CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

216482Orig1s000

PRODUCT QUALITY REVIEW(S)

Office of Pharmaceutical Quality

New Drug Application (NDA) 216482
Integrated Quality Assessment Template

Table of Content Links

RECOMMENDATION

☒ Approval
☐ Approval with Post-Marketing Commitment
☐ Complete Response

NDA 216482
Assessment #1

Drug Product Name	Mycophenolate Mofetil Oral Suspension
Dosage Form	Suspension
Proposed Strengths	200 mg/mL
Route of Administration	Oral
Rx/OTC Dispensed	Rx
Applicant	Liqmeds Worldwide Lts.
US agent, if applicable	MA Pharmaceutical Consulting, Inc.

Submission(s) Assessed	Document Date	Discipline(s) Affected
Original (SD 1)	3/8/2022	All
Quality Amendment (SD 5)	5/11/2022	Manufacturing, Biopharmaceutics, and Microbiology
Quality Amendment (SD 6)	5/17/2022	Drug Product
Quality Amendment (SD 8)	5/26/2022	Drug Product
Quality Amendment (SD 12)	9/16/2022	Manufacturing
Quality Amendment (SD 15)	10/11/2022	Labeling
Quality Amendment (SD 17)	11/14/2022	Biopharmaceutics
Quality Amendment (SD 18)	11/15/2022	Labeling
Quality Amendment (SD 19)	11/21/2022	Labeling

QUALITY ASSESSMENT DATA SHEET

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
(b) (4)	II		(b) (4)	Adequate	10-MAR-2021	
	III			N/A		Sufficient information in NDA
	III			N/A		See DMF (b) (4) below
	III			Adequate	10-SEP-2012	
	IV			Adequate	15-MAR-2022	

B. OTHER DOCUMENTS: *IND, RLD, RS, Approved NDA*

Document	Application Number	Description
PIND	140359	Presubmission for mycophenolate mofetil oral suspension

2. CONSULTS

Discipline	Status	Recommendation	Date	Assessor
Biostatistics	N/A			
Pharmacology/Toxicology	N/A			
CDRH-ODE	N/A			
CDRH-OC	N/A			
Clinical	N/A			
Other				

NDA Executive Summary

1. Application/Product Information

NDA Number.	216482
Applicant Name	Liqmeds Worldwide Ltd.
Drug Product Name	Mycophenolate Mofetil
Dosage Form.	Suspension
Proposed Strength(s)	200 mg/mL
Route of Administration	Oral
Maximum Daily Dose	3000 mg
Rx/OTC Dispensed	Rx
Proposed Indication	Mycophenolate Mofetil is an antimetabolite immunosuppressant indicated for the prophylaxis of organ rejection in recipients of allogeneic kidney, heart or liver transplants, and should be used in combination with other immunosuppressants. The drug product can be used in both adult and pediatric populations.
Drug Product Description	Mycophenolate mofetil oral suspension (200 mg/mL) is a white to off-white suspension for oral administration and is an immunosuppressant indicated for the prophylaxis of organ rejection. LiQMeds is filing the application under 505(b)(2) and references mycophenolate mofetil for oral suspension of NDA 50759. The drug product is formulated with compendial grade excipients in glycerin (b) (4))/water (b) (4) (sorbitol), a proprietary flavor, and is (b) (4) (pH 6.0-8.0). The suspension also includes paraben (b) (4) and simethicone (b) (4). Glycerol is used (b) (4) and the container (HDPE bottle) contacts the formulation for prolonged time. The applicant has addressed this with extractables/leachables studies. There is nothing unusual about the manufacturing which mainly involves (b) (4)

	In-process controls include (b) (4) The stability data support the physical stability of the suspension. (b) (4) (b) (4) the formulation ready to use as compared to the reference drug product.		
Co-packaged product information	N/A		
Device information:	N/A		
Storage Temperature/ Conditions	Store at 20°C to 25°C (68° F to 77° F); excursions permitted to 15°C to 30°C (59° F to 86° F) [See USP Controlled Room Temperature].		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Friedrich Burnett	Lawrence Perez
	Drug Product/ Labeling	Craig M. Bertha	Hong Cai
	Manufacturing	Khalid Khan	Lane Christensen
	Biopharmaceutics	Leah Falade	Tapash Ghosh
	Microbiology	Koushik Paul	Jesse Wells
	Other (specify):	N/A	
	RBPM	Teshara Bouie	
	ATL	Craig M. Bertha	
Consults	N/A		

2. Final Overall Recommendation: Adequate

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

There are no remaining deficiencies or pending issues, with the exception of minor editorial labeling revisions.[1]

b. Is the overall recommendation in agreement with the individual discipline recommendations? Yes

Recommendation by Subdiscipline:

Drug Substance	**-**	**Adequate**
Drug Product	**-**	**Adequate**
Quality Labeling	**-**	**Pending**[1]
Manufacturing	**-**	**Adequate**
Biopharmaceutics	**-**	**Adequate**
Microbiology	**-**	**Adequate**

Environmental Assessment: Categorical Exclusion - Adequate
QPA for EA(s): No

5. Life-Cycle Considerations

Established Conditions per ICH Q12: No
Comments:

Comparability Protocols (PACMP): No
Comments:

Additional Lifecycle Comments:

N/A

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[1] The labeling review decision is pending for this IQA due to ongoing negotiations with the applicant. There are only minor labeling deficiencies from the CMC perspective and we expect the applicant will accept our recommendations. Refer to the CMC sections of the final approved labeling.

CHAPTER IV: LABELING

1.0 PRESCRIBING INFORMATION

Assessment of Product Quality Related Aspects of the Prescribing Information:
Note: this assessment is based on the proposed PI and Carton and Contain labeling and labels submitted on 3/8/2022 (SN0001) as amended on 11/21/2022 (SN0019). Yellow highlighted items are deficiencies or issues that were resolved.

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

Item	Information Provided in the NDA	Assessor's Comments
Product Title in Highlights		
Proprietary name	No	Proprietary name not in current draft package insert, however a separate submission proposed (b) (4) but DMEPA 1 concludes that this proprietary name is vulnerable to medication errors
Established name(s)	No	If approved without a proprietary name, Mycophenolate Mofetil should be revised to be all UPPERCASE
Route(s) of administration	Yes	
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system.	Yes	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other	N/A	

package terms include pharmacy bulk package and imaging bulk package.		

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)

Item	Information Provided in the NDA	Assessor's Comments
DOSAGE AND ADMINISTRATION section		
Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents, storage conditions needed to maintain the stability of the reconstituted or diluted product)	N/A	

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

Item	Information Provided in the NDA	Assessor's Comments
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Yes	
Strength(s) in metric system	Yes	
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance	N/A	
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, and imprinting	No	Formulation described only as a suspension; revise to also describe the identifying characteristics as per 21 CFR 201.57(c)(4)(ii) (e.g., color)
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	
For injectable drug products for parental administration, use appropriate labeling term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package.	N/A	

1.2.3 Section 11 (DESCRIPTION)

Item	Information Provided in the NDA	Assessor's Comments
DESCRIPTION section		
Proprietary and established name(s)	Yes	See evaluation of HIGHLIGHTS section with regard to the proprietary name
Dosage form(s) and route(s) of administration	Yes	
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per FDA Guidance.	N/A	
List names of all inactive ingredients. Use USP/NF names. Avoid Brand names.	Yes	Unsatisfactory; (b) (4) should be revised to Monobasic Sodium Phosphate Dihydrate
For parenteral injectable dosage forms, include the name and quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect.	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Statement of being sterile (if applicable)	N/A	
Pharmacological/ therapeutic class	Yes	
Chemical name, structural formula, molecular weight	No	Chemical name (b) (4)
If radioactive, statement of important nuclear characteristics.	N/A	

Other important chemical or physical properties (such as pKa or pH)	No	However, the applicant has proposed the identical wording from the reference product labeling, which is not in complete agreement with the data in their application in S.1.3.

Section 11 (DESCRIPTION) Continued

Item	Information Provided in the NDA	Assessor's Comments
For oral prescription drug products, include gluten statement if applicable	N/A	
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity"	N/A	

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)

Item	Information Provided in the NDA	Assessor's Comments
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s)	Yes	
Strength(s) in metric system	No	The strength should be in mg/mL
Available units (e.g., bottles of 100 tablets)	No	Labeling should clarify that the 225 mL bottles contain 175 mL of suspension formulation
Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number	Yes	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.	N/A	

Section 16 (HOW SUPPLIED/STORAGE AND HANDLING) (Continued)

Item	Information Provided in the NDA	Assessor's Comments
Special handling about the supplied product (e.g., protect from light, refrigerate). If there is a statement to "Dispense in original container," provide reason why (e.g. to protect from light or moisture, to maintain stability, etc.)	No	This section should be revised to include the in-use period of 60 days once the bottle is opened for use.
If the product contains a desiccant, ensure the size and shape differ from the dosage form and desiccant has a warning such as "Do not eat."	N/A	
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	Yes	The storage condition should be revised to reflect what is proposed for the bottle and carton labels, for consistency.
Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of natural rubber latex, state: "Not made with natural rubber latex. Avoid statements such as "latex-free."	N/A	
Include information about child-resistant packaging	No	Revise the section to indicate that the container closure system has child-resistant caps

CMC sections of the Package Insert:

Assessment: Adequate as amended on 11/21/2022. See associated deficiencies and resolutions as outlined below.

1.2.5 Other Sections of Labeling

There may be other sections of labeling that contain product-quality related information. For example, there are specific required/recommended warnings for certain inactive ingredients [e.g., aspartame, aluminum in large and small volume parenterals, sulfites, FD&C Yellow Number 5 (tartrazine), and benzyl alcohol]. Please notify the prescription drug division if the product contains any of these inactive ingredients.
Please include your comments about other sections of labeling if they contain product quality information.

1.2.6 Manufacturing Information After Section 17 (for drug products)

Item	Information Provided in the NDA	Assessor's Comments
Manufacturing Information After Section 17		
Name and location of business (street address, city, state and zip code) of the manufacturer, distributor, and/or packer	Yes	

2.0 PATIENT LABELING

Product Quality Related Aspects of Patient Labeling (e.g., Medication Guide, Patient Information, Instructions for Use):

The Med Guide has a section that answers the question: "**How should I store** (b) (4) The first part of the answer is: " (b) (4)

This storage condition is not consistent with that listed in the How Supplied/Storage and Handling section of the package insert, nor with that on the bottle and carton labels.

Assessment: Adequate as amended on 11/21/2022. See associated deficiencies and resolutions as outlined below.

3.0 CARTON AND CONTAINER LABELING

3.1 Container Label

2 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

Item	Information Provided in the NDA	Assessor's Comments about Carton Labeling
Proprietary name, established name, and dosage form (font size and prominence	Yes	See evaluation of HIGHLIGHTS section with regard to the proprietary name
Dosage strength	Yes	
Route of administration	Yes	
If the active ingredient is a salt, include the equivalency statement per FDA Guidance	N/A	
Net contents (e.g. tablet count)	No	The bottle label should be revised to include the net content (i.e., 175 mL)
"Rx only" displayed on the principal display	Yes	
NDC number	Yes	
Lot number and expiration date	Yes	
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new BUD.	Yes	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use)	N/A	
Other package terms include pharmacy bulk package and imaging bulk package which require "Not for direct infusion" statement.	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Bar code	Yes	

Item	Information Provided in the NDA	Assessor's Comments about Carton Labeling
Name of manufacturer/distributor	No	Currently LiQMeds Worldwide Ltd. is listed as the "MA Holder." The applicant should revise the carton and container labels to comply with 21 CFR 201.1.
Medication Guide (if applicable)	Yes	
No text on Ferrule and Cap overseal	N/A	
When a drug product differs from the relevant USP standard of strength, quality, or purity, as determined by the application of the tests, procedures, and acceptance criteria set forth in the relevant compendium, its difference shall be plainly stated on its label.	N/A	
And others, if space is available	N/A	

Assessment of Carton and Container Labeling: Adequate as amended on 11/21/2022. See associated deficiencies and resolutions below.

ITEMS FOR ADDITIONAL ASSESSMENT

Deficiency: Revise the Med Guide and the HOW SUPPLIED/STORAGE AND HANDLING section of the package insert to have storage conditions consistent with that on the bottle and carton labels.

Initial Assessment and Associated Deficiencies:

There were deficiencies in the labels and labeling as outlined below:

1. Currently the draft package insert (PI) does not include a proprietary name. If no proprietary name is included in the PI, revise Mycophenolate Mofetil to be in all UPPERCASE lettering.

2. Revise the DOSAGE FORMS AND STRENGTHS section of the package insert to include identifying characteristics as per 21 CFR 201.57(c)(4)(ii) (e.g., color).

3. Revise the DESCRIPTION section of the package insert to provide the chemical name of mycophenolate mofetil as per the USP Dictionary.

4. Revise the description of the drug substance in the DESCRIPTION section of the packaging insert such that it is consistent with the information provided for the drug substance in section S.1.3 of your application.

5. Revise the DESCRIPTION section of the packaging insert and revise [redacted] (b) (4) to "Monobasic Sodium Phosphate," per the official USP title.

6. Revise the DESCRIPTION section of the packaging insert and revise [redacted] (b) (4) " to "Dibasic Sodium Phosphate," per the official USP title.

7. Revise the HOW SUPPLIED/STORAGE AND HANDLING section of the package insert to include the in-use period of 60 days once the product is opened for use.

8. Revise the HOW SUPPLIED/STORAGE AND HANDLING section of the package insert such that the strength of the drug product is given in mg/mL.

9. Revise the HOW SUPPLIED/STORAGE AND HANDLING section of the package insert to indicates that 225 mL bottles have 175 mL of suspension formulation.

10. Revise the HOW SUPPLIED/STORAGE AND HANDLING section of the package insert to indicate that the container closure system has child-resistant caps.

11. Revise the Med Guide and the HOW SUPPLIED/STORAGE AND HANDLING section of the package insert to have storage conditions consistent with that on the bottle and carton labels.

12. Revise the bottle labels to include the net content (i.e., 175 mL).

13. Revise the bottle and carton labels to comply with 21 CFR 201.1.

The comments above were sent to the applicant on 11/9/2022. An amendment with a response was received 11/21/2022 and is evaluated below.

Final Assessment of Amended Labeling and Recommendation:

Pending. The applicant has adequately addressed comments 1-3 and 5-13 above. The applicant did not make any changes in the DESCRIPTION section of the package insert based on comment 4. The current wording in the package insert regarding the solubility, [redacted] (b) (4) is identical to what is in the reference drug labeling. From section S.1.3 of the application, [redacted] (b) (4) values are said to be sourced from [redacted] (b) (4). It is suspected that these values calculation-based. The source of the solubility information is not stated. The slight difference in the solubility in aqueous solution is inconsequential as the drug substance is practically insoluble. Thus, in order to maintain consistency and prevent confusion, including the information from the approved reference drug labeling is acceptable.

Based on the Labeling tool recommendations, there are additional minor editorial labeling deficiencies in the CMC and title section of the package insert. However, we expect that the applicant will accept our recommendations regarding them. Refer to those portions of the final approved labeling.

Primary Labeling Assessor Name and Date: Craig M. Bertha, 11/22/2022
Secondary Assessor Name and Date (and Secondary Summary, as needed): Hong Cai, Acting Branch Chief and Division Director

Craig Bertha

Digitally signed by Craig Bertha
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Comments: I think this is more cohesive and clear.

Hong Cai

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CHAPTER VI: BIOPHARMACEUTICS

NDA Number	NDA-216482-ORIG-1
Assessment Cycle Number	1
Drug Product Name/ Strength	Mycophenolate Mofetil Oral Suspension/200 mg/mL
Route of Administration	Oral
Applicant Name	Liqmeds Worldwide Limited
Therapeutic Classification/ OND Division	/Division of Rheumatology and Transport Medicine
RLD/RS Number	N050759 for CellCept® Powder for Oral Suspension, 200 mg/mL
Proposed Indication	For the prophylaxis of organ rejection in recipients of allogeneic kidney, heart, or liver transplants, and should be used in combination with other immuno-suppressants

Assessment Recommendation: **Adequate**

Assessment Summary:
The Applicant is seeking approval to market Mycophenolate Mofetil Oral Suspension,200 mg/mL following the 505(b)(2) regulatory pathways relying on the previously established safety and efficacy for the Listed Drug (LD) CellCept® Powder for Oral Suspension, 200 mg/mL (NDA 050759).

The proposed product is a ready-to-drink oral liquid formulation of mycophenolate mofetil. The proposed product is intended for the same indication to be administered at the same dose, has the same dosing regimen, and route of administration as the LD. The ready-to-use formulation provides an alternative dosage form to CellCept® for patients with difficulty swallowing.

The clinical package in support of this NDA includes two pivotal clinical studies conducted using the proposed product comparing it to CellCept® under fasting and fed conditions. These studies will be assessed by the Office of Clinical Pharmacology.

The Biopharmaceutics review focuses on the evaluation and acceptability of:

1) **Dissolution method and acceptance criterion:**
The Applicant's dissolution method (USP Apparatus 2 (paddle) at 40 rpm, with 900 mL 0.1 N HCl/37°C) is adequately justified and considered acceptable for batch release and stability testing. Data was provided to support the discriminating ability of the method by altering the target formulation by changing the excipients (b) (4)

(b) (4) and API particle size distribution. Since the solubility is pH-dependent and high in 0.1 N HCl, the API releases very rapidly (b) (4) Therefore, the discriminating ability of the method is not applicable. A data-driven acceptance criterion was recommended. The Applicant accepted the recommended acceptance criterion on 11/14/2022.

2) **Bridging of formulations:**
The formulation used in the clinical pivotal studies is the same of the to-be-marketed (TBM) formulation. The commercial batches will be manufactured at the same site as the biobatch, (b) (4) . Therefore, formulation bridging is not needed.

Recommendation
From a Biopharmaceutics perspective, NDA-216482-ORIG-1 for the proposed Mycophenolate Mofetil Oral Suspension,200 mg/mL is recommended for **approval**.

FDA-Approved Dissolution Method and Acceptance Criterion for batch release and stability testing for Mofetil Oral Suspension:

USP Apparatus	Speed	Medium/Temperature	Volume	Acceptance Criterion
2 (Paddle)	40 rpm	0.1 N HCl/37°C	900 mL	Q= (b) (4) % in 15 min

List Submissions Being Assessed:

Document(s) Assessed	Date Received
Seq 0001	03/08/2022
Seq 0005	05/11/2022
Seq 0017	11/14/2022

Concise Description of Outstanding Issues:
None

B.1 DISSOLUTION METHOD AND ACCEPTANCE CRITERIA

Assessment: *Adequate*
The Applicant used the FDA Dissolution Database method as a starting point for the method development of the test product:

USP Apparatus	Speed	Medium	Volume
2 (Paddle)	40 rpm	0.1 N HCl	900 mL

Solubility

(b) (4) . Therefore, 0.1 N HCl was selected as the dissolution medium. Based on the submitted data, the selection of the dissolution medium is justified and acceptable.

Table 1. Solubility of Mycophenolate Mofetil at Different pH

Name of media	In-House Solubility (mg/mL)	Dose solubility volume (Highest strength 1000 mg)	Dose solubility volume × 3	OGD recommended media volume	Sink condition
(b) (4)				900 mL	(b) (4)
0.1 N HCL	3.99	250.6 mL	751.9 mL		Possible

Rotation Speed

The Applicant tested paddle rotation speeds of 40 (b) (4) rpm. (b) (4) The Applicant therefore selected (b) (4) paddle speed of 40 rpm for their proposed dissolution method. This Reviewer considers the selection of the rotation speed justified and acceptable.

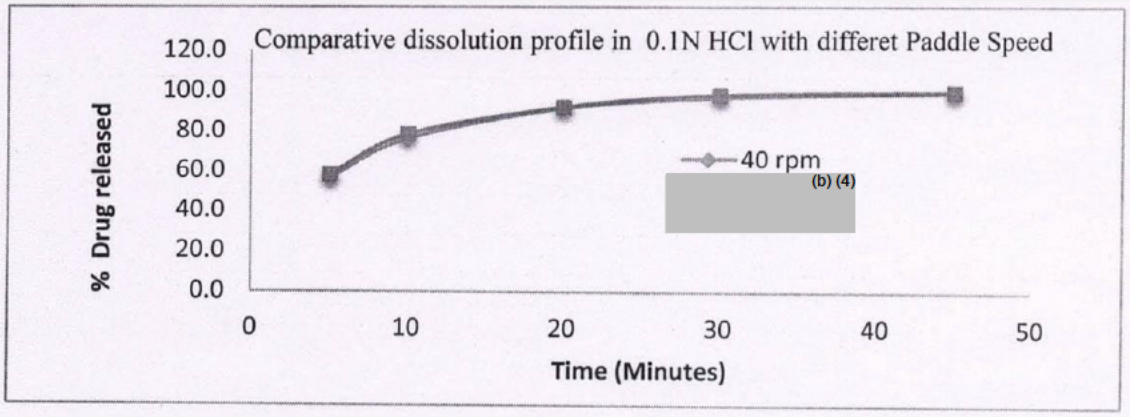

Figure 1. Comparative Dissolution Profile in 0.1 N HCl with Different Rotation Speeds

Discriminating Ability

Formulations were manufactured with different levels of [redacted] (b) (4). [redacted] (b) (4) , there is no variation observed due to the high solubility in 0.1 N HCl.

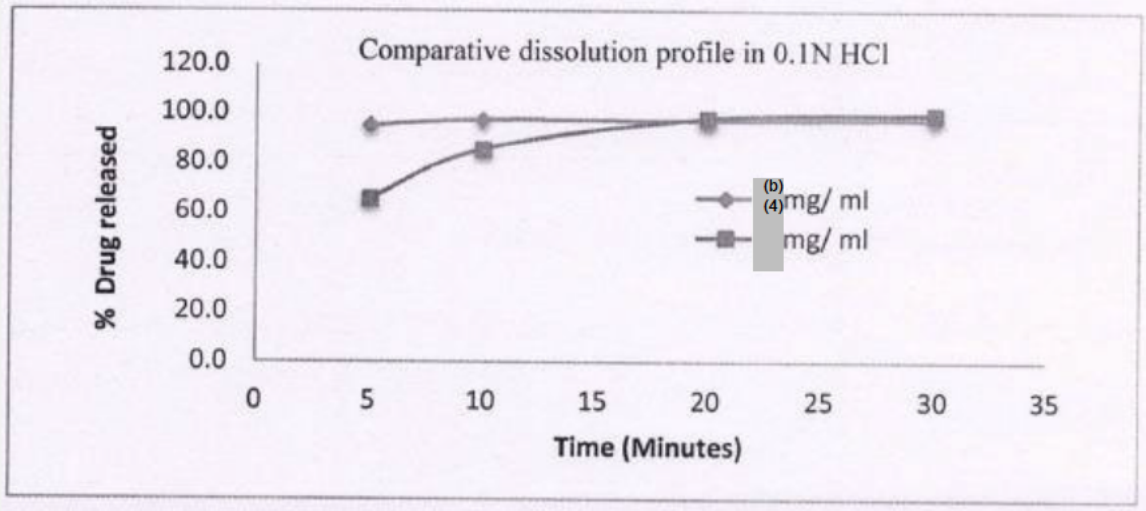

Figure 2. Comparative Dissolution Profile in 0.1 N HCl with Different Concentrations [redacted] (b) (4)

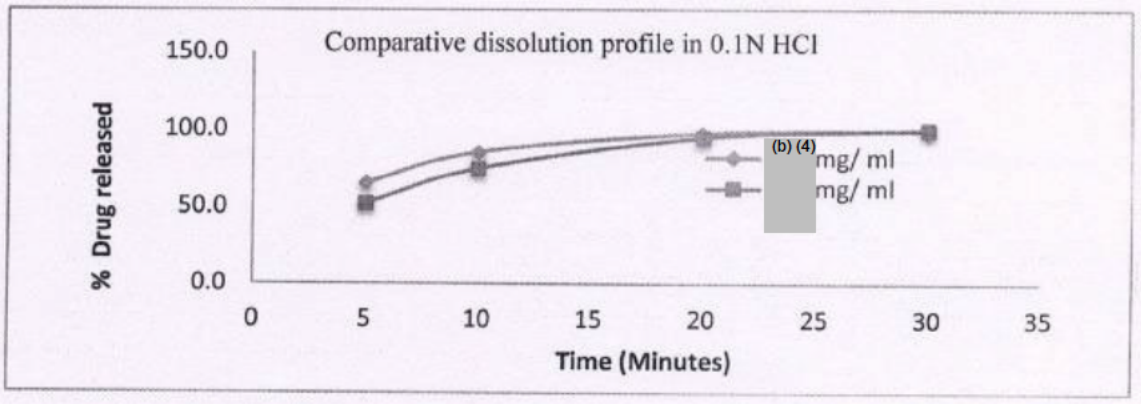

Figure 3. Comparative Dissolution Profile in 0.1 N HCl with Different Concentrations [redacted] (b) (4)

Formulations were manufactured with different particle size distribution (PSD). [redacted] (b) (4) . Since the solubility is pH-dependent and high in 0.1 N HCl, [redacted] (b) (4) . Therefore, the discriminating ability of the method is not applicable.

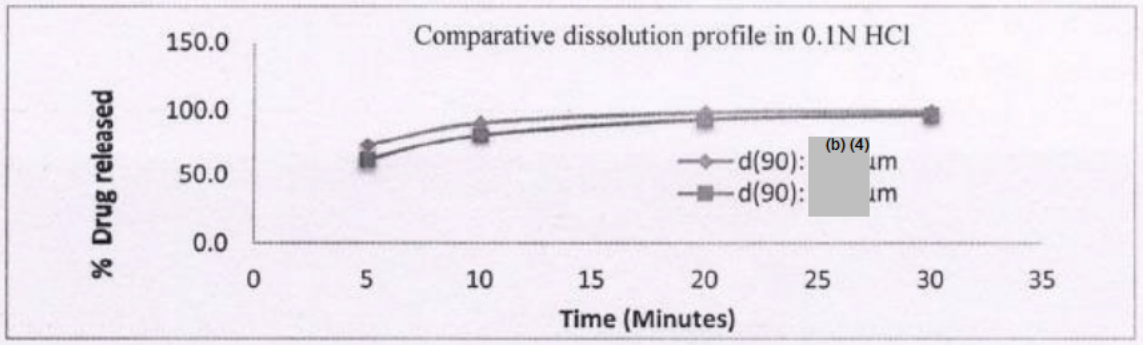

Figure 4. Comparative Dissolution Profile with Different Particle Size of Drug Substance

Acceptance Criterion

The Applicant proposed an acceptance criterion of "Q (b) (4)% in (b) (4) min." In response to the Information Request (Seq 0005), the Applicant provided the individual unit data on the pivotal clinical batch and lot VAL/18/0072 using the proposed dissolution method. The pivotal clinical batch was aged 4 months at the time of dissolution testing while the other registration batch was aged 34 months.

Table 2. Dissolution Data of Registration Batch and Biobatch, n=12

Lot/Time (min)	5	10	15	20	30	45
Lot Val-18-0072	(b) (4)					
Range						
%CV						
Lot MYC20001-(Bio-batch)						
Range						
%CV						

The Applicant's proposed acceptance criterion was permissive. Based on the submitted data of the pivotal clinical batch, "Q= (b) (4)% in 15 min" was recommended. In response to the IR on 11/14/2022, the Applicant accepted the acceptance criterion.

B.2 BRIDGING OF FORMULATIONS

Assessment: *Adequate*

The to-be-marketed (TBM) formulation was used for the pivotal clinical studies and was manufactured at the proposed commercial site (b) (4) (b) (4) Therefore, formulation bridging is not needed.

BIOPHARMACEUTICS LIST OF DEFICIENCIES

None

Primary Biopharmaceutics Assessor's Name and Date: Leah W. Falade, Ph.D., 11/15/2022

Secondary Assessor Name and Date: Tapash Ghosh, Ph.D., 11/15/2022

Leah Falade

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Tapash Ghosh

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MICROBIOLOGY

Product Background: For the prophylaxis of organ rejection in recipients of allogeneic kidney, heart, or liver transplants, and should be used in combination with other immunosuppressants.

NDA: 216482

Drug Product Name / Strength: Mycophenolate Mofetil Oral Suspension, 200mg/mL.

Route of Administration: Oral Suspension.

Applicant Name: Liqmeds Worldwide Limited.

Manufacturing Site: (b) (4) (b) (4)

Method of Sterilization: This is a nonsterile product.

Review Recommendation: **Adequate**

Theme (ANDA only): **N/A**

Justification (ANDA only): N/A

Review Summary: (b) (4)

List Submissions Being Reviewed: 03/08/2022 and 05/11/2022.

Highlight Key Outstanding Issues from Last Cycle: N/A

Remarks: The submission is **recommended** for approval on the basis of sterility assurance.

Concise Description Outstanding Issues Remaining: None.

Supporting Documents: Microbiology review (b) (4) MR01.doc, dated 07/16/2020.

List Number of Comparability Protocols (NDA only): None.

S Drug Substance – non-sterile

Reviewer's Assessment: The drug substance is not the subject of this review.

P.1 Description of the Composition of the Drug Product

Description of the Composition of the Drug Product

(*3.2.P.1 description-and-composition-description-and-comp.pdf)*

Mycophenolate Mofetil Oral Suspension, 200mg/mL is an antimetabolite immunosuppressant indicated for the prophylaxis of organ rejection in recipients of allogeneic kidney, heart, or liver, transplants, and should be used in combination with other immunosuppressants. The composition of the drug product is provided below.

Table 2: Qualitative and Quantitative Composition and Function of Drug Product Ingredients

Ingredients	Quality Standard	Function	% w/v	Quantity/mL (mg/mL)
Mycophenolate Mofetil[1]	USP	Active Pharmaceutical Ingredient	20.00	200.000
Methylparaben, NF (b) (4)	NF	(b) (4)	0.252	2.520
Propylparaben, NF (b) (4)	NF		0.056	0.560
Xanthan Gum	NF		(b) (4)	
Glycerin	USP			
Sorbitol Solution (b) (4) (b) (4)	USP			
(b) (4) Simethicone Emulsion[3]	USP			
Polysorbate 80	NF			
Monosodium phosphate dihydrate	USP			
Dibasic Sodium Phosphate, Dihydrate	USP			
Raspberry flavour	-			
Purified Water	USP			

Description of container closure system –

(*3.2.P.1 description-and-composition-description-and-comp.pdf and 3.2.P.7 container-closure-system-sum-cont-clos-system.pdf)*

Mycophenolate Mofetil Oral Suspension, 200mg/mL is packaged in 225mL HDPE Bottles with a 28mm White Child Resistant Closures. A complete description of the container/closure system is provided in.P.7.

Table 6: Container Closure System for Mycophenolate Mofetil Oral Suspension, 200 mg/mL

Strength	Configuration	Component	Description	Material Used
200 mg/mL	225 mL	Container	Translucent 225 cc round HDPE bottle	(b) (4)
		Closure	28 mm (b) (4) (b) (4) caps (Child Resistant Closures)	

Reviewer's Assessment: Based on the above information the reviewer has concluded that the applicant has provided adequate description of the drug product composition and the packaging system to support the manufacturing process for the drug product.

Acceptable

P.2 Pharmaceutical Development

(b) (4)

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Jesse Wells

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Koushik Paul

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