/ digital signature of Registered Pharmacist in-charge.

(4) The e-pharmacy registration holder shall inform the Central Licensing Authority `in writing inthe event of any change in the constitution of the firm operating under the registration. Where any change in the constitution of the firm takes place, the current registration shall be deemed to be valid for a maximum period of three months from the date on which change takes place unless, in the meantime, a fresh registration has been taken from Licencing Authority in the name of the firm with the changed constitution.

(5) The e-pharmacy registration holder shall not carry out e-pharmacy with respect to the drugs covered under the categories of the Narcotic and psychotropic as referred to in the Narcotic Drugs and Psychotropic Substances Act, 1985 (61 of 1985), tranquilizers and the drugs as specified in the Schedule X of Drugs and Cosmetics Rules, 1945.

(6) The e-pharmacy shall mention the following details on its e-pharmacy portal, -

(i) registration issued in Form 21AA;

(ii) constitution of the firm including details of the Directors, partners or persons having ownership of the E-pharmacy;

(iii)official logo of the e-pharmacy portal, if any.

(iv) details of the logistic service provider;

(v) return policy of dispensed drugs;

(vi) name of the registered pharmacist, with the Regd. No. and name of Pharmacy Council where the pharmacist has been registered, who validates the prescription prior to forward it to dispense the drugs;

(vii) contact details of e-pharmacy including telephone number, mobile number, e-mail, address;

(viii) procedure for lodging grievances, complaints etc. on the e-pharmacy portal and complaintredressal mechanism.

67N. Grant of registration of e-pharmacy. - (1) The Central Licencing Authority, may, after scrutiny of the information and documents furnished with the application in Form 18AA and such further enquiry, if any, as may be considered necessary, -

(i) if satisfied, that the provisions of this Part have been complied with, shall grant registration to the applicant in Form 21AA.

(ii) if not, reject the application, for reasons to be recorded in writing, within a period of thirty days, from the date the application made under rule 67L;

(iii) in case, where the Licencing Authority considers that there are some deficiencies in the application and the same can be rectified, the Central Licensing Authority shall inform the applicant of the deficiencies within a period of thirty days;

(iv) the applicant may, after being informed under clause (iii), rectify the deficiencies within a reasonable period specified by the Licencing Authority;

(v) in case where the applicant rectifies the deficiency, within the period referred to in clause (iv) and provides required information and documents, the Licencing Authority shall scrutinise the application again and if satisfied that the provisions of this Part have been complied with, shall grant registration to the applicant in Form 21AA or if not satisfied, reject the application within a period of thirty days reckoned from the day when the required information and documents furnished.

(vi) the Central Licencing Authority after registration of any e-pharmacy, shall list all the registered e-pharmacy on its website from time to time for information to all stakeholders.

(2) Notwithstanding anything contained in these rules, Licencing Authority may refuse to grant registration to any applicant in respect of whom it is satisfied that by reason of his conviction of anoffence under the Act or this Part, or the previous cancellation or suspension of any licence granted thereunder, he is not a fit person to whom a licence should be granted under this rule. Every such order shall be communicated to the licencee as soon as possible.

(3) An applicant who is aggrieved by the decision of the Central Licensing Authority under sub-rule (1), may file an appeal within forty-five days from the date of receipt of such rejection before the Central Government in the Ministry of Health and Family Welfare, which may after such enquiry and after giving an opportunity of being heard to the appellant, dispose of the appeal within a period of sixty days. 67-O. Periodic Inspection of e-pharmacy, - The premises from where the e-pharmacy business is conducted shall be inspected, every two years, by a team of officers authorised by the Central Licensing Authority, with or without the experts in the relevant field or the officers authorised by the concerned State Licensing Authority.

67P. Procedure for distribution or sale, of drugs through e-Pharmacy, - (1) On receipt of prescription, through e-pharmacy portal, the registered pharmacist on behalf of the e-pharmacy registration holder shall verify the details of the patient, Registered Medical Practitioner and arrange for the dispense of the drugs as per the instructions of the Registered Medical Practitioner, if not already found dispensed;

(2) The e-pharmacy registration holder who has received prescription in sub-rule (1) shall dispense and made arrangement for supply of drugs from any retail or wholesale licenced premises under the Drugs and Cosmetics Act, 1940 and rules made thereunder;

(3 The details of the drugs dispensed including the patient details shall be maintained on the e-pharmacy portal.

(4) In case of e-prescription, the prescription shall be uploaded on the e-pharmacy portal and shall be kept in record by the dispenser.

67Q. Validity of registration of e-pharmacy, - A registration issued to any person in Form 21AA shall remain valid for a period a three years from the date of its issue.

67R. Renewal of Registration of e-pharmacy.- An e-pharmacy registration holder of e-pharmacy who intend to renew the registration issued under rule 67N in Form 21AA, shall make an application inForm 18AA along with the a fee of fifty thousand rupees and the documents as specified in Form18AA:

Provided that if the application for renewal of registration is made before its expiry or if the application is made within three months of its expiry, the registration shall continue to be in force until orders are passed on the application. The registration shall be deemed to have expired if application for its renewal is not made within six months after its expiry.

67S. Prohibition of advertisement of drugs through e-pharmacy, - No e-pharmacy shall advertise any drug on radio or television or internet or print or any other media for any purpose.

67T. Suspension or cancellation of registration. - (1) Where the e-pharmacy registration holder contravenes any provision of the Drugs and Cosmetics Act, 1940 and this Part, the Central Licensing Authority, shall, after giving the e-pharmacy registration holder an opportunity to show cause as to why such an order should not be passed, shall, by an order and for reasons to be recorded in writing, suspend it for such period as it considers necessary or cancel the registration.

(2) An e-pharmacy registration holder whose registration has been suspended or cancelled by the Central Licensing Authority, under sub-rule (1), may within forty-five days of the receipt of a copy of the order by such authority, prefer an appeal to the Central Government in the Ministry of Health and Family Welfare, and that Government, shall after giving the appellant an opportunity of being heard, confirm, reverse or modify such order.

(3) Where the licence of any e-pharmacy registration holder, as provided in the Proviso to sub-rule(2) of rule 67P, is cancelled by two or more States, the e-pharmacy registration granted by the Central Licencing Authority under rule 67N shall deemed to have been cancelled for all purposes.

67U. Complaint Redressal mechanism, - (1) In the event of suspicion of supply of a Not of Standard Quality or adulterated or misbranded or spurious drug through e-pharmacy to any customer, that customer may file a complaint in writing to the concerned State Drugs Controller, by whatever name called, in that State Licensing Authority, as the case may be.

(2) On receipt of the complaint as referred in sub-rule (1), that State Drugs Controller or whatever name called, shall take action as per the procedure specified in the Drugs and Cosmetics Act, 1940 and Rules made thereunder to decide the complaint of the customer.

(3) Without prejudice to sub-rule (2), the customer shall have a right to seek relief under the Consumer Protection Act, 1986 and rules made thereunder.

67V. Monitoring of e-pharmacy, - (1) The e-pharmacy registration holder shall maintain and update, from time to time, the information regarding the drugs availability, types of drugs offered for sale, supply channels or vendor lists, details of registered pharmacists, registered medical practitioner (if any) and any other requirements of the Drugs and Cosmetics Act and rules thereunder, on the e-pharmacy portal.

(2) The Central Licensing Authority and the State Licensing Authority shall monitor the data or information as referred to in sub-rule (1), periodically to ensure compliance with the provisions of the Drugs and Cosmetics Act, 1940 and Rules thereunder.

(3) without prejudice to anything contained in these rules, the Central Licencing Authority or State Licencing Authority, as the case may be, at any time, may direct any e-pharmacy registration holder to provide prescription on the basis of which the drugs have been dispensed for the purpose of transaction audit.

Explanation: For the purpose of this rule, "transaction audit" means audit of the received prescription by the e-pharmacy registration holder and the drugs dispensed on that basis for the risk based data samples or system generated random data samples.

67W. Mode of payment of fee. — The fee prescribed under this Part, payable to the Central Government, shall be paid through challan or by electronic mode, in the Bank of Baroda, Kasturba Gandhi Marg, New Delhi-110001 or any other branch of Bank of Baroda, or any other bank, notified by the Ministry of Health and Family Welfare in the Central Government, to be credited under the Head of Account "0210- Medical and Public Health, 04-Public Health, 104-Fees and Fines.".

3. In the said rules, after Form 18A, the following Forms shall be inserted, namely, -

"FORM 18AA
[See rule 67L, 67N and 67R]
Application for grant of Registration or Renewal to distribute and sell, stock or exhibit or offer for sale, drugs through e-pharmacy

1. I/We ..... of ..... hereby apply for a registration or renewal to distribute or sale of drugs other than those specified under the categories of the Narcotic and Psychotropic as referred to in the Narcotic Drugs and Psychotropic Substances Act, 1985 (61 of 1985), tranquilizers and the drugs as specified in the Schedule X of Drugs and Cosmetics Rules, 1945.

2. Whether applicant is Individual or HUF or Company or Partnership or Limited liability partnership or public sector or any other entity details may be given along with proof.

3. Address of the e-pharmacy owner …….…….. (Specify the Name, location, premises number, etc.)

4. Name of the Pharmacist In-charge of the e-pharmacy…….

5. URL/Mobile application/mode of e-pharmacy and mode of customer care
……..……

6. Fee paid on …… Rs……. receipt/challan/transaction id …….

7. I undertake to comply with all the conditions required to obtain registration as specified in PART VIB of the Drugs and Cosmetics Rules, 1945.

Place: _____
Date: _____

Signature
(Name & Designation)
Seal/Stamp of authorized/
Signature/Digital signature

Documents or Information to be enclosed by the applicant:

(i) A copy of identity and address proof of the applicant, any one of the followings:
valid passport, voter ID card, valid permanent driving license, adhaar card;

(ii) Constitution details of the applicant; whether proprietorship or partnership or limited liability partnership or company;
Details of mode of helpline facility for counselling the patient or his representative with respect to drug usage, its method of administration, warnings, contra-indications and any other information relating to the drugs sold through e-pharmacy;

(iii) any other relevant information which may be required for the purpose of verifying the correctness of the statements made by the applicant, if any;"

4. In the said rules, after Form 21A, the following Forms shall be inserted, namely,-

"FORM 21AA
[See rule 67M, 67N, 67Q and 67R]
Registration to distribute and sell, stock or exhibit or offer for sale, drugs through e-pharmacy

Registration No: Date: .....

1. ..... having situated at ..... is hereby registered to distribute or sell, stock or exhibit or offer for sale by retail dealing for the categories of drugs, other than those specified under the categories of the Narcotic and Psychotropic as referred to in the Narcotic Drugs and Psychotropic Substances Act, 1985 (61 of 1985), tranquilizers and the drugs as specified in the Schedule X of Drugs and Cosmetics Rules, 1945 and to operate a e-pharmacy subject to the conditions specified below to the provisions of the Drugs and Cosmetics Act, 1940 and the Rules made thereunder.

2. The registration shall be in force from ..... to.....

3. The e-pharmacy shall operate through …….. (URL/Mobile application/mode of e-pharmacy).
4. Name and registration number of registered pharmacist in-charge: ……

Central Licensing Authority
Signature
(Name and designation)

Condition of Registration

The registration holder shall comply with the provisions of the Drugs and Cosmetics Act,1940 and the Rules made thereunder amended from time to time.

[F.No.X.11035/1010/2016-DRS-Vol-I]
SUDHIR KUMAR, 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. …… dated …….

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MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 21st August, 2018

"**G.S.R. 794(E)**.—In exercise of the powers conferred by section 26A of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government hereby further amends the notification of the Government of India, Ministry of Health and Family Welfare (Department of Health and Family Welfare) No. G.S.R. 411(E), dated 27th April, 2018 published in Part II - Section 3 - Sub-section (i) of the Gazette of India, Extraordinary, namely,—

In the said notification, in para 1, in sub-para 5, for clauses (v) and (vi), the following clause shall be substituted, namely,—

"(v) The Oxytocin formulations manufactured by the public sector companies or undertakings licensed under the Drugs and Cosmetics Rules, 1945 shall be distributed or sold in accordance with such rules."

[F. No. X.-11014/3/2018-DR]
SUDHIR KUMAR, Jt. Secy.

Note : The principal notification was published in the Gazette of India Extraordinary, Part II, Section 3, sub-section (i) vide number G.S.R. 411(E), dated the 27th April, 2018 and was last amended videnotification number G.S.R. 602(E), dated the 29th June, 2018.

NOTIFICATION
New Delhi, the 21st August, 2018

G.S.R. 795(E).—Whereas a draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required under sections 12 and 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. 763(E), dated the 10th August, 2018, in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), inviting objections and suggestions from persons likely to be affected thereby, before the expiry of a period of 7 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 the 10th August, 2018;

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

And whereas, circumstances have arisen making it necessary to publish this notification without prior consultation of the Drugs Technical Advisory Board and the consultation shall be made in accordance with section 12 and section 33 of the said Act.

Now, therefore, in exercise of the powers conferred under sections 12 and 33 of the Drugs and Cosmetics Act, 1940, the Central Government 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, 2018.

(2) They shall come into force on the First day of September, 2018.

2. In the Drugs and Cosmetics Rules, 1945, —
(a) In Schedule H the entry at serial number 382 relating to Oxytocin shall be omitted;

(b) In Schedule H1 at the end after entry at serial number 46 the following entry shall be inserted, namely,—

"47. Oxytocin ".

[F. No. X.-11014/3/2018-DR]
SUDHIR KUMAR, Jt. Secy.

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 was last amended vide notification number G.S.R. 602(E), dated the 29th June, 2018.

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MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

ORDER

New Delhi, the 11th July, 2018

S.O. 3400(E).—In exercise of the powers conferred by subsection (2) of section 20 of the Drugs and Cosmetics Act, 1940 (23 of 1940) read with sub rule (1) of rule 18 of the Medical Devices Rules, 2017, the Central Government hereby designates the following Government Analysts as Medical Device Testing Officers in respect of the Medical Devices as specified in the Table given below:-

TABLE

Serial No.	Name of Government Analyst	Name of Laboratory	Medical Device
(1)	(2)	(3)	(4)
1. 2. 3.	Dr. N. Murugesan Mrs. C. Vijayalakshmi Dr. J. Uma Maheswari	the Central Drugs Testing Laboratory, Chennai	Condoms
4. 5. 6. 7. 8.	Shri C. Hariharan Dr. Saroj Kumar Ghosh Dr. Rakesh Kumar Rishi Dr. Nandita Saha Dr. Anjan Pal	the Central Drugs Laboratory, Kolkata	Surgical dressing, Surgical cotton, Surgical bandages, Disinfectant, Disposable Hypodermic Syringes, Disposable Hypodermic Needles, Disposable Perfusion sets and Intravenous Cannulas
9. 10.	Dr. Raman Mohan Singh Mrs. S.U Warde	the Central Drugs Testing Laboratory, Mumbai	Intra Uterine Device(IUD) and Falope rings
11. 12. 13. 14.	Dr. Reba Chhabra Dr. J.P. Prasad Ms. Kanchan Ahuja Ms. Ajanta Sircar	the National Institute of Biologicals, Noida	Human Immunodeficiency Virus (HIV), Hepatitis B surface Antigen (HBsAg), Hepatitis C Virus (HCV), Blood grouping reagents, Glucose test strips and fully automated analyser based glucose reagents
15.	Dr. Partha Jyoti Gogoi	the Regional Drugs Testing Laboratory, Guwahati, Assam	Disposable Hypodermic Syringes, Disposable Hypodermic Needles, Disposable Perfusion sets and Intravenous Cannulas

2. This Order shall come into force from the date of publication in the Official Gazette.

[F. No. X.11014/1/2018-DR]
SUDHIR KUMAR, Jt. Secy.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 1st August, 2018

G.S.R. 729(E).—Whereas a draft of certain rules to amend the Medical Device Rules, 2017 was published as required under sections 12 and 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 412(E) dated 27.04.2018 in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i) by the Central Government, inviting objections and suggestions from all persons likely to be affected thereby, before the expiry of a period of thirty days from the date on which copies of the said Official Gazette containing the said notification were made available to the public;

And whereas, copies of the Official Gazette containing the said notification were made available to the publicon the 27th April, 2018;

And whereas, all objections and suggestions received in response to the said draft notification have been duly 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, namely:-

1. (1) These rules may be called the Medical Devices (Amendment) Rules, 2018.
(2) They shall come into force on the date of their publication in the Official Gazette.

2. In the Medical Devices Rules, 2017, in the Fourth Schedule, in Part II, in paragraph (ii), for clause (h), the following clause shall be substituted, namely:-

"(h) In case of in-vitro diagnostic medical devices, performance evaluation report by the manufacturer shall be submitted by the applicant:

Provided that when the State Licensing Authority specifically requires for Class B or the Central Licence Authority for Class B, Class C and Class D in-vitro diagnostic medical devices, as the case may be, applicant shall submit the report issued by the central medical devices testing laboratory or a medical device testing laboratory registered under rule 83 or by any laboratory accredited by the National Accreditation Board for Testing and Calibration Laboratories or by any hospital accredited by National Accreditation Board for Hospitals and Healthcare Providers or by any Central Government or State Government Laboratory of any hospital or of any institute, specified by the concerned State Licensing Authority or the Central Licensing Authority.".

[F. No. X.11014/5/2018-DR]
SUDHIR KUMAR, Jt. Secy.

Note : The principal rules were published in the Gazette of India vide notification number G.S.R 78(E), dated the 31st January, 2017.

List of Fixed Dose combination Drugs banned by Ministry of Health and Family Welfare, as on 7th September 2018.

S. No	Gazette No.	Drug Name
1.	S.O. 4379(E)	Aceclofenac + Paracetamol + Rabeprazole
2	S.O. 4380(E)	Nimesulide + Diclofenac
3	S.O. 4381(E)	Nimesulide + Cetirizine + Caffeine
4	S.O. 4382(E)	Nimesulide + Tizanidine
5	S.O. 4383(E)	Paracetamol + Cetirizine + Caffeine
6	S.O. 4384(E)	Diclofenac + Tramadol + Chlorzoxazone
7	S.O. 4385(E)	Dicyclomine + Paracetamol + Domperidone
8	S.O. 4386(E)	Diclofenac + Tramadol + Paracetamol
9	S.O. 4387(E)	Diclofenac + Paracetamol + Chlorzoxazone + Famotidine
10	S.O. 4388 (E)	Naproxen + Paracetamol
11	S.O. 4389 (E)	Nimesulide + Serratiopeptidase
12	S.O. 4390 (E)	Paracetamol + Diclofenac + Famotidine
13	S.O. 4391 (E)	Nimesulide + Pitofenone + Fenpiverinium + benzyl alcohol
14	S.O. 4392 (E)	Omeprazole + Paracetamol + Diclofenac
15	S.O.4393 (E)	Nimesulide + Paracetamol injection
16	S.O. 4394 (E)	Tamsulosin + Diclofenac
17	S.O. 4395 (E)	Paracetamol + Phenylephirine + Chlorpheniramine + Dextromethorphan + Caffeine
18	S.O. 4396 (E)	Diclofenac + Zinc Carnosine
19	S.O. 4397 (E)	Diclofenac + Paracetamol + Chlorpheniramine maleate + magnesium trisillicate
20	S.O. 4398 (E)	Paracetamol + Pseudoephedrine + Cetirizine
21	S.O. 4399 (E)	Phenylbutazone + Sodium Salicylate
22	S.O. 4400 (E)	Lornoxicam + Paracetamol + Trypsin
23	S.O. 4401 (E)	Paracetamol + Mefenamic Acid + Ranitidine + Dicyclomine
24	S.O. 4402 (E)	Nimesulide + Dicyclomine
25	S.O. 4403 (E)	Heparin + Diclofenac
26	S.O. 4404 (E)	Glucosamine + Methyl Sulfonyl Methane + Vitamin D3 + Manganese + Boron + Copper + Zinc
27	S.O. 4405 (E)	Paracetamol +Tapentadol
28	S.O. 4406 (E)	Tranexamic Acid + Proanthocyanidin
29	S.O. 4407 (E)	Lornoxicam + Paracetamol + Tramadol
30	S.O. 4408 (E)	Lornoxicam + Paracetamol + Serratiopeptidase
31	S.O. 4409 (E)	Diclofenac + Paracetamol + Magnesium trisilicate
32	S.O. 4410 (E)	Paracetamol + Domperidone + Caffeine
33	S.O. 4411 (E)	Ammonium Chloride + Sodium Citrate + Chlorpheniramine Maleate + Menthol
34	S.O. 4412(E)	3 tablets of Serratiopeptidase(enteric coated 20000 units) + Diclofenac Potassium & 2 tablets of Doxycycline
35	S.O. 4413 (E)	Nimesulide + Paracetamol suspension

S. No	Gazette No.	Drug Name
36	S.O. 4414 (E)	Aceclofenac + Paracetamol + Famotidine
37	S.O. 4415 (E)	Aceclofenac + Zinc Carnosine
38	S.O. 4416 (E)	Paracetamol + Disodium Hydrogen Citrate + Caffeine
39	S.O. 4417 (E)	Paracetamol + DL Methionine
40	S.O. 4418 (E)	Disodium Hydrogen citrate + Paracetamol
41	S.O. 4419 (E)	Paracetamol + Caffeine + Codeine Phosphate
42	S.O. 4420 (E)	Aceclofenac (SR) + Paracetamol
43	S.O. 4421 (E)	Diclofenac + Paracetamol injection
44	S.O. 4422 (E)	Azithromycin + Cefixime
45	S.O. 4423 (E)	Amoxicillin + Dicloxacillin
46	S.O. 4424 (E)	Azithromycin + Levofloxacin
47	S.O. 4425 (E)	Cefixime + Linezolid
48	S.O. 4426 (E)	Amoxicillin + Cefixime + Potassium Clavulanic Acid
49	S.O. 4427 (E)	Ofloxacin +Nitazoxanide
50	S.O. 4428 (E)	Cefpodoxime Proxetil + Levofloxacin
51	S.O. 4429 (E)	Combikit of Azithromycin, Secnidazole and Fluconazole
52	S.O. 4430 (E)	Levofloxacin + Ornidazole + Alpha Tocopherol Acetate
53	S.O. 4431 (E)	Nimorazole + Ofloxacin
54	S.O. 4432 (E)	Azithromycin + Ofloxacin
55	S.O. 4433 (E)	Amoxycillin +Tinidazole
56	S.O. 4434 (E)	Doxycyclin + Serratiopeptidase
57	S.O. 4435 (E)	Cefixime + levofloxacin
58	S.O. 4436 (E)	Ofloxacin + Metronidazole + Zinc Acetate
59	S.O. 4437 (E)	Diphenoxylate + Atropine + Furazolidone
60	S.O. 4438 (E)	Combikit of Fluconazole Tablet,Azithromycin Tablet and OrnidazoleTablets
61	S.O. 4439 (E)	Ciprofloxacin + Phenazopyridine
62	S.O. 4440 (E)	Amoxycillin + Dicloxacillin + Serratiopeptidase
63	S.O. 4441 (E)	Azithromycin + Cefpodoxime
64	S.O. 4442 (E)	Lignocaine + Clotrimazole + Ofloxacin + Beclomethasone
65	S.O. 4443 (E)	Cefuroxime + Linezolid
66	S.O. 4444 (E)	Ofloxacin + Ornidazole + Zinc bisglycinate
67	S.O. 4445 (E)	Metronidazole + Norfloxacin
68	S.O. 4446 (E)	Ciprofloxacin + Fluticasone + Clotrimazole + Neomycin
69	S.O. 4447 (E)	Metronidazole + Tetracycline
70	S.O. 4448 (E)	Cephalexin + Neomycin + Prednisolone

S. No	Gazette No.	Drug Name
71	S.O. 4449 (E)	Azithromycin + Ambroxol
72	S.O. 4450 (E)	Cilnidipine + Metoprolol succinate + Metoprolol tartrate
73	S.O. 4451 (E)	L-Arginine + Sildenafil
74	S.O. 4452 (E)	Atorvastatin + Vitamin D3 + Folic acid + Vitamin B12 + Pyridoxine
75	S.O. 4453 (E)	Metformin + Atorvastatin
76	S.O. 4454 (E)	Clindamycin + Telmisartan
77	S.O. 4455 (E)	Olmesartan + Hydrochlorothiazide + Chlorthalidone
78	S.O. 4456 (E)	L-5- Methyltetrahydrofolate calcium + Escitalopram
79	S.O. 4457 (E)	Paracetamol + Promethazine
80	S.O. 4458 (E)	Betahistine + Ginkgo Biloba Extract + Vinpocetine + Piracetam
81	S.O. 4459 (E)	Cetirizine + Diethyl Carbamazine
82	S.O. 4460 (E)	Doxylamine + Pyridoxine + Mefenamic Acid + Paracetamol
83	S.O. 4461 (E)	Drotaverine + Clidinium + Chlordiazepoxide
84	S.O. 4462 (E)	Flupentixol + Escitalopram
85	S.O. 4463 (E)	Gabapentin + Mecobalamin + Pyridoxine + Thiamine
86	S.O. 4464 (E)	Imipramine + Chlordiazepoxide + Trifluoperazine + Trihexyphenidyl
87	S.O. 4465 (E)	Chlorpromazine +Trihexyphenidyl
88	S.O. 4466 (E)	Ursodeoxycholic Acid + Silymarin
89	S.O. 4467 (E)	Metformin 1000/ 1000/ 500/ 500 mg + Pioglitazone 7.5/ 7.5/ 7.5/ 7.5 mg + Glimepiride 1/ 2/ 1/ 2 mg
90	S.O. 4468 (E)	Gliclazide 80 mg + Metformin 325
91	S.O. 4469 (E)	Voglibose + Metformin + Chromium Picolinate
92	S.O. 4470 (E)	Pioglitazone 7.5/ 7.5 mg + Metformin 500/ 1000 mg
93	S.O. 4471 (E)	Glimepiride 1mg/ 2mg/ 3mg + Pioglitazone 15mg/ 15mg/ 15mg + Metformin 1000mg/ 1000mg/ 1000mg
94	S.O. 4472 (E)	Glimepiride 1mg/ 2mg + Pioglitazone 15mg/ 15mg + Metformin 850mg/ 850mg
95	S.O. 4473 (E)	Metformin 850mg + Pioglitazone 7.5 mg + Glimepiride 2mg
96	S.O. 4474 (E)	Metformin 850mg + Pioglitazone 7.5 mg + Glimepiride 1mg
97	S.O. 4475 (E)	Metformin 500mg/ 500mg + Gliclazide SR 30mg/ 60mg + Pioglitazone 7.5mg/ 7.5mg
98	S.O. 4476 (E)	Voglibose + Pioglitazone + Metformin
99	S.O. 4477 (E)	Metformin + Bromocriptine
100	S.O. 4478 (E)	Metformin + Glimepiride + Methylcobalamin
101	S.O. 4479 (E)	Pioglitazone 30 mg + Metformin 500 mg
102	S.O.4480 (E)	Glipzide 2.5 mg + Metformin 400 mg
103	S.O. 4481 (E)	Pioglitazone 15 mg + Metformin 850 mg
104	S.O.4482 (E)	Metformin ER + Glicazide MR + Voglibose
105	S.O. 4483 (E)	Chromium Polynicotinate + Metformin

S. No	Gazette No.	Drug Name
106	S.O. 4484 (E)	Metformin + Gliclazide + Pioglitazone + Chromium Polynicotinate
107	S.O. 4485 (E)	Metformin + Gliclazide + Chromium Polynicotinate
108	S.O. 4486 (E)	Metformin (Sustained release) 500 mg + Pioglitazone 15 mg + Glimepride 3 mg
109	S.O. 4487 (E)	Metformin (SR) 500 mg + Pioglitazone 5 mg
110	S.O. 4488 (E)	Chloramphenicol + Beclomethasone + Clotrimazole + Lignocaine
111	S.O. 4489 (E)	Chloramphenicol + Ofloxacine + Glycerine and propylene gclycol
112	S.O. 4490 (E)	Chloramphenicol + Lignocaine + Betamethasone + Clotrimazole + Ofloxacin + Antipyrine
113	S.O. 4491 (E)	Ofloxacin + Clotrimazole + Betamethasone + Lignocaine
114	S.O. 4492 (E)	Gentamicin Sulphate + Clotrimazole + Betamethasone + Lignocaine
115	S.O. 4493 (E)	Ofloxacin + Clotrimazole + Beclomethasone + Lignocaine
116	S.O. 4494 (E)	Beclomethasone + Clotrimazole + Chloramphenicol + Lignocaine ear drop
117	S.O. 4495 (E)	Flunarizine + Paracetamol + Domperidone
118	S.O. 4496 (E)	Rabeprazole + Zinc carnosine
119	S.O. 4497 (E)	Magaldrate + Famotidine + Simethicone
120	S.O. 4498 (E)	Cyproheptadine + Thiamine
121	S.O. 4499 (E)	Magaldrate + Ranitidine + Pancreatin + Domperidone
122	S.O. 4500 (E)	Ranitidine + Magaldrate + Simethicone
123	S.O. 4501 (E)	Magaldrate + Papain + Fungal diastase + Simethicone
124	S.O.4502 (E)	Rabeprazole + zinc + Domperidone
125	S.O. 4503 (E)	Famotidine + Oxytacaine + Magaldrate
126	S.O. 4504 (E)	Ranitidine + Domperidone + Simethicone
127	S.O. 4505 (E)	Alginic Acid + Sodium Bicarbonate + Dried Aluminium Hydroxide + Magnesium Hydroxide
128	S.O. 4506 (E)	Clidinium + Paracetamol + Dicyclomine + Activated Dimethicone
129	S.O. 4507 (E)	Furazolidone + Metronidazole + Loperamide
130	S.O. 4508 (E)	Rabeprazole + Diclofenac + Paracetamol
131	S.O. 4509 (E)	Ranitidine + Magaldrate
132	S.O. 4510 (E)	Norfloxacin + Metronidazole + Zinc Acetate
133	S.O. 4511 (E)	Zinc Carnosine + Oxetacaine
134	S.O. 4512 (E)	Oxetacaine + Magaldrate + Famotidine
135	S.O. 4513 (E)	Pantoprazole (as Enteric Coated Tablet) + Zinc Carnosine (as Film Coated Tablets)
136	S.O. 4514 (E)	Zinc Carnosine + Magnesium Hydroxide + Dried Aluminium Hydroxide + Simethicone
137	S.O. 4515 (E)	Zinc Carnosine + Sucralfate
138	S.O. 4516 (E)	Mebeverine & Inner HPMC capsule (Streptococcus Faecalis + Clostridium butyricum + Bacillus mesentricus +lactic Acid Bacillus
139	S.O. 4517 (E)	Clindamycin + Clotrimazole + Lactic Acid Bacillus
140	S.O. 4518 (E)	Sildenafil + Estradiol Valerate

S. No	Gazette No.	Drug Name
141	S.O. 4519 (E)	Clomifene Citrate + Ubidecarenone + Zinc + Folic Acid + Methylcobalamin + Pyridoxine + Lycopene + Selenium + LevocarnitineTartrate + L-Arginine
142	S.O. 4520 (E)	Thyroxine + Pyridoxine + Folic Acid
143	S.O. 4521 (E)	Gentamycin + Dexamethasone + Chloramphenicol + Tobramycin + Ofloxacin
144	S.O. 4522 (E)	Dextromethorphan + Levocetirizine + Phenylephrine + Zinc
145	S.O. 4523 (E)	Nimesulide + Loratadine + Phenylephrine + Ambroxol
146	S.O. 4524 (E)	Bromhexine + Phenylephrine + Chlorepheniramine Maleate
147	S.O. 4525 (E)	Dextromethorphan + Bromhexine + Guaiphenesin
148	S.O. 4526 (E)	Paracetamol +Loratadine + Phenylephrine + Dextromethorphan + Caffeine
149	S.O. 4527 (E)	Nimesulide + Phenylephrine + Caffeine + Levocetirizine
150	S.O. 4528 (E)	Azithromycin + Acebrophylline
151	S.O. 4529 (E)	Diphenhydramine + Terpine + Ammonium Chloride + Sodium Chloride + Menthol
152	S.O. 4530 (E)	Nimesulide + Paracetamol + Cetirizine + Phenylephrine
153	S.O. 4531 (E)	Paracetamol + Loratadine + Dextromethorphan + Pseudoepheridine + Caffeine
154	S.O. 4532 (E)	Chlorpheniramine Maleate + Ammonium Chloride + Sodium Citrate
155	S.O. 4533 (E)	Cetirizine + Phenylephrine + Paracetamol + Zinc Gluconate
156	S.O. 4534 (E)	Ambroxol + Guaiphenesin + Ammonium Chloride + Phenylephrine + Chlorpheniramine Maleate + Menthol
157	S.O. 4535 (E)	Dextromethorphen + Bromhexine + Chlorpheniramine maleate + Guaiphenesin
158	S.O. 4536 (E)	Levocetirizine + Ambroxol + Phenylephrine + Guaiphenesin
159	S.O. 4537 (E)	Dextromethorphan + Chlorpheniramine + Chlorpheniramine maleate
160	S.O. 4538 (E)	Cetirizine + Ambroxol + Guaiphenesin + Ammonium chloride + Phenylephrine + Menthol
161	S.O. 4539 (E)	Chlorpheniramine + Phenylephrine + Caffeine
162	S.O. 4540 (E)	Dextromethorphan + Triprolidine + Phenylephrine
163	S.O. 4541 (E)	Terpin hydrate + Dextromethorphan + Menthol
164	S.O. 4542 (E)	Dextromethorphan + Phenylephrine + Zinc Gluconate + Menthol
165	S.O. 4543 (E)	Chlorpheniramine + Codeine + Sodium citrate + Menthol syrup
166	S.O. 4544 (E)	Chlorpheniramine +Codeine + Sodium citrate + Menthol syrup + Enrofloxacin + Bromhexin
167	S.O. 4545 (E)	Bromhexine + Dextromethorphan + Phenylephrine + Menthol
168	S.O. 4546 (E)	Levofloxacin + Bromhexine
169	S.O. 4547 (E)	Levocetirizine + Ranitidine
170	S.O. 4548 (E)	Levocetirizine + Phenylephrine + Ambroxol + Guaiphenesin + Paracetamol
171	S.O. 4549 (E)	Cetirizine + Dextromethorphan + Phenylephrine + Zinc gluconate + Paracetamol + Menthol
172	S.O. 4550 (E)	Paracetamol + Pseudoephedrine + Dextromethorphan + Cetirizine
173	S.O. 4551 (E)	Diphenhydramine + Guaiphenesin + Ammonium chloride + Bromhexine
174	S.O. 4552 (E)	Chlorpheniramine + Dextromethorphan + Phenylephrine + Paracetamol
175	S.O. 4553 (E)	Dextromethorphan + Promethazine

S. No	Gazette No.	Drug Name
176	S.O. 4554 (E)	Diethylcabamazine Citrate + Cetirizine + Guaiphenesin
177	S.O. 4555 (E)	Pseudoephedrine + Dextromethorphan + Cetirizine
178	S.O. 4556 (E)	Chlorpheniramine + Phenylephrine + Dextromethorphan + Menthol
179	S.O. 4557 (E)	Ambroxol + Terbutaline + Dextromethorphan
180	S.O. 4558 (E)	Dextromethorphan + Chlorpheniramine + Guaiphenesin
181	S.O. 4559 (E)	Terbutaline + Bromhexine + Guaiphenesin + Dextromethorphan
182	S.O. 4560 (E)	Dextromethorphan + Triprolidine + Phenylephrine
183	S.O. 4561 (E)	Paracetamol + Dextromethorphan + Chlorpheniramine
184	S.O. 4562 (E)	Pholcodine + Phenylephrine + Promethazine
185	S.O. 4563 (E)	Codeine + Levocetirizine + Menthol
186	S.O. 4564 (E)	Dextromethorphan + Ambroxol + Guaifenesin + Phenylephrine + Chlorpheniramine
187	S.O. 4565 (E)	Cetirizine + Phenylephrine + Dextromethorphan + Menthol
188	S.O. 4566 (E)	Roxithromycin + Serratiopeptidase
189	S.O. 4567 (E)	Paracetamol + Phenylephrine + Triprolidine
190	S.O. 4568 (E)	Acetaminophen + Loratadine + Ambroxol + Phenylephrine
191	S.O. 4569 (E)	Cetirizine + Acetaminophen + Dextromethorphan + Phenylephrine + Zinc gluconate
192	S.O. 4570 (E)	Diphenhydramine + Guaifenesin + Bromhexine + Ammonium Chloride + Menthol
193	S.O. 4571 (E)	Cetirizine + Dextromethorphan + Zinc Gluconate + Menthol
194	S.O. 4572 (E)	Paracetamol + Phenylephrine + Desloratadine + Zinc Gluconate + Ambroxol
195	S.O. 4573 (E)	Levocetirizine + Montelukast + Acebrophylline
196	S.O. 4574 (E)	Dextromethorphan + Phenylephrine + Ammonium chloride + Menthol
197	S.O. 4575 (E)	Dextromethorphan + Bromhexine + Guaiphenesin+ Menthol
198	S.O. 4576 (E)	Acrivastine + Paracetamol + Caffeine + Phenylephrine
199	S.O. 4577 (E)	Naphazoline + Carboxy Methyl cellulose + Menthol + Camphor + Phenylephrine
200	S.O. 4578 (E)	Dextromethorphan + Cetirizine
201	S.O. 4579 (E)	Nimesulide + Paracetamol + Levocetirizine + Phenylephrine + Caffeine
202	S.O. 4580 (E)	Terbutaline + Ambroxol + Guaiphenesin + Zinc + Menthol
203	S.O. 4581 (E)	Codeine + Chlorpheniramine + Alcohol syrup
204	S.O. 4582 (E)	Dextromethorphan + Phenylephrine + Guaifenesin + Triprolidine
205	S.O. 4583 (E)	Diethylcarbamazine + Cetirizine + Ambroxol
206	S.O. 4584 (E)	Ethylmorphine + Noscapine + Chlorpheniramine Maleate
207	S.O. 4585 (E)	Cetirizine + Dextromethorphan + Ambroxol
208	S.O. 4586 (E)	Ambroxol + Guaifenesin + Phenylephrine + Chlorpheniramine
209	S.O. 4587 (E)	Paracetamol + Phenylephrine + Chlorpheniramine + Zinc Gluconate
210	S.O. 4588 (E)	Dextromethorphan + Phenylephrine + Cetirizine + Paracetamol + Caffeine

S. No	Gazette No.	Drug Name
211	S.O. 4589 (E)	Levocetirizine + Dextromethorphan + Zinc
212	S.O. 4590 (E)	Paracetamol + Phenylephrine + Levocetirizine + Caffeine
213	S.O. 4591 (E)	Chlorpheniramine + Ammonium Chloride + Sodium Chloride
214	S.O. 4592 (E)	Paracetamol + Dextromethorphan + Bromhexine + Phenylephrine + Diphenhydramine
215	S.O. 4593 (E)	Salbutamol + Bromhexine + Guaiphenesin + Menthol
216	S.O. 4594 (E)	Chlorpheniramine + Ammonium Chloride + Noscapine + Sodium Citrate
217	S.O. 4595 (E)	Cetirizine + Dextromethorphan + Bromhexine + Guaifenesin
218	S.O. 4596 (E)	Diethylcarbamazine + Chlorpheniramine + Guaifenesin
219	S.O. 4597 (E)	Ketotifen + Cetirizine
220	S.O. 4598 (E)	Terbutaline + Bromhexine + Etofylline
221	S.O. 4599 (E)	Ketotifen + Theophylline
222	S.O. 4600 (E)	Ambroxol + Salbutamol + Theophylline
223	S.O. 4601 (E)	Cetirizine + Nimesulide + Phenylephrine
224	S.O. 4602 (E)	Chlorpheniramine + Phenylephrine + Paracetamol + Zinc Gluconate
225	S.O. 4603 (E)	Acetaminophen + Guaifenesin + Dextromethorphan + Chlorpheniramine
226	S.O. 4604 (E)	Cetirizine + Dextromethorphan + Phenylephrine + Tulsi
227	S.O. 4605 (E)	Cetirizine + Phenylephrine + Paracetamol + Ambroxol + Caffeine
228	S.O. 4606 (E)	Guaifenesin + Dextromethorphan
229	S.O. 4607 (E)	Levocetirizine + Paracetamol + Phenylephrine + Caffeine
230	S.O. 4608 (E)	Ketotifen + Levocetrizine
231	S.O. 4609 (E)	Paracetamol + Levocetirizine + Phenylephrine + Zinc Gluconate
232	S.O. 4610 (E)	Paracetamol + Phenylephrine + Triprolidine + Caffeine
233	S.O. 4611 (E)	Caffeine + Paracetamol + Phenylephrine + Cetirizine
234	S.O. 4612 (E)	Dextromethorphan + Phenylephrine + Guaifenesin
235	S.O. 4613 (E)	Ambroxol + Levocetirizine + Phenylephrine + Guaiphenesin + Menthol
236	S.O. 4614 (E)	Pseudoephedrine + Cetirizine
237	S.O. 4615 (E)	Dextromethorphan + Chlorpheniramine + Ammonium Chloride + Menthol
238	S.O. 4616 (E)	Paracetamol + Caffeine + Phenylephrine + Chlorpheniramine
239	S.O. 4617 (E)	Salbutamol + Aminophylline + Guaifenesin
240	S.O. 4618 (E)	Salbutamol + Theophylline + Bromhexine
241	S.O. 4619 (E)	Chlorpheniramine + Dextromethorphan + Guaifenesin + Phenylephrine
242	S.O. 4620 (E)	Caffeine + Paracetamol + Chlorpheniramine
243	S.O. 4621 (E)	Ammonium Chloride + Dextromethorphan + Cetirizine + Menthol
244	S.O. 4622 (E)	Dextromethorphan + Paracetamol+ Cetirizine + Phenylephrine
245	S.O. 4623 (E)	Chlorpheniramine +Terpin + Antimony Potassium Tartrate + Ammonium chloride + Sodium Citrate + Menthol

S. No	Gazette No.	Drug Name
246	S.O. 4624 (E)	Terbutaline Sulphate + Etofylline + Ambroxol
247	S.O. 4625 (E)	Paracetamol + Codeine + Chlorpheniramine
248	S.O. 4626 (E)	Paracetamol + Pseudoephedrine + Cetirizine + Caffeine
249	S.O. 4627 (E)	Chlorpheniramine + Ammonium Chloride + Menthol
250	S.O. 4628 (E)	N-Acetyl Cysteine + Ambroxol + Phenylephrine + Levocetirizine
251	S.O. 4629 (E)	Dextromethorphan + Phenylephrine + Triprolidine + Menthol
252	S.O. 4630 (E)	Salbutamol + Cetirizine + Ambroxol
253	S.O. 4631 (E)	Dextromethorphan + Phenylephrine + Bromhexine + Guaifenesin + Chlorpheniramine
254	S.O. 4632 (E)	Nimesulide + Cetirizine + Phenylephrine
255	S.O. 4633 (E)	Naphazoline + Chlorpheniramine + Zinc Sulphate + Boric Acid + Sodium Chloride + Chlorobutol
256	S.O. 4634 (E)	Dextromethorphan + Phenylephrine + Guaifenesin + Cetirizine + Acetaminophen
257	S.O. 4635 (E)	Guaifenesin + Bromhexine + Chlorpheniramine + Paracetamol
258	S.O. 4636 (E)	Chlorpheniramine + Ammonium Chloride + Chloroform + Menthol
259	S.O. 4637 (E)	Salbutamol + Choline Theophyllinate + Ambroxol
260	S.O. 4638 (E)	Pseudoephedrine + Bromhexine
261	S.O. 4639 (E)	Cetirizine + Phenylephrine + Paracetamol + Caffeine + Nimesulide
262	S.O. 4640 (E)	Dextromethorphan + Cetirizine + Guaifenesin + Ammonium Chloride
263	S.O. 4641 (E)	Ambroxol + Salbutamol + Choline Theophyllinate + Menthol
264	S.O. 4642 (E)	Paracetamol + Chlorpheniramine + Ambroxol + Guaifenesin + Phenylephrine
265	S.O. 4643 (E)	Chlorpheniramine + Vasaka + Tolubalsam + Ammonium Chloride + Sodium Citrate + Menthol
266	S.O. 4644 (E)	Bromhexine + Cetirizine + Phenylephrine + Guaifenesin+ Menthol
267	S.O. 4645 (E)	Dextromethorphan + Ambroxol + Ammonium Chloride + Chlorpheniramine + Menthol
268	S.O. 4646 (E)	Dextromethorphan + Phenylephrine + Cetirizine + Zinc + Menthol
269	S.O. 4647 (E)	Terbutaline + N-Acetyl L- Cysteine + Guaifenesin
270	S.O. 4648 (E)	Calcium Gluconate + Levocetirizine
271	S.O. 4649 (E)	Paracetamol + Levocetirizine + Pseudoephedrine
272	S.O. 4650 (E)	Salbutamol + Choline Theophyllinate + Carbocisteine
273	S.O. 4651 (E)	Chlorpheniramine + Vitamin C
274	S.O. 4652 (E)	Calcium Gluconate + Chlorpheniramine + Vitamin C
275	S.O. 4653 (E)	Chlorpheniramine + Paracetamol + Pseudoephedrine + Caffeine
276	S.O. 4654 (E)	Guaifenesin + Bromhexine + Chlorpheniramine + Phenylephrine + Paracetamol + Serratiopeptidase (as enteric coated granules)10000 SP Units
277	S.O. 4655 (E)	Paracetamol + Pheniramine
278	S.O. 4656 (E)	Betamethasone + Fusidic Acid + Gentamycin + Tolnaftate + Iodochlorhydroxyquinoline (ICHQ)
279	S.O. 4657 (E)	Clobetasol + Ofloxacin + Miconazole + Zinc Sulphate
280	S.O. 4658 (E)	Clobetasole + Gentamicin + Miconazole + Zinc Sulphate

S. No	Gazette No.	Drug Name
281	S.O. 4659 (E)	Levocetirizine + Ambroxol + Phenylephrine + Paracetamol
282	S.O. 4660 (E)	Permethrin + Cetrimide + Menthol
283	S.O. 4661 (E)	Beclomethasone + clotrimazole + neomycin + iodochlorohydroxyquinone
284	S.O. 4662 (E)	Neomycin + Doxycycline
285	S.O. 4663 (E)	Ciprofloxacin + Fluocinolone + Clotrimazole + Neomycin + Chlorocresol
286	S.O. 4664 (E)	Clobetasol + Ofloxacin + Ketoconazole + Zinc Sulphate
287	S.O. 4665 (E)	Betamethasone + Gentamicin + Tolnaftate + Iodochlorhydroxyquinoloine
288	S.O. 4666 (E)	Clobetasol + Gentamicin + Tolnaftate + Idochlorhydroxyquinone + Ketoconazole
289	S.O. 4667 (E)	Allantoin + Dimethieone + Urea + Propylene + Glycerin + Liquid paraffin
290	S.O. 4668 (E)	Acriflavine + Thymol + Cetrimide
291	S.O. 4669 (E)	Betamethasone + Neomycin + Tolnaftate + Iodo Chloro Hydroxy Quinoline + Chlorocresol
292	S.O. 4670 (E)	Clobetasol + Neomycin + Miconazole + Clotrimazole
293	S.O. 4671 (E)	Ketoconazole + Tea Tree oil + Allantion + zinc Oxide + Aloe Vera + Jojoba oil + Lavander oil + Soap noodles
294	S.O. 4672 (E)	Clobetasol + Ofloxacin + Ornidazole + Terbinafine
295	S.O. 4673 (E)	Clobetasol + Neomycin + Miconazole + Zinc Sulphate
296	S.O. 4674 (E)	Beclomethasone + Neomycin + Tolnaftate + Iodochlorhydroxyquinoline + Chlorocresol
297	S.O. 4675 (E)	Betamethasone + Gentamycin + Zinc Sulphate + Clotrimazole + Chlorocresol
298	S.O. 4676 (E)	Borax + Boric acid + Naphazoline + Menthol + Camphor + methyl hydroxy benzoate
299	S.O. 4677 (E)	Bromhexine + Dextromethorphan
300	S.O. 4678 (E)	Dextromethorphan + Chlorpheniramine + Bromhexine
301	S.O. 4679 (E)	Menthol + Anesthetic Ether
302	S.O. 4680 (E)	Dextromethorphan + Chlopheniramine + Ammonium Chloride + Sodium Citrate + Menthol
303	S.O. 4681 (E)	Ergotamine Tartrate + Belladona dry extract + Caffeine + Paracetamol
304	S.O. 4682 (E)	Gliclazide 40mg + Metformin 400mg
305	S.O. 4683 (E)	Paracetamol + Ambroxol + Phenylephrine + Chlorpheniramine
306	S.O. 4684 (E)	Ofloxacin + Ornidazole suspension
307	S.O. 4685 (E)	Albuterol + Etofylline + Bromhexine + Menthol
308	S.O. 4686 (E)	Albuterol + Bromhexine + Theophylline
309	S.O. 4687 (E)	Salbutamol + Hydroxyethyltheophylline (Etofylline) + Bromhexine
310	S.O. 4688 (E)	Paracetamol + Phenylephrine + Levocetirizine + Sodium Citrate

S. No	Gazette No.	Drug Name
311	S.O. 4689 (E)	Paracetamol + Propyphenazone + Caffeine
312	S.O. 4690 (E)	Guaifenesin + Diphenhydramine + Bromhexine + Phenylephrine
313	S.O. 4691 (E)	Dried Aluminum Hydroxide Gel + Propantheline + Diazepam
314	S.O. 4692 (E)	Bromhexine + Phenylephrine + Chlorpheniramine + Paracetamol
315	S.O. 4693 (E)	Beclomethasone + Clotrimazole + Gentamicin + Iodochlorhydroxyquinoline
316	S.O. 4694 (E)	Telmisartan + Metformin
317	S.O. 4695 (E)	Ammonium Citrate + Vitamin B 12 + Folic Acid + Zinc Sulphate
318	S.O. 4696 (E)	Levothyroxine + Pyridoxine + Nicotinamide
319	S.O. 4697 (E)	Benfotiamine + Metformin
320	S.O. 4698 (E)	Thyroid + Thiamine + Riboflavin + Pyridoxine + Calcium Pantothenate + Tocopheryl Acetate + Nicotinamide
321	S.O. 4699 (E)	Ascorbic Acid + Manadione Sodium Bisulphate + Rutin + Dibasic Calcium Phosphate + Adrenochrome mono Semicarbazone
322	S.O. 4700 (E)	Phenylephrine + Chlorpheniramine + Paracetamol + Bromhexine + Caffeine
323	S.O. 4701 (E)	Clotrimazole + Beclomethasone + Lignocaine + Ofloxacin + Acetic Acid + Sodium Methyl Paraben + Propyl Paraben
324	S.O. 4702 (E)	Nimesulide + Levocetirizine
325	S.O. 4703 (E)	Ofloxacin + Ornidazole injection
326	S.O. 4704 (E)	Gemifloxacin + Ambroxol
327	S.O. 4705 (E)	Glucosamine + Ibuprofen
328	S.O. 4706 (E)	Etodolac + Paracetamol
329	S.O. 4707 (E)	Benzoxonium Chloride + Lidocaine
330	S.O. 4708 (E)	Paracetamol + Prochlorperazine Maleate
331	S.O. 4709 (E)	Amoxicillin 250 mg + Potassium Clavulanate Diluted 62.5 mg
332	S.O. 4710 (E)	Paracetamol + Prochlorperazine
333	S.O. 4711 (E)	Glimepiride + Pioglitazone + Metformin
334	S.O. 4712 (E)	Glibenclamide + Metformin (SR) + Pioglitazone

OBITUARY

We regret to inform, Dr. K. A. Narendra Nath, passed away on 16th October 2018

He started his career as senior executive in M/s. TTK Health Care Ltd., and elevated to Vice President (Technical). He was also Director – R & D, American Remedies.

He was a founder Trustee of our Trust, since 1989. He was an active Governing Body Member for the last 15 years. He had been participating in all the meetings and guiding us for the activities for the Trust. He was also actively involved in "Indian Pharmaceutical congress" held in Chennai.

Our condolences to his family members and pray for his soul be rest in peace.

INFORMATION

M. PHARM & PHARM D SCHOLARSHIPS 2017-18 AWARDED BY TNPSWT

Profile of 3rd Rank

PHARMACEUTICS

Name: Ms. R. Nivetha

Project Title: Activity enhancement of Euphorbia hirta plant extracts by nano phytosomal formulation for the treatment of psoriasis

College: Arulmigu Kalasalingam College of Pharmacy, Krishnankoil

Guide's Name: Dr. V. Lavakumar

PHARMACEUTICAL CHEMISTRY

Name: Mr. Katike Basheer Ahmed

Project Title: In-silico design, synthesis and evaluation of coumate analogues as estrogen receptor Inhibitors for breast cancer therapy

College: J. S. S College of Pharmacy, Ooty

Guide's Name: Dr. S. Jubie

PHARMACEUTICAL ANALYSIS

Name: Ms. Tshamata Shakya

Project Title: Stability indicating studies of Omega-3 Fatty Acids in Flaxseed Oil to improve shelf life of the moderators and their genotoxicity studies of the degraded product(S).

College: J. S. S College of Pharmacy, Ooty

Guide's Name: Dr. M. R. Jeyaprakash

PHARMACOLOGY

Name: Mr. Navaf M T

Project Title: Evaluation of the neuro-protective activity of Desferrioxamine in combination with Dextromethorphan in 6- OHDA induced Parkinson's Rat model.

College: J. S. S College of Pharmacy, Ooty

Guide's Name: Ms. K. S. Santilna

PHARMACOGNOSY

Name: Mr. K. Rajkumar

Project Title: Green Synthesis of Silver nanoparticle using marine seagrass and the evaluation of anti-diabetic activity on Halodule piniflia.

College: College of Pharmacy, Madras Medical College, Chennai

Guide's Name: Dr. P. Muthusamy

Name: Ms. R. Suganya

Project Title: Studies on the leaves of Cardiospermum halicacabum L. and experimental assessment on lipid absorption inhibition and cardio protection of its bioactive insulinomimetic D-pinitol fraction

College: College of Pharmacy, Madurai Medical College, Madurai

Guide's Name: Dr. K. Periyanayagam

PHARMACY PRACTICE

Name: Ms. Rittumol Varghese

Project Title: Determination of health related quality of life in stroke patients and managing the post stroke spasticity at a tertiary care teaching Hospital in south India.

College: COP, Sri Ramakrishna Institute of Paramedical Sciences, Coimbatore

Guide's Name: Dr. S. Sriram

PHARM D

Name: Ms. Kolli Sowjanya,
Mr. Rawa Nawzad Najm,
Mr. Tulasi Raja

Project Title: A comparative study on clinical safety and efficacy of Trimetazidine as an add on with conventional therapy among coronary artery disease patients.

College: SRM College of Pharmacy, SRM University, Kattankulathur

Guide's Name: Mrs. S. Sarumathy

EVENTS

Pharma Knowledge and Training Institute (Finishing School)
7th Training on
Industrial Orientation Training for Production and Quality Management Personnel

The 7th 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 **10th September 2018 to 29th September 2018.** The total 34 trainees from Karpagam College of Pharmacy, Coimbatore, Madras Medical College, Chennai, PSG College of Pharmacy, Coimbatore, KMCH College of Pharmacy, Coimbatore, Annai Velanakanni College of Pharmacy, Chennai students were trained in this training programme.

The Inaugural function of the training programme was held on 10th September 2018, and the guest of honnour's were Mr. J. Jayaseelan, Vice President, IPA Industry Pharmacy division, Dr. A. Jerad Suresh, Principal, COP, MMC, Chennai and Dr. S. Mohan, Principal, Karpagam College of Pharmacy, Chennai.

The students were given training both theoretically and practical on the subject of "Industrial Orientation Training on Production and Quality management Personnel". 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, and Maintenance of record of Drugs & Pharmaceuticals.
- Calibration of QC equipments, Reference Standards and Working Standards, Reference / retention samples storage.
- cGMP's for manufacturing including entry & exit procedures.
- Plant Design & Site Master File.
- ICH guidelines for production & Quality Control of Pharmaceuticals.

- 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 Assessment.
- Change control, Deviation control and their importance.
- 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.
- Documentation and records in Production and QC
- Standard Operating Procedures
- Sampling of Raw Materials, Packing materials, In- process Materials and Finished products.
- What is Pharmacopoeia, various Pharmacopoeias used world over, how to use pharmacopoeia, monographs, their explanation & general notices in Pharmacopeia and Reference Standards.
- Tablets - 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.
- 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.
- Preventive maintenance, Predictive maintenance & Break down maintenance.
- Introduction to Theory of Chromatography & Spectrophotometry.
- TLC Gas Chromatography (GC), High Performance Liquid Chromatography (HPLC) a brief introduction.
- Basic Calculations in Quality Control, Dilutions and Statistical Analysis, Qualitative Analysis, Quantitative Analysis & Elemental Analysis.
- Analytical method validation

- Dissolution & its Importance, Methods used in Dissolution Testing.
- General requirements for Tablets, Capsule, Oral liquids & external preparations.
- Air Systems, Water Systems, their sampling and testing.
- Microbiology - An Introduction, Microbiology for non-sterile preparations.
- 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.
- Stability Testing, Accelerated and Real Time Studies, Packaging Material Stability, Their Testing, Their Importance with Respect to the Product Stability.
- 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.
- Capsules - 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.
- Batch Manufacturing Records, Batch Packing Records and importance of online recording Basics of production planning & Inventory Control.
- Quality by Design (QbD)
- 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-
- Preparation and Standardization of Herbal Formulations.
- Soft Skill

The above subjects were taught by well experienced senior level pharma industry manufacturing and quality assurance technical personnel through power point presentation. The faculties who had taken theory classes on the above subjects are as follows.

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

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

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

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

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

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

Mr. N. Chandar, Pharma Consultant,

Dr. D. Natarajan, Pharma Consultant

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

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

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

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

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

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

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

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

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

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

Mr. V. Saravanan, IICMS, Chennai

Dr. Devasena Kannan, IICMS, Chennai

Dr. Balaji, IICMS, Chennai

Ms. Soujanya, IICMS, Chennai

Dr. R. Ilavarasan, Assistant Director (S-3) Institute In-charge, Captain Srinivasa Murthy Regional Ayurveda Drug Development Institute, Chennai

Mrs. Jusna, Manager, L & D, Ripe Consulting Services Pvt. Ltd., Chennai

PKTI – 7th Training Programme

Inaugural address by Dr. A. Jerad Suresh

Felicitation to Dr. S. Mohan

Felicitation to Mr. N. Chandar

Lecture by Mr. S. Sridhar

Trainees

Lecture by Ms. Soujanya

Group Photo of Trainees

Valedictory function guest & Trainees

Valedictory address by our chairman Mr. S. Veerramani

Prize distribution to Trainees

Certificate distribution

Address by Mr. Sanjay Kumar Dasmohapatra

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 for 6 days.

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 3 merit awards given during the valedictory function.

Valedictory Function

The Valedictory function was held on 1st October 2018. The Chief guest of the function was Mr. S. V. Veerramnai, Chairman of our Trust and M/s. Fourrts (India) Labs Pvt Ltd., Prof. K. Chinnaswamy, President, Tamilnadu Pharmacy Council, Mr. Sanjay Kumar Dasmohapatra, Vice President, M/s. Medopharm, Mr. A. Krishna Dev, Vice Chairman, TNPSW Trust, . R. Sabapathy, Executive Director, M/s. Medopharm, Dr. N. Murugesan, Director – CDTL, Chennai, Mr. D. Srinivasa Rao, GM – Plant Operations, M/s. Apex Laboratories P Ltd., were the guest of honours. R. Narayanaswamy, Director, PKTI Welcomed the gathering and explained about the 7thtraining programme. Certificates were distributed all the trainees. Mr. N. Sreenivasen, Secretary, TNPSWT proposed vote of thanks.

Placement Interview

Placement interview conducted for the trainees on 1st October 2018 and the participants companies were M/s. Apex Laboratories Pvt. Ltd., Alathur, Chennai, M/s. The Madras Pharmaceuticals, OMR, Chennai and M/s. Scitus Pharma Services Pvt. Ltd., Chennai.

All the trainees who are interested in job got the placement.

DEVELOPING STRATEGIES FOR FFECTIVE IMPLEMENTATION OF REVISED PHARMACY CURRICULUM

Faculty of Pharmacy, a Constituent College of Sri Ramachandra Institute of Higher Education and Research (DU), conducted a Continuing Education Program (CEP) for three days from 16th to 18th July 2018, for 31 pharmacy teachers across South India. The theme of the program was “Developing strategies for effective Implementation of revised Pharmacy Curriculum”. The CEP was supported by the PCI in the form of funding and resources. The program was inaugurated by the Guest of Honour was Dr. B. Suresh, President of the PCI, New Delhi, and Prof. K. Chinnasamy, President, Indian Association of Colleges of Pharmacy, Tamil Nadu State Pharmacy Council, delivered the felicitation address. Eminent members of the PCI, Dr. B. Jayakar, Registrar, Vinayaka Missions Research Foundations (DU), Salem and Dr. T. K. Ravi, Principal, Sri Ramakrishna Institute of Pharmaceutical Sciences College of Pharmacy, Coimbatore, and Prof. V. Gopal, Principal, College of Pharmacy, Academic Registrar, MTPG&RIHS, Puducherry delivered lectures on Curricular aspects, teaching learning methodologies and Mr. J. Jayaseelan, Delvin Formulations, Chennai, delivered a lecture on Industry expectations from a Pharmacy graduate. Other lecture and hands on sessions included framing of objectives, competency based curriculum, question paper setting, teaching learning styles, ICT enabled teaching and internal assessment strategies. A panel discussion was held on the third day with the panellists Dr. A. Ravikumar, Dean Education, SRIHER (DU), Dr. V. Gopal, Principal and Registrar MTPG & RIHS, Puducherry, Dr. D. Chamundeeswari, Principal, Faculty of Pharmacy, SRIHER (DU), Dr. C. Uma Maheswara Reddy, Professor & Head, Dept. of Pharmacology, Faculty of Pharmacy, SRIHER (DU), and Dr. R. Jothi Malar, Professor, Department of Biochemistry, SRIHER (DU). The program concluded with a Valedictory on 18/7/2018.

NSS DAY CELEBRATION, MADRAS MEDICAL COLLEGE

The NSS Day Celebration was organised at Madras Medical College on 24.09.2018. The Dean, Dr. R. Jayanthi, MD, FRCP(GLASG) was the Chief Guest for the function. Dr. Narayanasamy, Medical Superintendent, Madras Medical College and Prof. Dr. Raghunanthan, Deputy Medical Superintendent, Madras Medical College were the other guests of honour. Dr. A. Jerad Suresh, Principal, College of Pharmacy, Madras Medical College, delivered the welcome address on the occasion. The agenda of the event as chalked out by Dr. N. Deattu, NSS Programme Coordinator, Madras Medical College, included Creating awareness on Ozone Layer depletion, Protecting the environment by avoiding plastics and Creating a green environment. As an initiative of making the campus green, The Dean, Madras Medical College, handed over saplings to the NSS Volunteers. The NSS Volunteers Pledge was taken by the volunteers to mark the significance of NSS Day.

WORLD PHARMACIST DAY CELEBRATIONS - SRI RAMACHANDRA INSTITUTE

Faculty of Pharmacy, Sri Ramachandra Institute of Higher Education and Research (Deemed to be University), (SRIHER) conducted World Pharmacists Day Celebrations on 24/9/2018 and 25/9/2018 in the campus. The celebrations started on 24/9/2018 with Elocution competition in English and Tamil on the theme (Pharmacists: Your Medicines experts" and a slogan competition on the theme. On 25/9/2018, Poster competitions, competition on role plays and skits were held on the theme, competition on Best out of waste were conducted and the participation included the Pharmacy students, the teaching and non-teaching faculty of Faculty of Pharmacy, and the hospital pharmacists of Sri Ramachandra Medical Center and Hospital. The celebrations and prize distributions started with a welcome address by Dr. D. Chamundeeswari, Principal, Faculty of Pharmacy, SRIHER(DU). Dr. P. V. Vijayaraghavan, Vice-Chancellor, SRIHER(DU), released the Annual report of Faculty of Pharmacy for the academic year 2017-2018 and delivered the felicitation address. Dr. K. Balaji Singh, Dean of students, SRIHER(DU), delivered the Presidential address.

Dr. S. P. Thyagarajan, Professor of Eminence & Dean (Research), SRIHER(DU), delivered the Keynote address. Mr. R. Thiruvengadam, Managing Director, Tablets (India) Ltd., Chennai was the Chief Guest of the Program. He delivered the inaugural address and distributed cash prizes for the winners of the competitions. Dr. S. Umamaheswari, Professor of Pharmacology, Faculty of Pharmacy, SRIHER(DU), proposed the vote of thanks. Around 300 students, pharmacists and faculty members participated.

WORLD PHARMACIST DAY CELEBRATIONS – IPA – COIMBATORE LOCAL BRANCH

Indian Pharmaceutical Association - Coimbatore Local Branch in coordination with PSG College of Pharmacy celebrated the World Pharmacist Day on 25th September 2018. The function was organized at PSG IMS&R Auditorium, Coimbatore.

Thirteen Pharmacy colleges in Coimbatore were participated in this event. Mr. J. Jayaseelan, Vice President – Industrial Division, Indian Pharmaceutical Association, Mumbai was the Chief Guest and Prof. (Dr.) K. Chinnasamy, President, Tamilnadu Pharmacy Council, Chennai and Thiru. Marimuthu, Senior Drug Inspector, Coimbatore Zone was the Guests of Honor.

Dr. S. Ramalingam, Dean, PSG IMS&R have consented to preside over the function. Dr. T. K. Ravi, President, IPA Coimbatore Local Branch, Principal, College of Pharmacy, SRIPMS welcomed the gatherings. Around 700 pharmacy students were attended this mega program. In this connection an Elocution competition has been organized for the Pharmacy students on the theme “Pharmacists are your medicine experts'. Fifteen students from different pharmacy colleges were participated in the competitions. 1st, 2nd & 3rd prizes were won by Ms. Hareni Iyer, B Pharm, PSG College of Pharmacy, Ms. Renny Rozario, B Pharm, Sri Ramakrishna College of Pharmacy and Ms. K. Bharathi, B Pharm, PSG College of Pharmacy respectively. The winners have received cash prize / certificate & a book written by APJ Abdul Kalam. The prizes were given to the winners by the dignitaries.

Dr. M. Ramanathan, Secretary, IPA Coimbatore Local Branch, Principal, PSG College of Pharmacy delivered the vote of thanks to all the IPA members and thanked PSG Management for sponsoring the event.

Antibiotics Becoming Ineffective for Neonates

First line antibiotics are becoming ineffective in treatment of neonates (under-28-day children) suffering from different sorts of bacterial infections, shows a study conducted by city-based doctors.

Commonly used antibiotic cefepime was found ineffective in 36% of patients suffering from sepsis and another most common antibiotic amoxyclav was found resistant in 52% of sepsis cases of neonates included in the study.

State's biggest government-run child-specialty JK Lon hospital doctors have come up with a study 'Clinical and Bacteriological Profile of Neonatal Sepsis with Emerging Resistance Patterns', which has also been published in International Journal of Contemporary Paediatrics' November-December edition. The findings in the study have expressed concern on neonatal sepsis with emerging resistance patterns against commonly used antibiotics.

"For the past 30 to 40 years, we have been using a set of first line antibiotics. Whenever a suspected case (neonate) of sepsis is brought to the hospital, we start empirical treatment with first line antibiotics, which belongs to cephalosporins class and aminoglycoside class. But, now we have found in the study that bacteria causing sepsis is now becoming resistant to most of the drugs belonging to these two class of antibiotics," said Dr Dhan Raj Bagri, who conducted the study, which was conducted in JK Lon Hospital.

The doctors use first line antibiotics in combination form. When a suspected sepsis neonate is brought to the hospital, the doctors immediately provide him treatment by using combination of drugs such as cefotaxime and amikacin, cefotaxime and gentamycin, ampicillin and amikacin and more such combination of first line antibiotic drugs. In the combination of antibiotic drugs, doctors use one antibiotic for killing gram positive organism and one for killing gram negative organism.

They use combination of drug as they are yet to ascertain what kind of organism (bacteria) is present in the blood causing sepsis. For ascertaining the kind of bacteria present in the blood, the doctors conduct culture test. The report of culture test is issued after 48 hours. The culture report also shows the sensitivity of particular drugs on bacteria causing sepsis.

The study shows the antibiotic sensitivity pattern using the culture report of 150 confirmed cases (neonates) of sepsis. The sensitivity pattern shows a high degree of resistance to commonly used antibiotics belonging to cephalosporins class and aminoglycoside class such as ampicillin, gentamycin, amikacin, cefotaxime, ceftriaxone, cefepime and Amoxyclav.

The study included 500 neonates, who were suspected cases of sepsis, brought to JK Lon hospital in past two years and were admitted to neonatal ICU (NICU). Out of 500 suspected cases of sepsis, 150 were culture proven sepsis. Culture proven sepsis means that they were tested positive for sepsis. In the study, only culture proven sepsis cases were included.

There are two different kinds of bacteria causing sepsis — gram positive and gram negative. The gram negative organism has the highest resistance to cefepime (36%),

while cefotaxime (24%), amikacin (22%), ceftriaxone (19%), gentamycin (13%) and amoxyclav were found ineffective in 10% of the cases.

For gram positive organisms' infection causing sepsis, highest resistance was noted from amoxyclav (52%) followed by azithromycin (34%), ciprofloxacin (32%), cefotaxime (30%), cefoxitin (28%) and cotrimoxazole (24%).

Source: *ET Healthworld, 27th October 2017*

Big Pharma Companies Set to Return to Double-digit Growth this Fiscal: Crisil

After two consecutive years of single-digit expansion, big Indian drug firms are expected to return to double-digit growth in the current fiscal aided by recovery in US sales, weakening of the rupee and revival of domestic demand, ratings agency Crisil said.

The return to double-digit growth would help the homegrown pharma companies, with turnover of Rs 1,000 crore or more, to weather a sharp rise in input costs.

As per Crisil, green shoots are already visible in the first quarter for 20 of these listed drug-makers, which account for three-fourths of the pharma industry revenue.

The US and the domestic markets contribute on average 30 per cent and 35 per cent of their revenues, respectively.

"The US market is witnessing an upturn after de-growth in five of the past eight quarters through June 2018," Crisil Ratings Senior Director Anuj Sethi said.

Revenue from US grew 7 per cent in the first quarter of this fiscal compared to a muted show in the same quarter of 2017-18, he added.

"We expect 6-7 per cent growth this fiscal, backed by lower intensity of regulatory issues, faster product approvals and improving share of complex products. This will also help offset pricing pressure faced in existing products," Sethi said.

"Domestic revenues of big pharma companies is expected to grow 12-13 per cent this fiscal, given better access to healthcare and deeper penetration of health insurance," Sethi noted.

The recovery is already reflected in the first quarter with the domestic segment growing 25 per cent year-on-year, albeit on a low base, as the first quarter of the previous year was severely impacted by retailers destocking ahead of the goods and services tax implementation, he added.

Source: *ET Healthworld, 29th October 2018*

Local Pharma Formulators to Benefit from New USFDA Generic Guidance: Report

The recent guidance from the US Food & Drug Administration (USFDA) on complex generics is expected to provide more clarity to US-focused Indian pharmaceutical formulators in preparing and submitting abbreviated new drug applications (ANDAs), says a report.

This will help domestic pharma formulators with pending ANDA approvals to reduce review cycles and expedite approvals, says a weekend report by India Ratings.

The current guidance dated October 9 is specific to complex transdermal and topical products.

The agency in its mid-year FY19 pharma outlook had identified the lack of scientific and regulatory clarity about complex drugs as one of the key hurdles for approvals of complex products.

Indian pharmaceutical formulators have indicated low double-digit pricing erosion for their base portfolio at end-FY18 and were exiting highly generic commercially unviable products and pruning R&D pipeline.

The regulatory clarity will benefit formulators such as Lupin (inhalation, injectable and ophthalmic), Cadila Healthcare (inhalation and injectable), Cipla (ophthalmic, injectable and inhalation), Torrent Pharmaceuticals (injectable, dermatology and ophthalmic), Aurobindo Pharma (ophthalmic and injectable) and Sun Pharmaceutical Industries (dermatology, ophthalmic and oncology) over the near to medium term.

In this scenario, a ramp-up in the less competitive complex generic portfolio through stepping up investments is a sustainable solution, Ind-Ra noted.

According to Ind-Ra's analysis, the US transdermal market consists of 19 molecules across pain management, cardiology, gynaecology, gastro-intestinal, neurology and anti -addiction.

Among these 10 molecules there is no generic player, six molecules with one generic player and three molecules with four generic players.

Among the 10 molecules with no generic players, the patents for five molecules have expired and balance have expiries over 2019-2020 and beyond.

The transdermal molecules had a cumulative market size in the range of USD 3.5 billion-4 billion at end-2017.

Some of the large molecules in terms of market size include clonidine, estradiol, fentanyl and testosterone.

According to the analysis, the US complex topical patch market consists of four molecules across dermatology and pain management therapies.

Out of these, one molecule has two generic players (non-Indian) while the other three molecules have not been generisied.

These three molecules have patent expiring in April 2019, June 2021 and August 2027, respectively.

These molecules had a cumulative market size of around USD1.5 billion at end-2017 with lidocaine the largest molecule in terms of market size, it said.

Lupin and Dr Reddys Laboratories are the only Indian players having a presence with one molecule each in the generic transdermal space.

Indian formulators such as Cadila Healthcare, Cipla and Glenmark Pharmaceuticalshave ANDAs pending approvals in the topical space while Cadila Healthcare is the only player with significant ANDA filings in the transdermal space and also has a dedicated manufacturing facility.

In FY17, Cadila Healthcare had also acquired one transdermal patch ANDA from Teva Pharmaceutical Industries.

The pharmaceutical industry now also looks forward to the receipt of similar guidance on scientific, regulatory and legal issues for other complex generics as highlighted by USFDA under the Drug Competition Action Plan.

Other than transdermal, clarity is being sought by generic developers for other complex differentiated platforms such as liposomal/colloidal formulations, inhalational drug- device combinations like metered dosage inhaler, extended release injectable and ophthalmic products pending for approvals from the regulator or under development.

Indian formulators have also resorted to the acquisitions of products and technology platforms, to build niche capabilities which are at various stages of integration.

However, their ability to compete/close the gap created by large established global peers in the complex generic space will remain critical, it added.

Source: *ET Healthworld, 28th October 2018*

High Trade Margins Push up Drug Prices: CCI

Concerned over the spiralling healthcare costs, the Competition Commission of India (CCI) has pointed at "unreasonably high trade margins" as responsible for exorbitant drug prices, highlighting the role of intermediaries in increasing prices of medicines along with need to promote generic medicines with quality assurance.

In a policy note, the anti-trust regulator said high margins are a form of incentive and an indirect marketing tool employed by drug companies. Essential medicines constitute over 60 per cent of out-of-pocket expenditure on healthcare in India.

"One major factor that contributes to high drug prices in India is the unreasonably high trade margins… Further, self-regulation by trade associations also contributes towards high margins as these associations control the entire drug distribution system in a manner that reduces competition," the country's fair play watchdog said in the note, titled 'Making Markets Work for Affordable Healthcare'.

CCI has shared the note with the ministry of corporate affairs, health, department of pharmaceuticals and Niti Aayog for any further

action on the issues highlighted in the policy paper. The anti-trust regulator said it received 52 cases pertaining to the pharmaceutical and healthcare sector in last nine years and while deciding on the cases, it observed information asymmetry sector significantly restricts consumer choice.

The note said in-house pharmacies of super speciality hospitals are "completely insulated from competition" as in-patients are not allowed to buy any product from outside pharmacies. "This calls for regulation that mandates hospitals to allow consumers to buy standardised consumables from the open market," it noted.

To allow access of essential medicines at lower prices, the CCI suggested efficient and wider public procurement and distribution of essential drugs to circumvent the challenges arising from the distribution chain and price regulation.

It also endorsed electronic trading of drugs with appropriate regulatory safeguards. CCI said e-pharmacies can bring in transparency and spur price competition among platforms and among retailers, as has been witnessed in other product segments.

Underlining quality perception behind proliferation of branded generics, the regulator stressed on the need for stringent quality control measures by the drug regulator and recommended "a one-company-one drug-one brand name-one price policy" to counter brand proliferation by introducing artificial product differentiation in the market, offering no therapeutic difference but allowing firms to extract rents.

"Worldwide, generic drugs are seen as a key competitive force against the patent-expired brand name drugs marketed at monopoly prices. In India, the pharmaceutical market is dominated by 'branded generics' which limit generic-induced price competition. The branded generic drugs enjoy a price premium owing to perceived quality assurance that comes with the brand name. Quality consideration may be a reason behind the prescription of branded generics by doctors. However, it is also equally possible that the brand proliferation is to introduce artificial product differentiation in the market, offering no therapeutic difference but allowing firms to extract rents," the note said.

Estimates show more than 70 per cent of the over Rs 1 lakh crore local pharmaceutical market is dominated by branded generics, whereas 9 per cent is patented medicines. Though there have been several policy proposals in the past suggesting to replace brand names by salt names of medicines on doctors' prescription, the government has not been able to implement any of these proposals given the pressure from the industry.

Source: *The Times of India, 26th October 2018*

Pharmacies Asked to Refer Fever Cases to Govt. Facilities

Paracetamol should not be sold without prescription: Director of Drug Control

In the light of dengue and H1N1 cases, the Tamil Nadu Drugs Control Department has instructed pharmacies across the State to refer persons seeking medications for fever without prescriptions to the nearest government medical facility.

K. Sivabalan, Director of Drugs Control, said there are 35,000 to 40,000 medical shops in the State. "We have instructed pharmacies through the assistant directors and drug inspectors of the department not to issue any tablets for fever over the counter. If persons seek medications over the counter, they should be referred to the nearest government hospital," he said.

Paracetamol tablets should not be sold without prescriptions, he said, adding that they have asked the assistant directors and drug inspectors to ensure that pharmacies have adequate stock of antiviral medicine, Oseltamivir — in tablet, capsule and syrup forms — for treating H1N1.

"If private nursing homes do not have Oseltamivir, they can approach the respective deputy director of health services for getting the stock," he said.

Easy availability

Earlier, Oseltamivir was in the list of Schedule 'X' drugs, but this was withdrawn to ensure its easy availability on ordinary licence. It is sold only on prescription, he said.

He added that there was continuous monitoring to ensure that quacks do not get drug supply. "Wholesale drug distributors should ensure that the order is placed by a registered medical practitioner and they should get the written order. If this is not done, legal action will be taken against them," he said.

Source: *The Hindu, 25th October 2018*

Drug Regulator Issues Notice to Amazon, Flipkart for Alleged Sale of Spurious Cosmetics

E-commerce giants -Amazon and Flipkart- have been issued notices by the country's drug regulator DCGI for allegedly selling "spurious and adulterated" cosmetics including imported brands, and have been warned of penal actions in case of failing to respond within 10 days.

The notice from the Drug Controller General of India (DCGI) follows raids by drug inspectors at various locations across the country on October 5-6, during which they found that some indigenously manufactured cosmetics without valid manufacturing licence and having ingredients imported without necessary registration certificates were being sold on the e-commerce platforms.

The law provides for penal actions ranging from monetary fine to imprisonment for sale of such "unapproved" products.

When contacted, an Amazon India spokesperson told the company takes strict action against sellers of "illegal or fake products" as and when such incidents are reported to it.

"Amazon.in is a third-party marketplace which enables sellers to list their products for sale to Indian customers. Sellers on Amazon.in own their respective products and are responsible for product compliances, as may be applicable.

"Amazon.in has a very high bar of customer experience and does take strict action against sellers who are selling illegal or fake products...in accordance with the due process of law, as and when such incidents are reported to us," the spokesperson said.

Among cosmetics being sold by these websites included imported brands without valid documents and containing ingredients in the "negative list" of the BIS (Bureau of Indian Standards).

Asking the companies to reply to its notice within 10 days, the DGCI has warned them of penal action for "offering for sale, sale and distribution of spurious, adulterated cosmetics and cosmetics manufactured without valid licence in contravention of the Drugs and Cosmetics Act, 1940."

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"In case, you fail to submit the reply within the stipulate period, it will be presumed that you have no reply to offer and appropriate action as deemed fit will be initiated against you," DCGI S Eswara Reddy said in the notice.

Under the Drug and Cosmetics Act, it is mandatory to get a registration certificate for import of cosmetics into India, while all cosmetics manufactured in the country need to have a valid licence.

Besides, cosmetics need to conform to the standards laid down by the BIS and cannot have any ingredient mentioned in its negative list.

A similar notice was also issued to the Indiamart, another e-commerce website, Reddy said. Reactions from Flipkart and Indiamart were not immediately available.

Illegal cosmetics estimated to be worth Rs four crore were seized during pan-India raids carried out after which the central drug regulator lodged five FIRs across three cities -- Mumbai, Pune and Delhi -- against manufacturers who were making these cosmetics without licence.

Asserting that the raids revealed the extent of illegal cosmetics in the market, Reddy also cautioned against purchase of such products.

Source: *ET Healthworld, 24th October 2018*

The Need for Disclosure

Tuberculosis patients in India are frequently ignorant of drug side-effects

Sunil Kumar, 28, a Delhi-based vegetable vendor, was diagnosed with drug-resistant tuberculosis (DRTB). The government hospital he visited for treatment prescribed a drug called bedaquiline. That year, even though India was giving bedaquiline to patients as part of a conditional access programme, there were questions about the medicine's toxic effects. There was no Phase 3 data, which is mandatory under the Indian regulatory regime for establishing a drug's safety. The only large randomised trial data on the drug came from a limited 161-patient Phase 2b study, which threw up paradoxical results.

While on the one hand patients on bedaquiline had shown TB-negative sputum more often compared to controls, on the other, comparatively more patients died in the Bedaquiline arm, suggesting that the drug might be killing patients. After an investigation did not find any link between the deaths and bedaquiline, the U.S. Food and Drug Administration fast-tracked the drug's approval on the condition that the drugmaker, Janssen Pharmaceuticals Inc, provide Phase 3 data by 2022. Given this, the World Health Organisation has suggested that all patients be told of bedaquiline's mortality risk as seen in the Phase 2b trial.

Kumar doesn't remember being told all this. “They didn't tell me anything. Nor did I sign any form,” he says. Even if he had been given the patient-information booklet (designed by India's Central TB division) for bedaquiline, he may not have learnt about the mortality risk.

While the patient information booklet mentions side-effects such as dizziness, it does not disclose the Phase 2b results. Such a lack of disclosure is "egregious,” says Jennifer J. Furin, an infectious diseases clinician at Harvard Medical School.

When questioned about the inadequacy of the patient booklet, V.S. Salhotra, the additional deputy director general (TB) at Delhi's Directorate General of Health Services, says

the booklet mentions all risks. He did not respond to a follow-up question about the phase 2b results.

Informed consent

Unfortunately, Kumar's experience is not uncommon. Interviews conducted by The Hindu show that Indian TB patients are frequently ignorant of drug side-effects. This is a problem because DRTB medicines can be highly toxic. Kanamycin, which belongs to the aminoglycoside class of antibiotics, can cause permanent hearing loss and is toxic to the kidneys. Another DRTB drug, cycloserine, can trigger suicidal thoughts, while the drug isoniazid has been linked with peripheral neuropathy (nerve damage).

Informing patients about these side-effects, or informed consent, is critical for several reasons. First, the patient has a right to know. Second, advance knowledge of risks makes it more likely that the patient will act to mitigate them. In the case of kanamycin, deafness is sometimes preceded by warning symptoms such as tinnitus, giving doctors an opportunity to intervene.

A third advantage is that it helps patients plan for painful side-effects. This, in turn, ensures they complete the treatment — something that often does not happen in DRTB. In the case of cycloserine, for example, a patient could choose to move in with her family during the treatment. “If you can't sleep for nights, and you have crazy dreams, what are you going to do? You have got to know that you need to put in place a support system before you jump into treatment,” says Aditi Krishnamurthy, an independent community health consultant in Bengaluru.

Patient literacy

Unfortunately, one of the biggest barriers to informed consent in India is patient literacy, say experts. Some poorly educated patients think of TB as a death sentence and do not see the point of taking medicines. Convincing them to do so is already an uphill task. Telling them about drug adverse effects without fully explaining the risk-benefit ratio is likely to push them further away, Krishnamurthy points out. “Informed consent is a double edged sword.”

Take the case of journalist Nandita Venkatesan, who was diagnosed with intestinal tuberculosis for the second time in 2013. She was admitted to a large private hospital in Mumbai where her doctors gave her kanamycin.

One afternoon, about a week after Venkatesan finished her course of the drug, she took a nap. When she woke up, she could hear absolutely nothing. Eventually, a ear-nose-throat specialist diagnosed her with over 90% hearing loss, and told her it was a side-effect of the drug.

Today, Venkatesan does not rue that she was prescribed the drug, given how ill she was. “I know the doctors who treated me did terrific work,” she recounts. What still rankles is that no one told her about the catastrophic impact it could have on her life. “I didn't even hear a whisper about this,” she says.

Source: *The Hindu, 21st October 2018*

70% City Patients Self-medicate: Study

S Muthukumaran, a 29-year-old chemist at a pharmacy in West Mambalam, always manages to offer his customers what they need.When one of his customers came with complaints of severe throat pain, body ache and fever, he reached out for a blue box and handed over a strip of Azithral 500, a brand name for azithromycin, an antibiotic.

"Once a day for three days. Have a paracetamol if there is fever. If you are too tired, add B complex," he said. And the customer walked out thanking

Though a prevalent practice, self-medication is increasingly worrying the public health department this monsoon. Azithromycin, like all antibiotics, requires a doctor's prescription. Antibiotics are prescribed only for bacterial infections. They are ineffective against viruses such as dengue, H1N1 or even flu. "We are beginning to see a spike in fever cases along with sporadic cases of H1N1and dengue and it is time to stop popping pills without prescriptions. There are many problems with self-medication. It increases complications and risks of death and also increases chances of diseases spreading," said director of public K Kolandaisamy.

In 2017, when there was a dengue outbreak, most people who died delayed the right treatment. "We have also been telling pharmacists not to give medicine without prescriptions," he said.

A recent city-based study shows that nearly seven out of ten patients in Chennai are opting for self-medication. The study done on 610 patients visiting a dental hospital showed that 4 of 5 patients selected antibiotics from their previous prescriptions. Less than one in 10 complained of adverse reactions, and more than half of them did not know what antibiotic misuse is.

The study, published in the Journal of Education and Health Promotion concluded the need for health care professionals and government bodies to enlighten the public about the harmful effects of self-medication with antibiotics to overcome the antibiotic resistance. "The government should consider steps to supervise or control the practice of self-medication by check on availability of the medicines without prescription, controlling over-thecounter medicines, and formulating guideline for the usage of the drugs by the physician and pharmacist," said the study's corresponding author Dr J Muruganandhan of Sri Venkateswara Dental College and Hospital.

Doctors say different antibiotics are used for different types of bacteria, so merely taking one does not mean it will cure an ailment. Taking the wrong antibiotic may cause worsened infections or allergic reactions.

"Most antibiotics need to be taken for five days to a week. When taken for only a few days, the likelihood of a mutation in a bacterium's genetic structure is increased. These changes can make the germs resistant to the antibiotics meant to kill them," said infectious diseases expert Dr V Ramasubramanian.

Source: *The Times of India, 21st October 2018*

Impact on the Pharmaceutical Industry After NPPA Fixed the Price for 92 Drug Formulations

NPPA has recently circulated three orders, dated 13 August 2018, to fix and revise the ceiling prices for a total of 92 drug formulations. This notification was made in accordance with Drugs Prices Control Order (DPCO 2013), which aims to benefits the retail consumers. The targeted medicines are used for multiple treatments including Cancer, Hepatitis-C, Migraine, and Diabetes.

Notification 3982(E) controls the prices of 72 formulations, 3983(E) revises the ceiling prices of 9 scheduled formulations, and 3984(E) revises the retail prices of 11 scheduled formulations of Schedule-I Drugs.

The National Pharmaceutical Pricing Authority (NPPA) is government run organization in India, which has the authority to fix and revise the prices of controlled drugs and formulations, along with enforcing the prices and availability of the medicines in the country.

Identifying a common man's standpoint on a regime of continuous medications, the working class is worst affected after shelling out a big portion of their monthly income, in order to recover from any unfortunate disease which requires prolonged dosages.

This decision made by NPPA would directly interest those patients who have to spend a considerable amount of money on treatments involving recurring drugs. Oncology, Hepatitis-C, and Migraine patients are mostly prescribed daily doses of scheduled drugs by their treating physicians, and this news could be a big relief for the public.

The Business Perspective.

Recognizing a trader's viewpoint, any price control notification for the Indian pharmaceutical industry portrays a visible impact on their profit margins and Top lines thereafter. Price capping restrictions have historically been a major factor responsible for the Better Discipline in the industry.

The manufacturers are only able to draw capital investments into the pharmaceutical industry, if a sustained growth rate is established over the past, but, with frequent circulars to regulate the retail prices, the companies are unable to set the prices for their own products.

Making a drug and getting it approved by the government at times become quite daunting. Modern medicines are mandated to prove their efficacy during numerous clinical trials, which take years to complete and hit the market. The underlying groundwork to develop a successful molecule, even a small pill, demands a strenuous amount of research and knowledge in the field of science, which happens in the laboratories and away from the public eye.

To cure a disease with better results, a pharma company has to invest in a team of expert staff, technology and development procedures, in order to discover a new and preferable medicine.

Let's imagine a scenario - You invent a new formula which heals influenza in a day. You had spent millions of dollars on the research, equipment and manpower to get your new medicine patented around the world, and finally be able to sell. Then, within months, another group comes forward and announces

the discovery of their advanced influenza vaccine, which would render your product obsolete.

If someone makes a better medicine, you can visualize the resulting business loss when doctors stop recommending your old product. The point is, the pharmaceutical industry is a highly competitive and a difficult business to sustain. Even on humanitarian grounds, any restriction on the prices incur a loss to the manufacturers.

With such regulations on the price of complex medications and the consequential profitability of the manufacturing companies, the cash inflow gets limited for further research and development. It is because money encourages the corporations to grow their business. However, when profits are cut short by the government due to such price controls, the stimulation of achieving extended goals (more money) is lessened. Hence the zeal for continuous innovation is dwindled at times.

With slower progressions in the field of medical science, the evolution of the pharmaceutical research shrinks. It is a fact generally endorsed by the industry executives, and they might be right.

So, how should a government help the poor and provide them access to affordable treatments? The answer is not simple.

The concept of 'developing vs developed economies' comes in picture. There are nations in the world which buy expensive medicines, just to distribute amongst people at a subsidized rate. It is all about running an administration and maintaining stability between conflicting aspects. Making pivotal decisions to benefit the society is a complicated part of a state organization like NPPA, but making quick conclusions is something the society prefers to do.

Acting as a medium between the consumers and the manufacturers, NPPA also monitors the recovering of overcharged amounts for controlled drugs and even keeps the prices of decontrolled drugs at reasonable levels, however as we know that pricing interventions should be implemented along with a strong market monitoring to prevent market distortions at all times.

Source: *ET Healthworld, 15th October 2018*

Dr Reddy's to Sell Hyderabad API Unit to Therapiva

Drug major Dr Reddy's Laboratories (DRL) Monday said it will sell its active pharmaceutical ingredient (API) business unit in Hyderabad to generics pharmaceutical company Therapiva Private Ltd. In a regulatory filing, Dr Reddy's Laboratories said it has entered into a definitive agreement for the sale of its API manufacturing business unit in Jeedimetla, Hyderabad, to Therapiva.

Therapiva is a joint venture between Omnicare Drugs India, a wholly owned subsidiary of Neopharma LLC, Abu Dhabi and Laxai Life Sciences.

The sale includes all related fixed assets (land and building), current assets, current liabilities, and its employees, the company said.

"The divestiture of our API manufacturing business unit is a step towards streamlining our manufacturing operations and optimising our cost structures," said Sanjay Sharma, Executive Vice President & Head, Global Manufacturing Operations of Dr Reddy's Laboratories.

The company however, did not disclose any financial details.

"this acquisition which will augment Neopharma's vertical integration advantage and provide us with a high quality manufacturing base in India. This is a key milestone in our acquisition strategy over the next few years to increase Neopharma's presence in the global generics space" said BR Shetty, Chairman of Neopharma LLC, Abu Dhabi.

Source: *ET Healthworld, 15th October 2018*

Sun Pharma Invests 120 Crore in Assam to Set up Production Line

Pharmaceutical Company, Sun Pharma has invested Rs 120 crore in Assam to set up production line which will boost the company's capacity to manufacture liquid vials, injectable, eye drops and tablets.

According to statement from Assam government the company has already invested Rs 700 crore in this manufacturing facility in the state and another Rs 200 crore is going to be invested. The company is providing employment to 595 people and 62 percent of this workforce is from the state.

“When we organised Advantage Assam: Global Investors' Summit in February, many people cast aspersions about its feasibility and rationale. But the success of summit has proved them wrong as many investors and big industrial players have come to the state for setting up their businesses as a result of the summit and now the state is witnessing an economic resurgence.” Chief Minister Sarbananda Sonowal said while inaugurating a new production line in the parenteral block of Sun Pharma's manufacturing facility at Palashbari on the city outskirts.

Sun Pharma is one of the companies which committed investment in the state during Advantage Assam summit, Sonowal said that Rs 79,000 crore investment committed during the summit is being realised as companies are setting up their bases here which is creating employment opportunities for the youth of the state.

He urged the global investors to take advantage of these changing times and set up their businesses in Assam so that they can take advantage of the state's growth and prosperity.

Managing Director of Sun Pharma Dilip Shanghvi thanked the state government for support and cooperation in setting up this plant and said that this plant is expected to become one of the largest facilities of the company to manufacture sterile products.

Source: *ET Healthworld, 14th October 2018*

Dr Reddy's Labs Recalls 35k Tubes of Skin Infection Cream from US

Dr Reddy's Laboratories' US arm is recalling over 35,000 tubes of Nystatin and Triamcinolone Acetonide cream on account of failed stability specifications, USFDA said. As per the US health regulator's Enforcement Report, Dr Reddy's Labs Inc is recalling 35,020 tubes of Nystatin and Triamcinolone Acetonide Cream, USP, 1,00,000 units/gm and 1 mg/gm from the American market.

The recall is on account of "failed stability specifications - an out of specification result was observed for the test parameter : composition of Nystatin during stability testing," it added.

The cream is used for treatment of cutaneous candidiasis, a skin infection.

The voluntary ongoing nationwide recall is a class II recall, United States Food and Drug Administration (USFDA)said.

As per USFDA, a class II recall is initiated in a situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.

Source: *ET Healthworld, 14th October 2018*

E-Pharmacies to Come Under Regulatory Scanner Soon

Online portals like Netmed, 1mg and PharmEasy selling medicines through internet will soon come under the regulatory scanner. Central Drugs Standard Control Organisation has proposed rules to monitor sale and distribution of drugs through e-pharmacy, bringing such portals under the purview of the drug law, official sources said.

Such portals will have to register and maintain proper information about stocks, transactions as well as prescription against any sale. The regulator will also do periodic inspection of e-pharmacies. In case of sale of substandard drugs, these portals will be penalised under the Drugs and Cosmetics Act, the draft rules said.

"The premises from where the e-pharmacy business is conducted shall be inspected, every two years, by a team of officers authorised by the Central Licensing Authority, with or without the experts in the relevant field or the officers authorised by the concerned State Licensing Authority," the draft rules for regulation of e-pharmacies said.

According to an official, public comments have been invited on the draft within 45 days, after which the rules will be notified through a final notification. The move assumes significance as in the last two years close to 500 players have entered the epharmacy space, despite strong opposition from the chemists running brick and mortar stores. While there are around 15 major players in the segment, a lot of traditional retailers are also gradually making the shift with growing internet penetration and online demand.

Official estimates show sales through e-pharmacy is pegged at Rs 3,000 crore annually and growing at 100%. “This segment has great growth potential because e-pharmacies can help make medicines accessible and affordable. This is a growing trend and it will be unfair to stop it so, instead of curtailing it we decided to regulate it,” drugs controller general of India S Eswara Reddy said

Source: *The Times of India, 2nd September 2018*

Drug Makers May Have to Pay 5 Times More for Pharma Imports

Drug makers importing medicines may soon have to pay the government up to five times more to register their products here and get their overseas manufacturing facilities audited by the Indian regulator. The move aims to increase domestic manufacturing of medicines.

India's current charges are a lot less than what Indian drug makers pay in other countries.

After a meeting between the Central Drugs Standard Control Organisation and industry stakeholders in August, the ministry is once again mulling a hike in fees for several regulatory submissions for foreign drug makers, said two senior health ministry officials. A similar move was suggested in December 2015 as well.

“All stakeholders present agreed, in principle, to a hike in fees (as per the 2015 draft notification),” stated a document that ET has viewed.

“Members also stressed (the need) to revise fees periodically after three years, instead of 15 years. The proposal for amendment in rules is under process.” Revision of fees is necessary, as rates have not been updated for more than 15 years, one of the officials said.

“India charges much less than other countries for regulatory licences,” the official told ET, on condition of anonymity. “Now, the Indian regulator will be at par with world regulators (in the fees that it charges).”

The health ministry is expected to soon release a draft proposing higher fees for import licences, registration certificates for manufacturing sites overseas and CDSCO's inspections of these sites, said the official.

For instance, the ministry is planning to increase the fees to register one manufacturing site to $10,000 from $1,500 currently. It has proposed that the fee for a registration certificate for one product be hiked to $5,000 from around $1,000 now and make it valid for three years, the second official said.

This fee increase will impact imported products and may be perceived as a tariff barrier, said A Vaidheesh, president, Organisation of Pharmaceutical Producers of India.

Source: *ET Healthworld, 13th October 2018*

Novartis Division Sandoz Recalls One Lot of Blood Pressure Drug

Novartis Sandoz division was recalling one lot of losartan tablets after finding traces of a probable carcinogen in the blood pressure drug.

The drug is made by China's Zhejiang Huahai Pharmaceutical Co Ltd. Last month, the European Medicines Agency placed the firm under high supervision after a probable carcinogen was found in its blood pressure drug valsartan.

A review was extended to other 'sartan' medicines, including candesartan, irbesartan, losartan, olmesartan and valsartan, after very low levels of a carcinogen was found in losartan made by Hetero Labs in India.

Novartis said Sandoz had not received any reports of adverse events related to this lot.

Source: *ET Helathworld, 9th November 2018*

Strides' Subsidiary Inks Pact With SUDA Pharmaceuticals for Migraine Drug

Strides Pharma Science, its step-down subsidiary has entered into an exclusive product development, licensing and supply agreement with Australia's SUDA Pharmaceuticals for its novel drug SUD-001H, used in the treatment of migraine. Strides Pharma Science said this partnership with SUDA is part of its specialty portfolio for the US market.

Under the terms of agreement, SUDA will receive an upfront cash payment of USD 0.4 million and a further payment of USD 0.6 million on reaching certain milestones including the pilot first-in-man clinical study, submission and approval of the product in the US," Strides Pharma Science said in a BSE filing.

On commercial sales, SUDA will also receive royalties plus a handling fee.

SUD-001H is an oral spray of sumatriptan to treat migraine headache.

"Sumatriptan is one of the most widely used drugs for the treatment of acute migraine in adults. SUD-001H is a first-in-class mint-flavoured oral spray formulation of sumatriptan (marketed in tablet form and in a nasal spray by GlaxoSmithKline under the brand name Imitrex)," it added.

Strides Pharma Science said the product will be filed with the US Food and Drug Administration (USFDA) and on approval is expected to be the first fast-acting oral spray of sumatriptan in the US market.

Strides said, the company will have a right of first refusal for additional territories including the European Union, Australia and New Zealand, Canada, South Africa and Japan.

"Execution of Strides' generic product pipeline for the US is nearing completion and is expected to have over 150 abbreviated new drug application (ANDA) filings by 2021. The company is now focusing on developing a portfolio of complex and specialty products," the company said.

The company through in-house development and partnerships will build a portfolio of limited competition products offering exclusivity for a sustainable period.

Source: *ET Helathworld, 9th November 2018*

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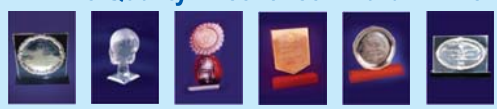

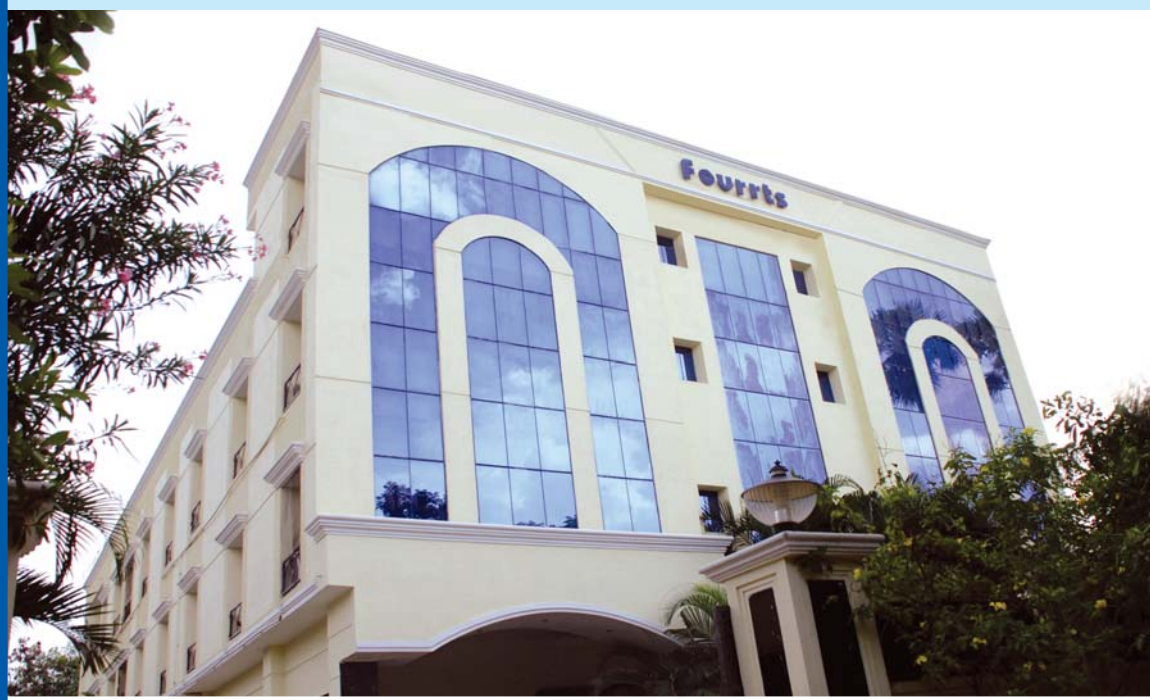

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