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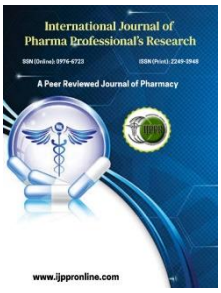

A Review Process of ANDA Filling in PMDA (Japan) & Calibration of UV in Accordance to its Regulatory Guidelines

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ABSTRACT: The Abbreviated New Drug Application (ANDA) filing system is an important regulatory process in Japan for the approval of generic drugs. This system allows pharmaceutical companies to submit an application for the marketing and sale of a generic drug, which has already been approved by the regulatory agency in another country. The ANDA system in Japan is similar to that of the United States and Europe, but there are some unique aspects that must be taken into account. For example, in Japan, the regulatory agency requires a separate drug master file for each active pharmaceutical ingredient, which can be a time-consuming process.

UV spectrophotometry is a widely used analytical technique for the characterization of pharmaceuticals, including active pharmaceutical ingredients and finished dosage forms. The Shimadzu UV-1800 spectrophotometer is a popular instrument for this purpose, which is widely used in Japan. This instrument has a range of features that make it particularly useful for pharmaceutical analysis, including a wavelength range of 190-1100 nm, a double-beam optical system, and a low stray light level. The Shimadzu UV-1800 is also compatible with a range of accessories, such as a multicell holder, which allows for the simultaneous measurement of multiple samples.

The combination of the ANDA filing system and UV spectrophotometry using the Shimadzu UV-1800 is an important tool for the development and approval of generic drugs in Japan. The ANDA system allows for a streamlined regulatory process for generic drug approval, while UV spectrophotometry provides a

reliable and accurate method for the characterization of pharmaceuticals. Together, these tools help to ensure the safety and efficacy of generic drugs in Japan.

Introduction: The Abbreviated New Drug Application (ANDA) filing system is commonly used in the world to approve generic versions of drugs that are already approved and marketed. However, Japan has a different filing system for generic drugs known as the "Yakki Kensa" or drug application review process. Under the Yakki Kensa process, an applicant must submit an application to the Ministry of Health, Labour and Welfare (MHLW). The MHLW reviews data on quality, safety, efficacy and other aspects related to manufacturing processes before granting approval for marketing authorization. According to a publication by Japan's Pharmaceuticals and Medical Devices Agency (PMDA), there are three types of applications under this system:

a. Full Review Applications- no existing product with similar compositions available.
b. Partial Change Applications - minor changes need to be made in an existing product (dosage form or packaging material).
c. Notification Applications - submitted if certain specified changes do not affect a drug's quality/safety/efficacy etc.

Furthermore, PMDA states that all applications should contain accurate information about composition/formulation/manufacturing methods/stability testing etc., along with clinical trial data demonstrating therapeutic equivalence between test/reference products where applicable.[1,2]

1.1 ANDA Filing System of Japan: The Abbreviated New Drug Application (ANDA) filing system is used in the United States to approve generic versions of drugs that are already approved and marketed. However, Japan has a different filing system for generic drugs known as the "Yakki Kensa" or drug application review process.

According to an article published by the US Food and Drug Administration (FDA), "Japan's regulatory framework for pharmaceuticals differs significantly from that in other countries, including the United States." The article goes on to state that Japanese regulations require companies to conduct extensive clinical trials before submitting their applications for approval.

1.1.1 ANDA Filling Process of Japan: The process for filing an Abbreviated New Drug Application (ANDA) in Japan is a bit different from that of the United States. In Japan, the process is called a "Generic Drug Application" (GDA), and it is regulated by the Pharmaceuticals and Medical Devices Agency (PMDA).

Here are the general steps involved in the GDA filing process in Japan:
1.1.1.1 Preparing the application: The applicant must prepare the GDA application, which includes data on the quality, safety, and efficacy of the generic product, as well as information on the manufacturing process, packaging, and labeling.

1.1.1.2 Submission of the application: The applicant submits the GDA application to the PMDA.

1.1.1.3 Application review: The PMDA reviews the application to ensure that it is complete and contains all necessary information. If the application is incomplete, the PMDA will request additional information from the applicant.

1.1.1.4 Facility inspection: The PMDA inspects the manufacturing facility to ensure that it complies with Good Manufacturing Practice (GMP) standards.

1.1.1.5 Clinical studies: If necessary, the PMDA may require the applicant to conduct clinical studies to demonstrate the safety and efficacy of the generic product.

1.1.1.6 Approval: If the PMDA is satisfied with the data provided by the applicant, it will grant approval for the generic product to be marketed in Japan.

It's worth noting that the GDA filing process in Japan is generally more rigorous than the ANDA filing process in the United States. This is because Japan has stricter requirements for generic drugs, and the PMDA places a greater emphasis on ensuring that these drugs are safe and effective.[3]

1.1.2 Preparing the Application: The preparation of an ANDA in Japan involves several steps to ensure that the application meets the PMDA's guidelines. Here are some of the key elements that need to be included in an ANDA submission to the PMDA:

1.1.2.1 Drug Substance: The drug substance, or active ingredient, should be identified and characterized in the ANDA. The applicant should provide information on the quality, purity, and stability of the substance.

1.1.2.2 Drug Product: The drug product is the finished dosage form that will be marketed to patients. The applicant should provide detailed information on the composition, manufacturing process, and quality control of the drug product.

1.1.2.3 Bioequivalence: In order to obtain approval for a generic drug in Japan, the applicant must demonstrate bioequivalence between the generic drug and the reference drug. This means that the generic drug must have the same pharmacokinetic properties as the reference drug. The applicant must provide data from bioequivalence studies conducted in accordance with PMDA guidelines.

1.1.2.4 Clinical Data: The applicant may be required to submit clinical data to support the safety and efficacy of the generic drug. The type and amount of clinical data required will depend on the specific drug and the PMDA's requirements.

1.1.2.5 Manufacturing: The applicant must provide detailed information on the manufacturing process, including information on the facilities, equipment, and controls used in the production of the drug.

It is important to note that the PMDA's guidelines for the preparation of an ANDA can change over time. Applicants should refer to the latest guidelines and consult with the PMDA to ensure that their ANDA meets the current requirements.[3]

1.1.3 Submission of the ANDA to PMDA: Once the ANDA has been prepared according to the PMDA's guidelines, it can be submitted for review. Here are the steps involved in the submission of an ANDA to the PMDA:

1.1.3.1 Electronic Submission: In Japan, the submission of an ANDA is done electronically through the PMDA's e-Submission Gateway.

1.1.3.2 Cover Letter: The applicant should provide a cover letter that includes a summary of the information contained in the ANDA.

1.1.3.3 Application Form: The applicant must complete the PMDA's application form, which includes information on the drug substance, drug product, manufacturing process, and clinical data.

1.1.3.4 Payment of Fees: The applicant is required to pay a fee for the review of the ANDA.

1.1.3.5 Supporting Documents: The applicant must provide supporting documents, such as the results of bioequivalence studies, analytical methods, and stability studies.

1.1.3.6 Authorization Letter: If the applicant is using a representative, such as a consultant or a legal entity, to submit the ANDA on their behalf, an authorization letter must be provided.

1.1.3.7 Submission Checklist: The applicant should include a submission checklist to ensure that all required documents have been included in the submission.

Once the ANDA has been submitted, the PMDA will review the application and may request additional information or clarification if necessary. The review process can take several months to complete, depending on the complexity of the application.[4,5,6]

1.1.4 Review of the ANDA by PMDA: The review of an ANDA by the PMDA involves a thorough evaluation of the application to ensure that the generic drug is safe, effective, and of high quality. Here are the steps involved in the review process:

1.1.4.1 Administrative Review: The PMDA first conducts an administrative review to ensure that the ANDA is complete and that all required documents have been submitted.

1.1.4.2 Screening: The PMDA then conducts a screening process to identify any major deficiencies in the application. If major deficiencies are identified, the PMDA may request additional information or clarification from the applicant.

1.1.4.3 Evaluation: The PMDA evaluates the ANDA based on scientific and regulatory criteria, such as the quality, safety, and efficacy of the drug. The evaluation includes a review of the data provided by the applicant, as well as a review of any relevant literature or data from other sources.

1.1.4.4 Inspections: The PMDA conducts inspections of the manufacturing facilities to ensure that they meet the required standards for quality and safety.

1.1.4.5 Consultation: The PMDA may consult with external experts or advisory committees to obtain additional input on the evaluation of the ANDA.

1.1.4.6 Decision: Based on the results of the evaluation, the PMDA will make a decision on whether to approve the ANDA or not. If the ANDA is approved, the PMDA will issue a marketing authorization.

The review process can take several months to complete, and the timeline may vary depending on the complexity of the application and the PMDA's workload. The applicant may be required to provide additional information or clarification during the review process, which can extend the timeline for approval.[7,8]

1.1.5 Inspection of the manufacturing facility by PMDA: As part of the ANDA review process, the PMDA conducts inspections of the manufacturing facilities to ensure that they meet the required standards for quality and safety. Here are some key points regarding the inspection of manufacturing facilities by the PMDA:

1.1.5.1 Purpose of the Inspection: The purpose of the inspection is to verify that the manufacturing facilities and processes used to produce the generic drug are in compliance with the PMDA's standards and guidelines.

1.1.5.2 Notification of Inspection: The PMDA will provide advance notice to the manufacturer of the inspection date and time.

1.1.5.3 Scope of the Inspection: The inspection may cover all aspects of the manufacturing process, including facilities, equipment, personnel, documentation, and quality control systems.

1.1.5.4 Inspection Team: The inspection team typically includes experts from various disciplines, such as chemistry, microbiology, and engineering, as well as inspectors from the PMDA.

1.1.5.5 Inspection Report: Following the inspection, the PMDA will issue an inspection report that summarizes the findings and identifies any deficiencies or areas of non-compliance. The manufacturer will be given an opportunity to respond to the findings and provide corrective actions.

1.1.5.6 Impact on Approval: The results of the inspection can have an impact on the approval of the ANDA. If the inspection reveals significant deficiencies or non-compliance, the PMDA may delay or deny approval of the ANDA until the issues have been resolved.

It is important for manufacturers to ensure that their manufacturing facilities and processes are in compliance with the PMDA's standards and guidelines to avoid delays or rejections in the approval process.[7-11]

1.1.6 Approval of the ANDA by PMDA: The approval of an ANDA by the PMDA is the final step in the process of obtaining marketing authorization for a generic drug in Japan. Here are some key points regarding the approval of an ANDA by the PMDA:

1.1.6.1 Decision on Approval: After conducting a thorough review of the ANDA and inspecting the manufacturing facility, the PMDA will make a decision on whether to approve the ANDA or not.

1.1.6.2 Approval Criteria: The PMDA will evaluate the ANDA based on scientific and regulatory criteria, including the quality, safety, and efficacy of the drug.

1.1.6.3 Conditions of Approval: If the ANDA is approved, the PMDA may impose conditions on the approval, such as restrictions on the indications, dosages, or patient populations for which the drug can be used.

1.1.6.4 Marketing Authorization: If the ANDA is approved, the PMDA will issue a marketing authorization, which allows the drug to be marketed and sold in Japan.

1.1.6.5 Post-Marketing Monitoring: The PMDA will continue to monitor the safety and quality of the drug after it has been approved and marketed, and may impose additional requirements or restrictions if necessary.

It is important to note that the approval criteria and conditions for an ANDA in Japan may differ from those in other countries, and may vary depending on the specific drug and the PMDA's requirements. It is recommended that applicants consult with the PMDA and seek professional advice to ensure that their ANDA is prepared and submitted correctly.[12-14]

1.1.7 Post-approval Monitoring by PMDA: Post-approval monitoring by the PMDA is a critical step in ensuring the safety and efficacy of generic drugs in Japan. Here are some key

points regarding the post-approval monitoring process:

1.1.7.1 Pharmacovigilance: The PMDA conducts pharmacovigilance activities to monitor the safety of drugs after they have been approved and marketed. This includes collecting and analysing reports of adverse events and taking appropriate actions if safety concerns arise.

1.1.7.2 Post-Marketing Surveillance: The PMDA conducts post-marketing surveillance to monitor the quality and efficacy of drugs after they have been approved and marketed. This includes monitoring the use of the drug in the real-world setting and evaluating its effectiveness.

1.1.7.3 Inspections: The PMDA conducts periodic inspections of manufacturing facilities to ensure that they continue to meet the required standards for quality and safety.

1.1.7.4 Labelling Changes: The PMDA may require changes to the labelling of a drug if new safety or efficacy information becomes available.

1.1.7.5 Regulatory Actions: If safety concerns arise, the PMDA may take regulatory actions, such as suspending or revoking the marketing authorization, or imposing additional requirements or restrictions on the drug.

It is important for manufacturers to cooperate with the PMDA and comply with post-approval monitoring requirements to ensure the safety and efficacy of their drugs. Failure to comply with post-approval requirements can result in regulatory actions that can have significant consequences for the manufacturer and the drug.[15-17]

2. UV spectroscopy: It is a widely used analytical technique that involves the measurement of the absorption of ultraviolet (UV) radiation by a sample. This technique is commonly used in the fields of chemistry, biochemistry, and pharmaceuticals to determine the concentration of a solute in a solution, identify unknown compounds, and study the structure of molecules.

The Shimadzu UV-Vis Spectrophotometer 1800 is a high-performance spectrophotometer that is designed for a wide range of applications, including quantitative analysis, wavelength scanning, and time-course measurements. The instrument uses a double-beam design, which allows for the measurement of both the sample and reference beams simultaneously, thereby reducing the effects of sample variability and instrument drift.

The Shimadzu UV-Vis Spectrophotometer 1800 is equipped with a number of features that make it a versatile and reliable instrument for UV spectroscopy. These features include a large colour LCD display, a range of measurement modes, an automatic wavelength calibration function, and a built-in printer for convenient data recording.

In addition to its high-performance capabilities, the Shimadzu UV-Vis Spectrophotometer 1800 is also user-friendly and easy to operate, making it an ideal instrument for both novice and experienced users.[18-33]

Overall, the Shimadzu UV-Vis Spectrophotometer 1800 is a powerful and versatile instrument that is widely used in the pharmaceutical industry for the analysis of drugs and pharmaceuticals. Its high-performance capabilities, user-friendly design, and range of features make it an ideal choice for a wide range of applications in research and quality control laboratories.[34-38]

2.1 Principles and Fundamentals of UV Spectroscopy in Pharmaceutical Analysis: UV spectroscopy is a widely used analytical technique in the pharmaceutical industry for the analysis of drugs and pharmaceuticals. The principle of UV spectroscopy is based on the measurement of the absorption of UV radiation by a sample. The absorption of UV radiation results in electronic transitions within the molecules of the sample, which causes the excitation of the electrons from the ground state to the excited state. The energy required for this transition is specific to the electronic structure of the molecule and is determined by the wavelength of the UV radiation. The intensity of the absorption is directly proportional to the concentration of the sample and is related to the molar absorptivity of the compound.

The fundamental components of a UV spectrophotometer include a UV source, a monochromator for selecting the desired wavelength, a sample holder, and a detector for measuring the intensity of the transmitted or absorbed light. The sample holder is usually a quartz cuvette, which is transparent to UV radiation and allows the sample to be placed in the path of the radiation.

UV spectroscopy is used in pharmaceutical analysis for a variety of applications, including quantitative analysis, identification of unknown compounds, and determination of drug purity. UV spectroscopy is particularly useful for the analysis of compounds that contain chromophores, which are functional groups that absorb UV radiation. Chromophores include groups such as carbonyl, aromatic, and conjugated double bonds.

The quantitative analysis of drugs using UV spectroscopy involves the measurement of the absorbance of the drug at a specific wavelength, which is related to the concentration of the drug in the sample. The Beer-Lambert law is used to relate the absorbance to the concentration of the drug.

Overall, UV spectroscopy is a powerful analytical technique in the pharmaceutical industry that allows for the quantitative and qualitative analysis of drugs and pharmaceuticals. It is a relatively simple and fast method that requires minimal sample preparation and is widely used in quality control and research laboratories.[39-45]

2.2 Objectives:

- To examine the regulatory guidelines and requirements for UV calibration in the context of ANDA submissions.
- To understand the importance of UV calibration in ensuring pharmaceutical quality control and compliance with regulatory standards.
- To evaluate the different parameters and criteria involved in UV calibration for ANDA submissions.
- To investigate the methods and techniques used for UV calibration in pharmaceutical laboratories.
- To develop a comprehensive framework or methodology for UV calibration in alignment with regulatory guidelines.
- To provide recommendations and best practices for effective UV calibration in the ANDA process.
- To contribute to the existing knowledge and understanding of UV calibration for ANDA submissions and its implications for pharmaceutical quality control.

3. Material and Method: Equipment and materials:

- Shimadzu UV-1800 UV-Vis spectrophotometer
- Quartz cuvettes
- UV-Vis compatible solvent
- Analytical balance
- Sample solutions for analysis

4. Experimental Work:

4.1 Standard Operating Procedure (SOP) Purpose: The purpose of this SOP is to provide guidelines for operating the Shimadzu UV-1800 UV-Vis spectrophotometer for quantitative and qualitative analysis of samples.

4.2 Scope: This SOP applies to the Shimadzu UV-1800 UV-Vis spectrophotometer in the specified laboratory.

4.3 Safety Precautions:

a. Follow all laboratory safety protocols, including the use of appropriate personal protective equipment (PPE).
b. Handle all chemicals and solvents with care and follow proper disposal procedures.

4.4 Instrument Setup and Initialization:

a. Ensure that the UV-1800 spectrophotometer is connected to a stable power source and turned on.
b. Allow the instrument to warm up for the recommended period, typically 30 minutes, to ensure stability and accuracy.
c. Verify that the wavelength calibration is up to date and accurate. Calibrate if necessary according to the manufacturer's instructions.

- Sample Preparation:
- Prepare the sample solutions according to the specific analysis requirements.
- Ensure that the samples are properly labelled and identified.
- Use UV-Vis compatible solvents for sample dilution or preparation.

4.5 Instrument Calibration:

a. Perform a blank measurement by placing the appropriate blank solvent into a cuvette and setting the baseline to zero absorbance.
b. For quantitative analysis, prepare a calibration curve using standard solutions of known concentrations.

4.6 Measurement Procedure:

a. Clean and dry the cuvettes before use to avoid contamination and stray absorbance.
b. Pipette the sample solution into a cuvette, ensuring it is filled evenly and without air bubbles.
c. Wipe the outside of the cuvette with a lint-free cloth to remove any fingerprints or smudges.
d. Place the cuvette into the sample holder, ensuring proper alignment.
e. Close the sample compartment lid to prevent stray light interference.
f. Set the desired wavelength on the UV-1800 spectrophotometer.
g. Click the "Start" button or select the appropriate measurement mode (e.g., Absorbance, transmittance) and acquisition parameters.
h. Record the measured absorbance or transmittance value for the sample.

Table 1. List of tests for calibration

S. No.	Test name
1	Control of Wave Length
2	Control of Absorbance
3	Limit of stray light
4	Resolution power
5	Baseline flatness
6	Specification of Cells

5. Data Analysis:

- Calculate the concentration or perform qualitative analysis based on the Obtained absorbance values using appropriate calibration curves or spectral comparisons.
- Record and analyse the data using suitable software or spreadsheets.

6. Post-Measurement:

- Clean the cuvettes thoroughly with a suitable solvent after each use to remove any residue.

- Turn off the UV-1800 spectrophotometer after completing the analysis.
- Clean the instrument exterior with a soft cloth as needed.

7. Documentation and Reporting:

- Record all relevant information, including sample details, measurement
- parameters, and results in a lab notebook or electronic database.
- Prepare reports or summaries of the analysis as required.

8. Maintenance and Troubleshooting:

- Perform routine maintenance tasks, such as cleaning the instrument,
- Checking Lamp intensity, and verifying wavelength accuracy, according to the manufacturer's instructions.
- Contact the appropriate personnel or service provider if any issues or malfunctions arise that are beyond routine maintenance or troubleshooting.

9. Calibration of UV-VIS Spectrophotometer: Calibration of a UV-VIS spectrophotometer is an important procedure to ensure accurate and reliable measurements of sample absorbance or transmittance. The following are the steps involved in the calibration of a UV-VIS spectrophotometer:

9.1 Control of Wavelength:

- Done using a known standard with a well-defined absorption spectrum is set to the specific wavelength of the standard, and the absorbance reading is recorded
- Process was repeated for several different wavelengths to ensure that the spectrophotometer is correctly calibrated across the entire range of wavelengths.

9.2 Control of Absorbance:

- Done using a known standard with a well-defined absorption spectrum and a known concentration.
- The spectrophotometer is set to the specific wavelength of the standard, and the absorbance reading is recorded.
- Process is repeated for several different concentrations to ensure that the spectrophotometer is correctly calibrated across the entire range of absorbance values.

9.3 Limit of Stray Light:

- Determined using a solution of potassium chloride.
- Involves measuring the absorbance of the solution at a specific wavelength and comparing it to the absorbance of a reference material at the same wavelength.

9.4 Resolution Power:

- Determined using a solution of toluene in hexane.
- Involves measuring the absorbance of the solution at two closely spaced wavelengths and calculating the resolution using the peak widths and the distance between the two wavelengths.

9.5 Photometric Linearity:

- Determined using a solution of potassium chromate in potassium hydroxide
- Involves measuring the absorbance of the solution at several concentrations and verifying that the absorbance values are proportional to the concentration values.

9.6 Baseline Flatness:

- Ability of the spectrophotometer to produce a flat and stable baseline signal in the absence of a sample.
- Determined by measuring the absorbance of deionized water or another suitable blank solution over a range of wavelengths.
- Resulting data is plotted, and any deviations from a flat baseline are noted.

9.7 Specification of Cells:

- It ensure that the cells used to hold samples meet the necessary standards for accuracy, precision, and reliability.

10. Result:

Figure 1 and table 2 shows the control wavelength.

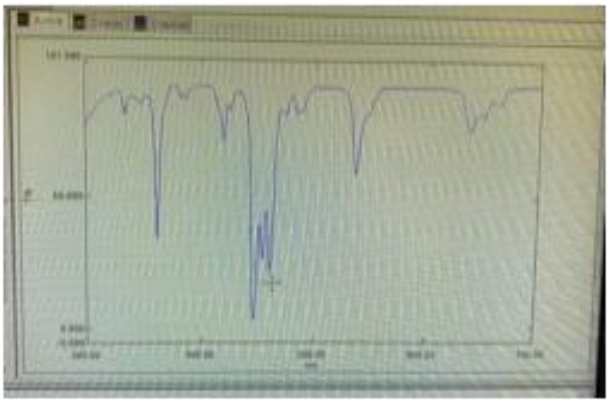

Figure 1. Wavelength of control

Table 2. Wavelength of control

S. No.	Wavelength	Observed Wavelength	Acceptance Criteria
1	241.15 nm	245.01 nm	240.15 to 242.15 nm
2	287.15 nm	288.01 nm	286.15 to 288.15 nm
3	361.50 nm	360.90 nm	360.50 to 362.50 nm
4	536.30 nm	534.30 nm	533.30 to 539.30 nm

Figure 2 and table 3 show the control absorbance.

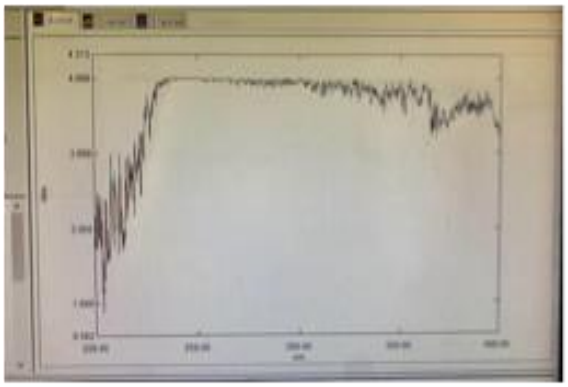

Figure 2. Control absorbance

Table 3. Control absorbance

S. No.	Wavelength	Observed Absorbance	Calculate Absorbance (1%, 1 cm)	Standard Absorbance (1%, 1cm)	Maximum Tolerance
1.	235 nm	1.48	24.12	124.5	112.9 to 126.2
2.	257 nm	1.74	154.7	144.5	142.8 to 146.2
3.	313 nm	0.58	48.61	48.6	47.0 to 50.3
4.	350 nm	1.29	108.31	107.3	105.6 to 109.0

Figure 3 and table 4 show the limit of stray light.

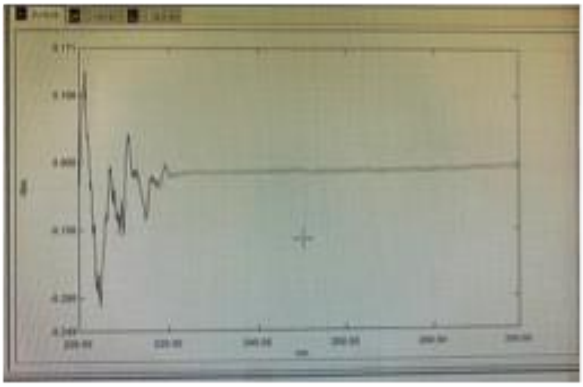

Figure 3. Limit of Stray light

Table 4. Limit of stray light

Test	Specification	Actual
Concentration of Potassium chloride	12g/ml	2g/ml
Absorbance at 200nm	The absorbance should be more than 2	0.136
Maximum at 269 m	0.002	-
Minimum at 266 m	0.001	-
Ratio of Absorbance	1.5	Ratio is not less than 1.5

Figure 4 and table 5 show the resolution power.

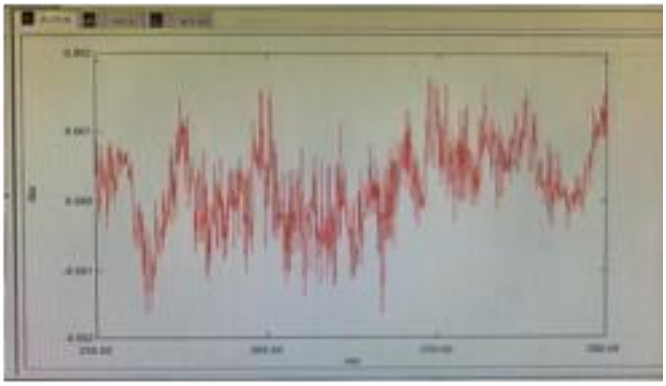

Figure 4. Resolution power

Table 5. Resolution power

Wavelength	Observed Absorbance	Maximum Tolerance

Figure 5 and table 6 show the baseline flatness.

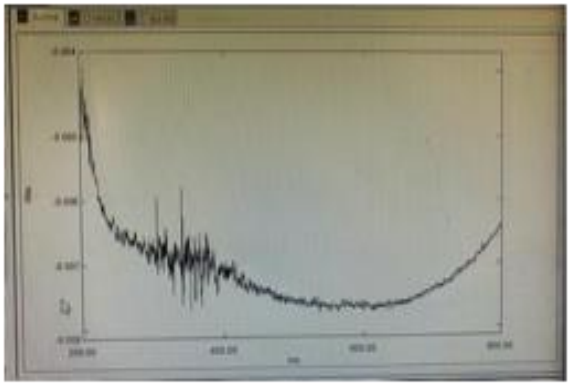

Figure 5. Baseline flatness

Table 6. Baseline flatness

Specification	Result
NMT 0.002 Abs	In Limit

Figure 6 and table 7 show the specification of cells.

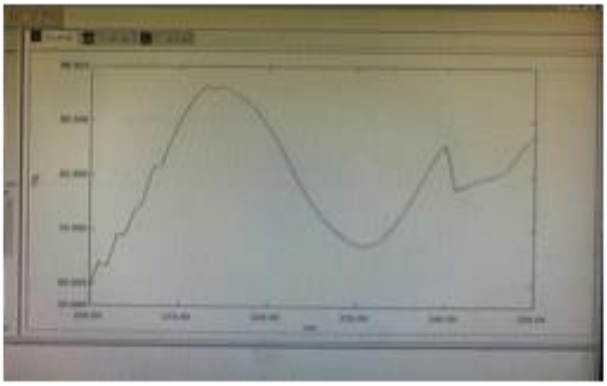

Figure 6. Specification of cells

Table 7. Specification of cells

Wavelength	Observed % Transmittance	Maximum Tolerance
200 nm	63.202	68 to 72 %
220 nm	96.252	80 to 84 %
240 nm	85.539	85 to 89 %

11. Conclusion: The Abbreviated New Drug Application (ANDA) filling system of Japan has been a significant contributor to the production and distribution of generic drugs globally. This system is designed to ensure that generic drugs are manufactured in compliance with regulatory requirements for safety, efficacy, and quality. The ANDA filing process allows manufacturers to produce bioequivalent versions of existing branded drugs after patent expiration without having to go through costly clinical trials.

One important aspect of ensuring compliance with these regulations involves developing calibration, validation, and standard operating procedures for equipment such as UV spectroscopy machines like Shimadzu 1800. These procedures help ensure that accurate measurements are taken during drug manufacturing processes under Good Manufacturing Practices (GMP) conditions.

Calibration is the process by which reference points are set up against which measurements can be compared. In the case of UV spectroscopy machines like Shimadzu 1800 used in drug manufacturing processes under GMP conditions, calibration ensures that the machine measures light intensity accurately at specific wavelengths. This helps ensure consistency in measurement across multiple tests.

Standard Operating Procedures (SOPs) provide written instructions detailing how specific tasks should be performed to ensure consistency and safety throughout an organization. Developing SOPs specifically tailored to use UV spectroscopy machines like Shimadzu 1800 which can help streamline operations by providing clear guidelines on how these instruments should be calibrated, validated, maintained & operated correctly.

Properly calibrated equipment combined with well-designed validation protocols leads to more accurate results when testing drugs before they leave production facilities; this ultimately leads to safer medications reaching patients around world

In conclusion, proper calibration/validation/standard operating procedure development for UV spectroscopy machines like Shimadzu 1800 is essential to maintaining high-quality standards during drug manufacturing processes under GMP conditions. This ensures that generic drugs produced using the ANDA filling system in Japan are safe and effective for patients worldwide. By ensuring that equipment is calibrated, validated, and operated correctly, manufacturers can produce high-quality generic drugs that meet the needs of patients while complying with strict regulatory standard.

12. References:

1. Pharmaceuticals and Medical Devices Agency. https://www.pmda.go.jp/english/review-services/reviews/approval- status/index.html

2. National Institute of Health Sciences. https://www.nihs.go.jp/drug/beiyaku- e.html
3. Pharmaceuticals and Medical Devices Agency. May 2021, Review and Inspection for Approval of Generic Drugs in Japan. https://www.pmda.go.jp/files/000226144.pdf
4. Pharmaceuticals and Medical Devices Agency. March 2020, Guideline on Clinical Development of Anticancer Drugs. https://www.pmda.go.jp/files/000153317.pdf
5. Pharmaceuticals and Medical Devices Agency. March 2020, Guideline for Clinical Evaluation of Antimicrobial Drugs. https://www.pmda.go.jp/files/000153318.pdf
6. Pharmaceuticals and Medical Devices Agency. March 2020, Guidelines for Nonclinical Studies of Drugs. https://www.pmda.go.jp/files/000153321.pdf
7. Pharmaceuticals and Medical Devices Agency. March 2020, Guideline on Clinical Evaluation of Generic Drugs. https://www.pmda.go.jp/files/000153316.pdf
8. Pharmaceuticals and Medical Devices Agency. March 2020, Guideline on Manufacturing and Quality Control of Drugs and Quasi-drugs. https://www.pmda.go.jp/files/000153353.pdf
9. Pharmaceuticals and Medical Devices Agency. May 2021, Review and Inspection for Approval of Generic Drugs in Japan. https://www.pmda.go.jp/files/000226144.pdf
10. Pharmaceuticals and Medical Devices Agency. March 2020, Guideline for Quality, Safety and Efficacy of Generic Drugs. https://www.pmda.go.jp/files/000153319.pdf
11. Pharmaceuticals and Medical Devices Agency. March 2020, Guideline on Clinical Evaluation of In Vitro Diagnostic Medical Devices. https://www.pmda.go.jp/files/000153314.pdf
12. Pharmaceuticals and Medical Devices Agency. March 2020, Guideline on Clinical Development of Vaccines. https://www.pmda.go.jp/files/000153315.pdf
13. Pharmaceuticals and Medical Devices Agency. March 2020, Guideline on Clinical Development of Regenerative Medicine Products. https://www.pmda.go.jp/files/000153320.pdf
14. Pharmaceuticals and Medical Devices Agency. March 2020, Guideline on Development of In Vitro Diagnostic Medical Devices. https://www.pmda.go.jp/files/000153354.pdf
15. Pharmaceuticals and Medical Devices Agency. March 2020, Guideline for the Conduct of Clinical Trials for Medical Devices. https://www.pmda.go.jp/files/000153355.pdf
16. Pharmaceuticals and Medical Devices Agency. March 2020, Guideline on Clinical Evaluation of Medical Devices. . https://www.pmda.go.jp/files/000153313.pdf
17. Pharmaceuticals and Medical Devices Agency. March 2020, Guideline for the Conduct of Good Clinical Practice. https://www.pmda.go.jp/files/000153350.pdf
18. Anda, Inc. (2021). Anda Filling System. https://www.andanet.com/services/anda-filling-system/
19. Pharmacy Times. (2019). Anda Launches Automated Filling System for Retail Pharmacies. https://www.pharmacytimes.com/view/anda-launches- automated-filling-system-for-retail-pharmacies
20. Anda, Inc. (2021). Anda Filling System. https://www.andanet.com/services/anda-filling-system/
21. Pharmacy Times. (2019). Anda Launches Automated Filling System for Retail Pharmacies. https://www.pharmacytimes.com/view/anda-launches- automated-filling-system-for-retail-pharmacies
22. Drug Store News. (2019). Anda launches robotic system for filling prescriptions. https://drugstorenews.com/technology/anda-launches-robotic- system-filling-prescriptions
23. Anda, Inc. (2021). Anda Filling System. https://www.andanet.com/services/anda-filling-system/

24. Pharmacy Times. (2019). Anda Launches Automated Filling System for Retail Pharmacies. https://www.pharmacytimes.com/view/anda-launches- automated-filling-system-for-retail-pharmacies
25. Drug Store News. (2019). Anda launches robotic system for filling prescriptions. https://drugstorenews.com/technology/anda-launches-robotic- system-filling-prescriptions
26. Wang Y et al., Strategies to optimize ANDA submissions and approval rates, Journal of Pharmaceutical Sciences. 2012; 101(8): 2707-2716.
27. Garrison LP Jr et al., The value-added medicines group: Advancing the science of medical practice through health economics & outcomes research in generic pharmaceuticals – a case history on how to do it right! Pharmacoeconomics, 2011; 29(3): 179-190.
28. Singh R, Yu LX, Regulatory science initiatives enabling better understanding and improving quality across the generic drug lifecycle at FDA's office of generic drugs, Therapeutic Innovation & Regulatory Science. 2012; 50(5): 562–570.
29. IQVIA Institute for Human Data Science (2020). Medicine Use And Spending In The U.S.: A Review Of 2019 And Outlook To 2023. https://www.iqvia.com/insights/the-iqvia-institute/reports/medicine-use-and- spending-in-the-us-review-of-2019-outlook-to-2023
30. BioPharm International Editors. (2018). ANDA Filing for Biosimilars. https://www.biopharminternational.com/view/anda-filing-biosimilars
31. United States Pharmacopeia. (2021). General Chapter <1058> Analytical Instrument Qualification. United States Pharmacopeial Convention.
32. Chen, X., & Wang, J. (2014). Current progress in automated pharmaceutical filling technology. Drug Development and Industrial Pharmacy, 2014; 40(12); 1561-1572.
33. Shimadzu Corporation. (2021). UV-VIS Spectrophotometer UV-1800. https://www.shimadzu.com/an/products/spectro/uv-vis/uv1800.html
34. Skoog DA, Holler FJ, Crouch SR, Principles of instrumental analysis. Cengage learning; 2017.
35. Shimadzu Corporation. (2021). UV-Vis Spectrophotometer 1800. https://www.shimadzu.com/an/products/spectro/uv-vis/uv-1800.html
36. Rehder DS, UV-visible spectroscopy in pharmaceutical analysis, Journal of Pharmaceutical and Biomedical Analysis. 2008; 48(3): 254-261.
37. Lopes NP, Kato MJ, HPLC and UV spectroscopy for the quality control of medicinal plants, Phytochemical Analysis. 2009; 20(3): 220-226.
38. Ali F, Hasan MM, Islam MS, An overview of UV-visible spectroscopy in pharmaceutical analysis, Journal of Analytical & Pharmaceutical Research. 2016; 2(4): 00024.
39. Cohatwal GR, Anand A, UV spectroscopy in pharmaceutical analysis. In Pharmaceutical Analysis, New Delhi: Himalaya Publishing House. 2004; 173-201.
40. Patil MS, Kulkarni PV, Patil S.R. UV spectroscopy for pharmaceutical analysis, International Journal of Pharmaceutical Sciences and Research. 2011; 2(12): 3059-3073.
41. Srivastava SK, Gupta A, Gupta U, Application of UV spectroscopy in pharmaceutical analysis, Journal of Pharmaceutical Science and Bioscientific Research. 2014; 4(2): 108-114.
42. Augsburger LL, Hoag SL, Quantitative and qualitative analysis of drugs using UV spectroscopy. In Pharmaceutical Analysis: A Textbook for Pharmacy Students and Pharmaceutical Chemists. London: Academic Press. 2013; 123-147.
43. Shimadzu Corporation. UV-VIS Spectrophotometer UV-1800.

https://www.shimadzu.com/an/spectro/uv/uv-1800.html

44. Analytical Instrument Resource. Shimadzu UV-1800 UV-Vis Spectrophotometer. https://www.airscientific.com/product/shimadzu-uv- 1800-uv-vis-spectrophotometer
45. Blandino A, Altimari P, Cappellin L, et al., UV-visible spectrophotometry as a tool for wine analysis, J Chem. 2015; 1-7.