HPLC METHODOLOGY MANUAL

DISTRIBUTED PHARMACEUTICAL ANALYSIS LABORATORY (DPAL)

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INTRODUCTION AND SCOPE

The goal of the Distributed Pharmaceutical Analysis Lab (DPAL) is to provide the highest quality analysis possible. However, it is important to acknowledge that as a coalition of research-based academic laboratories, the level of quality assurance, maintenance and record keeping may not be equivalent to that of a commercial or government analytical laboratory. DPAL participants are expected to conduct all experiments in accordance with proper analytical methodology and report all results in a transparent manner.

DPAL procedures for quantifying the active ingredients in pharmaceutical dosage forms are based on monographs published in the United States Pharmacopeia (USP) or British Pharmacopeia (BP). Modifications are made to these methods to adjust for the resources available. For example, since the samples are single packages that do not contain a large number of tablets, DPAL analyzes individual drug tablets rather than pooled samples of 20-50 tablets.

LEGAL CONSIDERATIONS

Participants in the DPAL should be aware of legal issues related to pharmaceutical analysis. These legal considerations help protect all those involved in the DPAL including those being served and those in academic laboratories.

Poor quality medications are reported to the World Health Organization (WHO) Rapid Alert system and to the Medical Regulatory Authority (MRA) in the country where the drugs originated. Since the DPAL conducts single tablet analysis, assay results must be replicated on several samples before triggering a report to the MRA or WHO. If a participant laboratory identifies a substandard product, Professor Lieberman will assist them in reporting the medication to the appropriate authorities. The DPAL may need to run additional tests such as LC-MS and/or the MRA may want to analyze the samples themselves to support legal action. Therefore, samples and their packaging must be preserved carefully.

Due to the nature of the samples, secure data sharing and sample reporting is very important. The DPAL utilizes Open Science Framework (OSF) for communicating information with the intention of transparent data sharing among participants. Since information uploaded to OSF is primary data which is used in formal reports to regulatory agencies, it is imperative that the data is authentic and accurate. Therefore, folder access is restricted to only those individuals who actively report data or supervise operations. This policy is in place to prevent accidental or intentional editing by unauthorized users. For any questions regarding OSF, please reference the OSF Handbook found in the DPAL folder in OSF.

Due to the prevalence of counterfeit and improperly labeled products in developing world markets, it is possible that manufacturer information (manufacturer name, lot number, expiration date, etc.) stated on packaging materials is falsified or missing. At the recommendation of legal counsel at the University of Notre Dame, the DPAL requires that participants always reference samples as "stated to be manufactured by (company name)" for all communications about specific pharmaceutical products.

All product-specific information, including but not limited to photographs or metadata, that is posted in a public forum (poster session, news article, web site, social media platform, etc.) must adhere to the previously described wording ("stated to be manufactured by") for reference to the origin of the medication, unless the manufacturer has confirmed that they made the product. In addition, all comments about the products must be factual and non-inflammatory. Students must obtain permission from their instructor before posting anything regarding product information. It is the responsibility of the instructor to certify that the posting is, indeed, factual and non-inflammatory.

DPAL ANALYSIS PROGRAM SET-UP

In order to provide quality analysis of pharmaceutical samples, several steps are necessary to ensure that the analytical methodology meets regulatory standards. The DPAL program is composed of distinct stages. The process begins with exploring a method based on published United States Pharmacopeia (USP) or British Pharmacopeia (BP) procedures. Once a functioning and efficient methodology has been established by one DPAL participant, other participants may use it if they can demonstrate system suitability to validate the method. Upon satisfactory completion of the system validation, the participant school will be sent pharmaceutical samples collected by our international partners to analyze.

Method Exploration
The appropriate USP or BP procedure is used as a starting point and assay conditions are optimized for the particular column and system. This process generally requires several hours in lab for a faculty member. Most assays require a standard 10-25 cm x 4.6 mm C18 column, HPLC grade methanol or acetonitrile as the organic solvent, buffer components, a pH meter and the appropriate reference standard. Samples must be syringe filtered. The DPAL can provide technical advice and funding assistance. Once a working method has been established, contact the DPAL to request expired samples for system suitability testing.

System Suitability
This stage occurs after the method conditions have been optimized and demonstrates that the instrument and developed method are in accordance with the standards laid out in USP <1226>. System suitability involves measuring the accuracy, precision, linearity, specificity, sensitivity, and limits of detection for the method. Detailed instructions for this stage can be found in the System Suitability Requirements Section. Demonstrating system suitability generally requires about 40 injections and makes for a good independent research or instrumental analysis team project. The DPAL will provide expired dosage forms for matrix recovery experiments. Data and results should be recorded in the System Suitability Spreadsheet Template (found in the DPAL folder on OSF). Other formats are acceptable as long as they contain all of the necessary information outlined in the System Suitability Requirements. The data from the system suitability experiments must be uploaded into OSF and reviewed before in-date pharmaceuticals are sent to the participant laboratory for analysis.

Sample Analysis
Running an assay consists of sample preparation, 1-3 injections of the sample, and analysis against an external reference. The external reference results are tracked as quality control (QC) samples and are run every five experimental samples. If the analytical metrics for a QC sample are out of the limits described in the protocol for a particular analyte, the results from all previous injections up until the last successful QC sample must be discarded and the samples re-

run. (The experimental work can be easily completed in a 3-hour lab session, although there are logistical issues if many students are trying to use a small number of HPLCs).

Assay data and results for all pharmaceutical samples run during a session must be reported together in the appropriate template Excel spreadsheet (found in the Data Processing Templates folder in the DPAL project on OSF). The template spreadsheet includes blanks for all the necessary data required for the DPAL. It is imperative that the spreadsheet be carefully completed to ensure proper data reporting. In addition, always maintain a current copy of the Control Chart (template found in the DPAL folder in OSF) for each analyte. Please see the OSF Handbook for full reporting procedures.

HPLC METHODS

It is imperative that DPAL participants submit detailed and exact descriptions of the methodologies being employed. This ensures that accurate records are kept and allows other members of the DPAL to replicate the procedure. To submit method development information, please use the Excel template in the DPAL folder on OSF. Once the HPLC Method spreadsheet, System Suitability Requirements Information and a current Control Chart have been uploaded to OSF, the method will be reviewed and incorporated into the next update of the HPLC Methodology Manual.

Experimental Set-Up Information

- Analyte
- Instrument make and model
- Detector type, make and model
- λ Detector
- Column (Brand, Dimensions, Packing)
- Temperature (Room temperature? Column heated?)

Sample Information

- Concentration
- Solvent
- Reference material source, cost, purity
- Notes on Sample Prep (degradation, storage, sonication, mixing, ect.)
- Injection volume

Isocratic Methods

- Mobile Phase (% water, % organic, buffer pH and conc., flow rate, additive conc.)
- Additive sources and costs
- How to make the buffer
- How to store the buffer
- Notes about the buffer
- Run Times

Gradient Methods

- Mobile Phase A (% water, % organic, buffer pH and concentration, additive conc.)
- Mobile Phase B (% water, % organic, buffer pH and concentration, additive conc.)
- How to make the buffer
- How to store the buffer
- Notes about the buffer
- Description of gradient (run times, mobile phase ratios, flow rates and ramp types)

Column Washing

- Description of column washing protocol

SYSTEM SUITABILITY REQUIREMENTS

General Information
Information regarding personnel and the location of analysis is required for reporting purposes and is used as a means of contacting those involved with the project in the event that there are questions or concerns about the data. It is important to remember that student emails are deactivated upon graduation; therefore, the DPAL strongly encourages all student researchers to provide their personal email. For all of the following tests, the required information includes the analyst's name, date of completion, and mentor verification (initials) indicating that the experiment was properly conducted.

Precision
The relative standard deviation (RSD) for the integrated intensities of 6 consecutive injections of the known normal standard should be below 0.020 (2%).
Required Information:

- Intensity value measured
- RSD (in decimal units)

Linearity
Prepare and run at least five calibration standards over the concentration range of 5% to 200% of the standard. Calculate a regression line for the calibration data. The correlation coefficient, R, should be 0.98 or higher and the y intercept should be zero (within the error of measurement).
Required Information

- Concentration values used
- Measurements for each point
- Calibration curve
- Slope and y-intercept (including units)
- R value
- Residual sum of squares

Establish Control Chart
Track metrics such as the peak shape, resolution, and integrated intensity of the known standard for each analyst and each day of operation. Use the Control Chart Excel Template found in the DPAL folder on OSF. Ensure that a current version is uploaded to OSF when submitting the System Suitability Report.

Accuracy & Range
Use volumetric techniques to accurately prepare overdosed (~150%), normal (~100%) and deficient (~35%) samples. Perform three replicate injections each of the overdosed sample (~150%), normal sample (100%), deficient sample (~35%), and a solvent blank (total of 12 determinations). Run the external standard after every 4 runs and check that the values of the integrated intensity for the external standard fall within 2% RSD. Use the average external standard signal to determine the

concentrations of the overdosed, normal, deficient, and blank samples. The measured concentration of each sample should be within ±2% of its true concentration.
Required Information

- True Concentration (T), Intensity, Measured Concentration (M) and (M-T)/T for all three of the runs for the overdosed sample, normal sample, deficient sample and solvent blank
- Listed intensities for the external standard (QC) samples
- RSD for QC samples

Accuracy via Spike Recovery
A sample of a pharmaceutical dosage form (tablet or capsule) of the target drug should be prepared for analysis and a portion spiked with an extra 30% of the API. Calculate the % recovery of the spike. It should be within 90-110%.
Required Information

- Description of how the sample was prepared and spiked
- % Recovery of spike

Specificity
This can be demonstrated by showing that a spike can accurately be recovered from a degraded dosage form matrix. Stress the dosage form by baking a tablet for an hour at 60˚C, then spike with an extra ~30% of the pure API and measure the spike recovery.
Required Information:

- Description of what was used as the matrix
- Description of how the matrix was spiked
- % recovery
- Chromatograms before and after the spike
- Calculated retention times and resolution for impurities

Normal Chromatograms
Include a chromatogram of a "normal" sample, analyzing the peak metrics as shown in the Analytical Metrics Section (p 10).

Limit of Detection (LOD) & Lower Limit of Quantification (LLOQ)
LOD and LLOQ determination are carried out using the slope of the calibration curve and the standard deviation of six low concentration samples. Best practice is to prepare the low concentration sample at about 2-3 times the expected LOD, which you can guess from your linearity plot. How ever one measures the LOD and LLOQ, samples near the LOD or LLOQ limit should be run and their chromatograms shown in the report.
Required Information

- Description of how LOD and LLOQ were measured and results of experiment
- (Or) Explanation of why this was not done

ANALYTICAL METRICS

Measuring Theoretical Plates

The DPAL recommends using the British Pharmacopia method due to the simplicity of measuring peak width at half max height. Note, that this method will slightly underestimate column efficiency.

$$N=5.54\left(\frac{t_r}{W_{0.5}}\right)^2$$

t_r=retention time of the peak

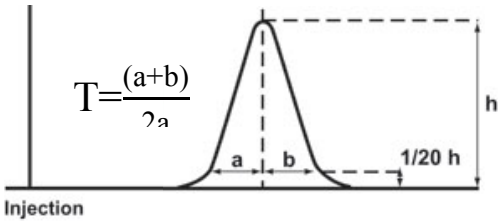
$W_{0.5}$=width of peak at half the height

Measuring Resolution of Two Peaks

For peaks with tailing, the DPAL uses a formula with peak widths measured at ½ max height.

$$R_s=\frac{2(t_2-t_1)}{1.7(W_{0.5,1}+W_{0.5,2})}$$

Measuring Tailing Factor



T=tailing factor (measured at 5% of peak height)

b=distance from the point at peak midpoint to the trailing edge

a=distance from the leading edge of the peak to the midpoint

Measuring Column Capacity Factor (Isocratic Methods Only)

$$k=\frac{(t_r-t_0)}{t_0}$$

t_r=peak retention time

t_0=dead volume of the column (measured by the elution time for the solvent front)

SAMPLE STORAGE AND TRACKING

The pharmaceuticals sent for analysis are forensic samples. Therefore, they must be stored in a way that does not promote degradation or contamination. It is imperative that thorough and accurate records of each sample are kept to ensure that the DPAL knows who performed what tests.

Samples must be stored in a cool, dark environment. The DPAL recommends storing samples in a plastic container with a tight lid in a refrigerator. Allow the samples to come to room temperature before working with them in order to prevent water from condensing on cold surfaces.

Each product sample in the batch you will receive consists of at least 3 tablets or capsules which will be shipped in a plastic bag labeled with a NDID tracking number (for example, the tracking number will be of the form "16-xxxx" for a sample cataloged in 2016). When tests are run on individual tablets or capsules, label them as "16-xxxxa, b, c". Students should sign out samples for analysis and use the NDID tracking number in their records and chromatogram labels.

SAMPLE PREPARATION

External Standards

External calibration standards are created from analytical grade reagents that are traceable to USP or BP standards. The standard should include a certificate of analysis, and the reagent purity, protonation state, and hydration state should all be taken into account when calculating final concentrations (see the Excel template for guidance). Store dry standards as directed on the bottle (most must be kept cold).

Paracetamol Standard	Sigma-Aldrich	PHR1005-1G	$57.00
Ampicillin Trihydrate Standard	Sigma-Aldrich	PHR1393-1G	$61.70
Amoxicillin Trihydrate Standard	Sigma-Aldrich	PHR1127-1G	$57.00
Potassium Clavulanate Standard	Sigma-Aldrich	33454-100MG	$129.50
Ciprofloxacin Standard	Sigma-Aldrich	PHR1167-1G	$57.00
Azithromycin Standard	Sigma-Aldrich	PHR1088-1G	$62.70

The "known" API standard should contain about 0.5 mg/mL of the active pharmaceutical ingredient (API) being analyzed (for amoxyclav analysis the standard should contain 0.5 mg/ml of amoxicillin plus 0.2 mg/ml of clavulanate). The precise concentration is not important, but the exact concentration must be known (use the analytical balance and volumetric fluid measurements). For most analytical balances, a minimum mass of 50.0 mg is required for suitable accuracy. This external standard will be used to determine the sample concentrations.

It is best practice to make a fresh standard sample every time it is needed. However, this protocol is expensive and time consuming. If a participant wants to reuse standards, the data and results of at least one experiment must be conducted in which the reused standard was assayed against a fresh one (it would be a good, short research project to run periodic chromatograms for a standard sample that is left out at room temperature or under refrigeration for several days).

For system suitability, you will need the known standard, five calibration standards; a set of normal, overdosed, and deficient "unknowns"; and a dosage form of the product that will be used for a spike-recovery experiment. The HPLC experiment only requires 20µL per injection, but in order to get accurate dilutions, one must prepare the solutions using volumetric glassware.

Calibration standards should span the range from 5% to 200% of the expected API concentration in the experimental samples. At least 5 standards should be used to construct the calibration curve. For example, use 5%, 20%, 80%, 120%, and 200% to establish linearity. A calibration curve generated on one day cannot be used to assay concentrations of samples run on another day. Since it takes 5 runs to do the calibration curve, the DPAL prefers to establish linearity, and then use a single-point external standard to assay concentrations of unknown samples.

Prepare a "normal" unknown sample in the 95-105% range, an "overdosed" sample in the 140-160% range, and a "deficient" sample in the 20-50% range. Also prepare a method blank, which is nominally 0%. For the spike recovery experiment, a dosage form (tablet or capsule) is required, which DPAL can send to participants. Prepare the sample as described below under "pharmaceutical dosage forms," weighing out at least 50 mg of the powdered tablet. Weigh out 25 mg of the API and add, then prepare and filter the sample as described below; the nominal concentration should be around 150% of the expected API content (calculate it exactly).

Pharmaceutical Dosage Forms

Samples for analysis should contain about 0.5 mg/mL of the API (0.5 mg/ml of amoxicillin and 0.2 mg/mL of clavulanate for amoxyclav analysis). This concentration may need to be adjusted to ensure that the samples are in the linear range for a particular system.

Accurately weigh a tablet or the contents of a gel capsule and take a portion of the powder that will give a 0.5 mg/ml solution of the API when diluted to volume. For capsules, weigh the contents of a gel cap by difference. Weigh the entire capsule, then remove the powder and use a stream of air to blow out any remaining powder, finally reweigh the empty capsule. For tablets, the entire tablet should be weighed and then crushed with a mortar and pestle. The powder from a tablet or capsule should be well mixed. For preparation of the analytical sample, weigh out at least 50 mg of powder on an analytical balance. The remaining powder should be labeled and frozen for storage. The label should include the date, API name, sample number, and analyst's initials.

For example, the total contents of an amoxicillin capsule with a nominal dose of 500 mg amoxicillin might weigh 627 mg due to excipients. To prepare a 0.5 mg/mL solution, a portion of roughly 63 mg would be accurately weighed and dissolved in 100 mL of solvent. Samples should be thoroughly mixed (by 5 minutes of sonication or 5 minutes on a magnetic stirrer) and an additional 2 minutes of hand shaking and inversion of the volumetric flask. All samples must be filtered through a fresh 0.45-micron syringe filter to remove particulates that might clog the HPLC column. The DPAL recommends filtering about 1 mL of the sample into an autosampler vial, discarding the first drops of filtrate.

COLUMN STORAGE, CONDITIONING AND WASHING

For 4.6 mm ID columns, typical column volumes are 4.2 mL for a 25 cm column, 2.5 mL for a 15 cm column, and 1.7 mL for a 10 cm column.

Column Storage
50% organic solvent (methanol or acetonitrile):50% water. It is good practice to label individual columns so students can record which column was used to produce each assay. Many columns are pre-labeled with a unique ID to facilitate tracking the usage.

Conditioning the Column
If a buffer solution is run through the column while it is full of 50% methanol, the buffer salts may precipitate and clog the column. Condition the column by running 95% water:5% methanol (initial water: organic ratio) for 5 column volumes. Use a flow rate that gives back pressures in the 1500-2400 psi range. Next run 95% buffer:5% methanol (initial conditions, with buffer) for 10 column volumes. Do a blank run and check that the background is clean. Conditioning will take 1-2 hours, during which time samples can be prepared.

Washing the Column
Do *not* leave the column with low-organic buffer solution (<30% methanol or acetonitrile) in it, because bacterial growth will occur. If the column needs to be stored for more than 10 hours, protect the column by washing it. Run 5 column volumes of 100% water to remove traces of buffer salts, then run 5 column volumes of 50% methanol:50% water (or 50% acetonitrile:50% water if the method uses acetonitrile). The column can be left on the HPLC or removed and capped for storage.

SAMPLE ASSAY AND QUALITY CONTROL PROCEDURES

Reproducibility
External calibration standards are created from analytical grade reagents as directed in section 4. Five injections of the external standard must show a peak area within 2% relative standard deviation (RSD), and the range of retention times must be within 0.5 minutes, before samples are assayed.

Control Chart
Each time the method is performed, record the date and the retention time and integrated intensity of the 5th external calibration standard. Also record changes to the method (for example, use of a new column or different batch of buffer). The intensities and retention times should be plotted on a graph. If the intensities or retention times vary outside the control limits, the system suitability is in question. Control chart problems are usually caused by clogged columns or instrumental problems such as bad valve blocks or buffer salt precipitation. These issues must be resolved before carrying on with assays.

Quality Check
After every five unknown sample runs, the standard is injected as a quality check and it must assay within 2% RSD of the 5 initial injections and be within the 0.5 minute time range of the initial injections. If a quality check fails, data after the last passed quality check cannot be used.

Replicate Samples
Typically, one pill from each package is analyzed. If a sample fails analysis (assay value <90% or >110% of stated API content) then two new samples are prepared independently from the remaining powdered pill material and re-assayed. Report all three assays and calculate their average and standard deviation. If the average also fails and you want to measure pill-to-pill variability in the packet, two more tablets may be assayed.

Record Keeping
All data and results must be collected and uploaded using DPAL templates on the OSF site. Please see the OSF Handbook for full instructions on uploading procedures.

METHODS

AMOXICILLIN AND AMOXICILLIN/CLAVULANATE (OR CLAVULANIC ACID)

Instrument: Waters e2695 High Performance Liquid Chromatograph
Detector: Waters 2998 Photodiode Array Detector
Analytical Wavelength: 220 nm
Column: Symmetry 100 x 4.6 mm, C18 column, 5 µm particle size and 100Å (An earlier procedure used a Kinetix column. Many C18 column types are acceptable for this assay.)
Column Temperature: Room temperature

Gradient Method

Sample Concentration: 0.5 mg/mL
Amoxicillin Sample Solvent: 20 mM monobasic sodium phosphate at pH of 4.4 in 18 MΩ water to make the samples. The pH is important, as amoxicillin hydrolyzes rapidly at basic pH. Keep standards and standard solutions refrigerated. Use standard solutions within 3 weeks. Alternatively, freeze for storage up to 2 months.
Amoxyclav Sample Solvent: 100% DI water. Clavulanate is thermally unstable. Samples should be used within 6 hours of preparation, or they may be held at -80˚C for up to 4 weeks with <2% degradation.
Mobile Phase A: 100% methanol
Mobile Phase B: 20 mM monosodium phosphate buffer, pH 4.4 in 18MΩ water
Sample Injection Volume: 18 µL
Gradient Description:

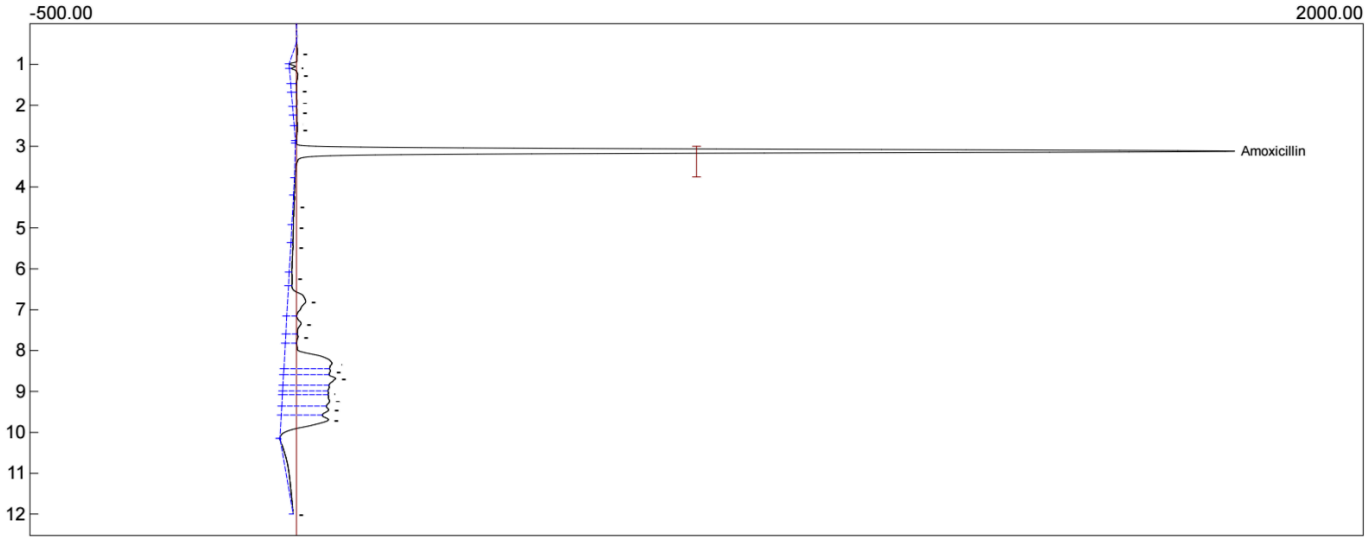
Time (min)	Mobile Phase A (%)	Mobile Phase B (%)	Flow (mL/min)	Ramp
0.5	5	95	0.5	None
7.0-8.0	90	10	0.5	Linear
8.0-11.0	90	10	0.5	None
11.0-12.0	5	95	0.5	Linear

Column Washing: After each analysis session, it is important to wash out accumulated buffer salts and degraded clavulanic acid. Use 5 column volumes of 95% water:5% methanol, 5 column volumes of 50% methanol:50% water, 5 column volumes of 95% methanol:5% water, then 5 column volumes of 50% methanol:50% water again.
Column Storage: 60% methanol: 40% water

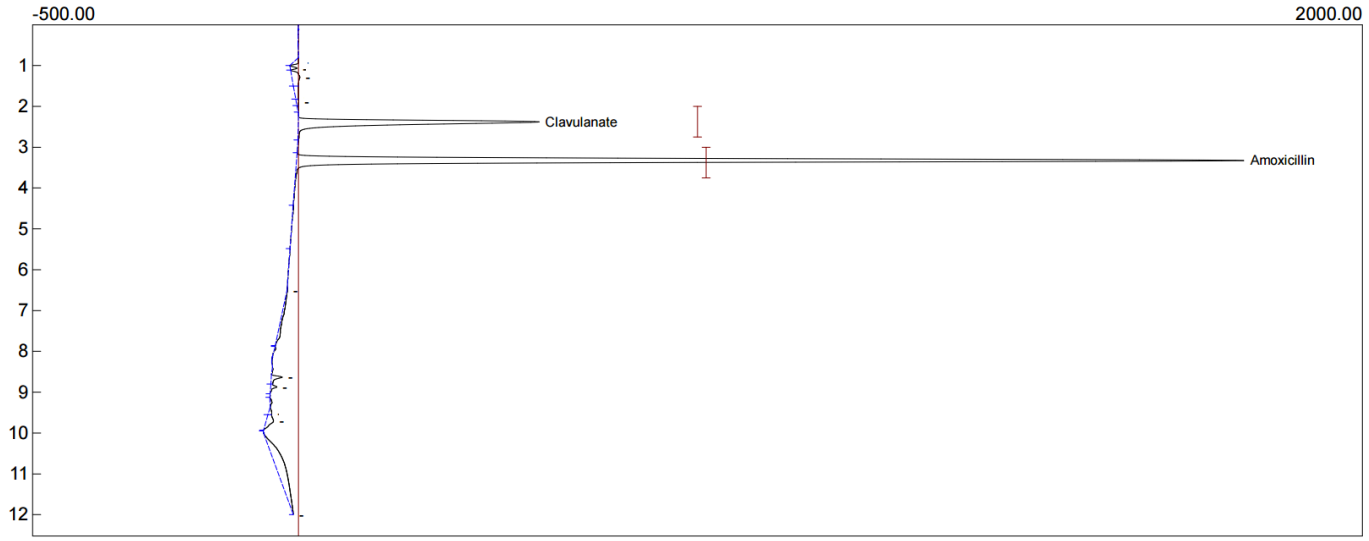
Analytical Metrics for Amoxicillin
Column Efficiency >1700 theoretical plates
Tailing Factor <2.5
RSD for Replicate Injections <2.0%

Analytical Metrics for Amoxyclav
Resolution between the amoxicillin and clavulanate peaks > 3.5
Column Efficiency >550 theoretical plates
Tailing Factor <1.5
RSD for Replicate Injections <2.0% for both APIs

Typical Amoxicillin Chromatogram



Typical Amoxyclav Chromatogram



METHODS

ALBENDAZOLE

Instrument: Waters e2695 High Performance Liquid Chromatograph
Detector: Waters 2998 Photodiode Array Detector
Analytical Wavelength: 254 nm
Column: XTerra 150 x 4.6 mm, C18 column, 3.5 µm particle size
Temperature: Room temperature

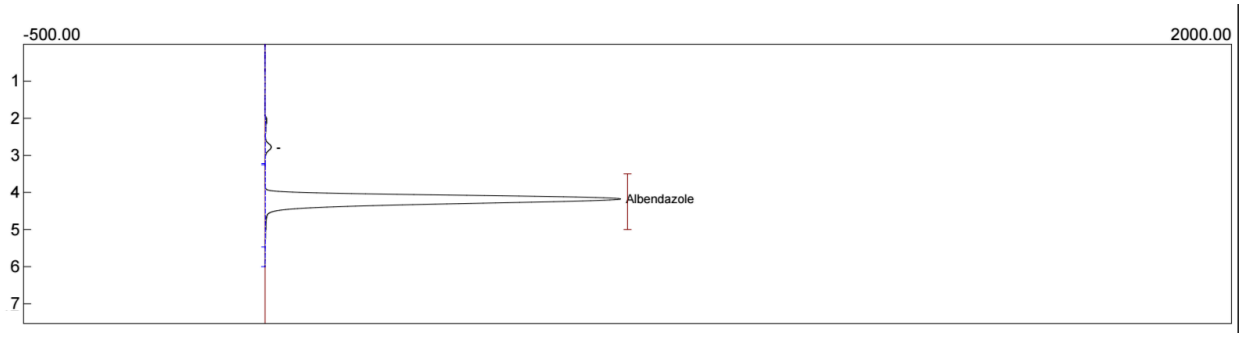
Isocratic Method

Sample Concentration: 0.5 mg/mL Standard Concentration (50 mg of tablet powder used to prepare 1 mg/mL solution)
Sample Solvent: Acidified methanol prepared by adding 1 mL of sulfuric acid to 99 mL of methanol. Sample prep involves dissolving 50 mg of powder in 5 mL of acidic methanol and 25 mL methanol in a 50 mL volumetric flask. Sonicate for 5 minutes and bring to volume with methanol.
Mobile Phase: Dissolve 0.50 g of monobasic ammonium phosphate in 400 mL of water. Add 600 mL of methanol, mix and filter. Bring pH to 1.7-2.0 by using a drop or two of sulfuric acid.
Flow Rate: 0.75 mL/min or 1.0 mL/min
Injection Volume: 15 µL
Run Time: 7 minutes
Column Washing: After each analysis session, rinse column with 10 column volumes of 50% water: 50% methanol.
Column Storage: 50% methanol: 50% water after rinsing.

Analytical Metrics

Column Efficiency >2000 theoretical plates
Tailing Factor <1.5
RSD for Replicate Injections <0.3%

Typical Albendazole Chromatogram



REVISION HISTORY

This manual was drafted 2014-11-04
Updated 2015-01-28 to fix errors in amoxicillin/amoxy-clav gradients
Updated 2015-04-16 to fix more gradient errors.
Updated 2015-05-15 to add QA/QC procedures
Updated 2015-05-19 to add information on column storage, washing, reconditioning

Initials/Date	Change	Purpose
NM 2015-08-07	Deleted Ampicillin analysis from the Amp, Amox, Amox/Clav analysis	The parameters are only valid for Amox and Amox/Clav. The analyses have been separated to shorten run time. A new section will be added for Ampicillin analysis.
NM 2015-08-07	Gradient for Amox and Amox/Clav has been changed from (time (min), %methanol, %buffer, gradient) (0.0, 5, 95, none; 10.0, 80, 20, linear; 13.0, 5, 95, linear; 18.0, 5, 95, none) flow = 0.5 mL/min	Run time is shorter
ML 2015-08-07	Corrected cipro buffer to include 3.5% acetonitrile	buffer description was incorrect
ML 2015-08-20	Added a form to summarize method	
NM & ML 2015-11-06	Rewrote some confusing text	Clarify verification requirements
ML 2016-03-25	Added Cipro sample prep directions	
ML & NM 2016-05-12	Make validation form more explicit/transparent	
MB 2016-06-28	Formatting Changes	Clarification and to use with electronic OSF templates for information submission
MB 2016-07-14	Added to Legal Considerations	OSF security considerations