



**Health & Population Department
PROVINCIAL QUALITY CONTROL BOARD, PUNJAB.**

263 Meeting of PQCB

Date: 27-06-2023

Time: 11:00 AM

Venue

**COMMITTEE ROOM OF DIRECTORATE GENERAL HEALTH SERVICES, PUNJAB, 24-
COOPER ROAD, LAHORE**

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ITEM No. 1

ADJOURNED CASES OF PREVIOUS MEETING

Case No. 1

DISTRICT LAHORE

PQCB/R-553/2021

Jinnah Hospital, Lahore

ATTENDANCE:

Secretary DQCB	<u>Accused Persons involved in subject case</u>
Drug Inspector	1. M/S Cotton Craft Pvt. Ltd, Plot 407, 408-Sundar Industrial Estate, Raiwind Road- Lahore, Pakistan through its Managing Director Salman Shahid
	2. Salman Shahid Managing Director (MD)
	3. Hafiz Tariq Mahmood Production Incharge/ Warrantor
	4. Nuzhat Kauser Mumtaz Quality Control Incharge
	Of M/S Cotton Craft Pvt. Ltd, Plot 407, 408-Sundar Industrial Estate, Raiwind Road- Lahore, Pakistan.

BRIEF FACTS OF THE CASE

Provincial Inspector of drugs Jinnah Hospital, Lahore reported that:-

- She on, on 22-09-2021, inspected the Main Medicine Store B of Jinnah Hospital, Lahore and took samples of drugs on Form No.04 for the purpose of test/analysis and sent the sample to Drug Testing Laboratory, Lahore vide memorandum no. 0000107495 dated 22-09-2021.
- Following drug sample, after test/analysis, was declared **Substandard** by Government Analyst, Drug Testing Laboratory, **Lahore** as detailed below:
- The drug inspector directed Store Keeper of Main Medicine Store B of Jinnah Hospital, Lahore not to dispose of stock in his possession vide Form 3 dated 09-12-2021.
- Store Keeper of Main Medicine Store B of Jinnah Hospital, Lahore submitted Invoice/warranty no. 1262 dated 21-09-2021 issued by M/S Cotton Craft Pvt. Ltd, Plot 407, 408-Sundar Industrial Estate, Raiwind Road- Lahore, Pakistan as a proof of its purchase of the said drug.
- Warrantor portion of the drug sample and a copy of test/analysis report were sent to M/S Cotton Craft Pvt. Ltd, Plot 407, 408-Sundar Industrial Estate, Raiwind Road- Lahore, Pakistan and they were asked to provide the requisite information in this regard.
- The company challenged the report of DTL Multan in the appellate laboratory and subject request for retesting of the drug sample was placed before the Provincial Quality Control Board (PQCB) under section 22 of The Drugs Act 1976 in its 244th meeting held on 31-05-2022 where the firm vide letter no. 786/0793/2022 dated 30-05-2022 requested to withdraw their re-

testing request. The board unanimously decided to approve their appeal for withdrawal of the re-testing request.

Name of drug	Batch No.	Name of manufacturer	DTL Report TRA No. & Date	DTL Test Report Results
Surgical Bandages (Open Wove Bandage 10CM*6M) Mfg.date: Sep-2021 Exp. date: Aug-2024 Regn No. 006272	30I21	M/S Cotton Craft Pvt. Ltd, Plot 407, 408-Sundar Industrial Estate, Raiwind Road-Lahore, Pakistan	TRA No. 01-73010151/DTL Dated:-26-11-2021	<u>Analysis with specifications applied:</u> BPC 1973 <u>Description:</u> B.P.C monograph of Open wove Bandage describes Standard description as “Cotton cloth of plain weave, bleached to a good white, in one continuous length containing no joints, clean, and reasonably free from weaving defects, leaf and shell; the edges are evenly cut, parallel with the wrap threads, and are reasonably free from loose threads”. <u>Observed:</u> Cotton cloth of plain weave, bleached to almost white, clean, and reasonably free from weaving defects, leaf and shell having size of 10cm * 5.9m. 12 units are observed and out of which 02 units are found to have joints (Not in one continuous length) while other 02 units have considerable loose threads. Therefore, 04 out of 12 units are not complying the standard specifications. (DOES NOT COMPLY) <u>Note:</u> Below are the results of 08 units that are complying the physical description and are in one continuous length. <u>Warps:</u> Limit: Average 17.1/cm Determined: 17.4/cm <u>Wefts:</u> Limit: Average 10.7/cm Determined: 10.89/cm <u>Weight per unit area:</u> Limit: Average 71g/m² Determined: 76.73 g/m² RESULT:

				The above sample is Sub-standard , on the basis of Description as per BPC.
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2. Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused persons who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended) / DRAP Act 2012 and Rules framed there under by the way of: -

- a. **Manufacture for sale/sale of the Substandard drug**
- b. **Issuance of false warranty**

3. Show cause Notice (s) issued to the accused person(s) Dated 29-09-2022.
4. Personal Hearing notice(s) issued to accused person(s) dated 05-06-2023.

PREVIOUS PROCEEDINGS & DECISION BY THE BOARD:

5. Case was considered by the Provincial Quality Control Board, under section 11 of the Drugs Act 1976 in its **262nd meeting** held on **13-06-2023** under the Chairmanship of Secretary, Primary and Secondary Healthcare Department, Punjab. Mr. Hassan Saeed, Secretary DQCB, Lahore was present along with original case record. No one among the nominated accused persons of **M/S Cotton Craft Pvt. Ltd, Plot 407, 408-Sundar Industrial Estate, Raiwind Road- Lahore, Pakistan** appeared before the Board. However, a written request for adjournment was received on behalf of the firm vide letter no. Ref:786/0629/2023 dated 12-06-2023.
6. The Board after due deliberation and discussion unanimously decided to **adjourn the case** in the best interest of justice. The Board further decided to provide another opportunity of hearing to the accused persons. Personal Hearing notice(s) issued to accused person(s) dated 05-06-2023.
7. Personal Hearing notice(s) issued to accused person(s) dated 19-06-2023.

Case is placed before the Board for Decision

Summary:

- **Manufacturing Date: 09-2021**
- **Expiry Date: 08-2024**
- **Sampling Date (Form 4): 22-09-2021**
- **Sent to DTL (Form 6): 22-09-2021**
- **Date of receipt in DTL: 22-09-2021**
- **DTL Report Date (Form 7): 26-11-2021**
- **Time Extension: Granted in 236th meeting dated 15-12-2021**
- **1ST DI Communication with firm on dated: 09-12-2021**
- **Date of Retesting Request of Firm: 21-12-2021**
- **Fate of Retesting: Board approved firm's appeal for withdrawal of retesting request in 244th meeting dated 31-05-2022**
- **Investigation Report Dated: 03-09-2022**

CURRENT PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 2

PQCB R-425/2020

(Tehsil and District Rajanpur)

ATTENDANCE:

Drug Inspector	<u>Accused Persons involved in subject case</u> 1. M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore through its Managing Director Salman Shahid 2. Salman Shahid Managing Director 3. Hafiz Tariq Mehmood Production Incharge/Warrantor 4. Nuzhat Kausar Mumtaz Quality Control Incharge of M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore
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BRIEF FACTS OF THE CASE

Provincial Inspector of drugs Rajanpur reported that:-

- His predecessor, on 17-06-2020, inspected the premises of Medicine Store situated at Chief Executive Officer, DHA, Rajanpur and took samples of nine different type of drugs on Form No. 04 for the purpose of test and analysis.
- One out of these nine drug samples, after test/ analysis was declared **Substandard** by Government Analyst Drug Testing Laboratory, Multan as detailed below:

Name of drug	Batch no.	Name of manufacturer	DTL Report TRA No. & Date	DTL Test Report Results
Bandages Elastocraft (Cotton crepe bandage 7.5cm*4.5m)	72B20	M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore.	TRA No.01-87001319/DTL dated: 13-07-2020	Analysis with specifications applied: BPC 1973 Description: Cotton crepe bandage of characteristic fabric of plain weave in one continuous length containing no joints, clean and reasonably free from weaving defects, cotton leaf, and shell having fast edges. (comply) Warps: Limits: Avg NLT 17/cm Determined: 16.10/cm (Does not Comply) Wefts: Limits: Avg NLT 78/10cm

				Determined: 84.64/10 cm (Comply) Weight g/m²: Limit: 140g/m² Determined: 132.53 g/ m² (Does not Comply) Result: The above sample is Sub-standard on the basis of tests performed...
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iii. Store keeper of Medicine Store situated at Chief Executive Officer, DHA, Rajanpur provided invoice/ Warranty No. 0887 dated 13-06-2020 issued by M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore as a proof of its purchase.

iv. Warrantor portion and copy of test report was sent to M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore with directions to explain their position and provide requisite information in this regard.

2. Drug Inspector requested for grant of permission for prosecution against the above- accused persons nominated in the instant case who have contravened the provisions of Section 23/27 of the Drugs Act 1976(as amended)/DRAP Act 2012 and Rules framed there under by the way of: -

- a. **Manufacture for sale/ Sale of Substandard Drug**
b. **Issuance of false warranty**

3. Show cause notice(s) issued to the accused vide 14-04-2021.

Reply to Show cause Notice:

The firm vide Ref No. 786/0731/2021 Dated 26-05-2021 submitted written reply to Show-Cause Notice stated That:

This is with reference to your Show Cause Notice No. PQCB/R-425-2020 dated 14-04-2021, received by us on 17-05-2021, served to this firm concerning the **(Elastocraft) Cotton Crepe Bandages BPC 7.5cm x 4.5M Batch No.72B20, Mfg. Feb-2020 Exp. Jan- 2025**, sample taken from Medicine Store of Chief Executive Officer, DHA, Rajanpur and declared sub-standard by the Government Analyst, Punjab DIL Multan vide report No.TRA-01-87001319/DTL dated 13-07.2020 on the basis of Description, Warps and Weight per Unit Area.

As far as the sample under reference is concerned, we are reporting here under the details of DTL report No. TRA-01-87001319/DTL dated 13-07-2020 along-with our explanations /comments are given here under for evaluation and kind consideration at your end please.

	Tests Performed		Stated Values		Determined/Observed
	Warp threads/cm		NLT 17/cm= 17.00/cm		16.10/cm =16.10cm
	Weft Threads/10cm		NLT 78/10cm=7.80/cm		84.64/10cm=08.464/cm

		Total=24.80/cm		24.564/cm $\pm$ 5%=25.7922/cm Total count almost complies Hence there is no concealment in the threads.
	Weight/m²		NLT 140g/m ²	132.22 $\pm$ 5%=139g/m ²

Here it is mentioning that as per Method of testing provided / approved by the Ministry of Health, Government of Pakistan, Islamabad a variation in the threads and weight is allowed $\pm$ 5%. We do understand that if the Thread count complies the specification, then it is understood that weight per unit area is also complies. And there is no question of any shortfall in the weight, hence we confirm the sample under reference is complies the required standards.

We understand it might happen in testing the sample casually and ensure it is up to the required limit. Please observe from the above that other than the above test all necessary parameters (Weft, Width, Length, Elasticity etc.) required under the BPC specification also complies as per DTL Multan vide his report No. TRA-01-87001861/DTL dated 21.08.2020 and confirms it is up to the standards. Hence our submissions are as under: -

We are very much conscious about the quality and quantity of the products and do not compromise on the quality of our product in any case.

It is confident to mention here that we tested the warrantor portion as well as retained sample of the said Batch No.72B20 of Cotton Crepe Bandage BPC 7.5cm x 4.5m at our Quality Control Lab and observe it is of "Standard Quality and there is no such shortfalls in the sample as reported by the Analyst in his report. **A copy of Test Report dated 05.09.2020 performed at our QC Lab is attached herewith for your ready reference.**

It is worthwhile to mention here that the Surgical Bandages (Cotton Crepe Bandage) is meant for external use only and it has many commercial usage other than medical purposes like Cleaning of Machinery, Polishing etc. In the light of above said explanation it is stated that the Product (Medical Device) under reference is complies all test according to the BPC specifications and observations find by the Analyst for declaring sub-standard are unfortunate, ignorable and we understand has no such effect in externally use on human body. Even though if the authority feels it necessary, we are ready to replace the seized stock with fresh stock of standard quality or otherwise forward the sample of the same product (Medical Device) under reference to the NIH for re-testing.

In the light of above said facts it is submitted that we have not contravened the provisions of Section 23/72 of the Drug Act 1976 (as amended) DRAP Act 2012 and Rules framed there under by the way of (a) Manufacturing for sale/Sale of Substandard drug (b) Issuance of false warranty.

Keeping in view the above said explanation it is stated that the product (Medical Device) under reference is complies all test according to the BPC specifications and observations find by the Analyst for declaring sub-standard is unfortunate, which may kindly be ignored and consider our request as under:

- i. Stock under reference may be accepted.
- ii. Allow to return "out of specification" seized stock to us with the conditions of replacement by fresh stock of standard quality to settle this issue at your level.
- iii. Forward the sample of the same product (Medical Device) under reference to the NIH for re-testing purposes.

Thanking you and assuring you our best cooperation for all the time we remain.

Personal Hearing notice(s) issued to accused person(s) on 19-06-2023.

Case is placed before the Board for Decision.

Note:

It is pertinent to mention here that in 236th Board meeting, dated: 15-12-2021, a Product Specific Inspection (PSI) of **M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore**, was marked in cases of similar nature having **same batch numbers**. The inspection was conducted with reference to:

- **Case No. PQCB/R-426/2020**
- **Case No. PQCB/R-427/2020**
- **Case No. PQCB/R-424/2020**

The committee after conducting the Product Specific Inspection (**PSI**) submitted the inspection report vide letter No. DPN/19373/DTL, dated: 17-11-2022. The firm submitted CAPA regarding the recommendations in PSI report and it was placed before the Board in **257th meeting, dated: 07-02-2023**.

The Board after careful perusal of the case record, the report of the product specific inspection and the corrective and preventive action submitted by the firm observed that in compliance to the recommendations by the committee, the firm has taken active measures in terms of improving the quality of raw material and also establish a separate Quality Assurance department to assure the quality of the products manufactured by them. Keeping in view the forgoing facts and the corrective and preventive actions taken by the firm, the Board after due deliberation and detailed discussion, unanimously decided to issue **Warning** to **M/S Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore, Pakistan** with directions to be careful in future.

Summary:

Manufacturing Date: 02-2020

Expiry Date: 01-2025

Sampling Date (Form 4): 17-06-2020

Sent to DTL (Form 6): 17-06-2020

Date of receipt in DTL: 17-06-2020

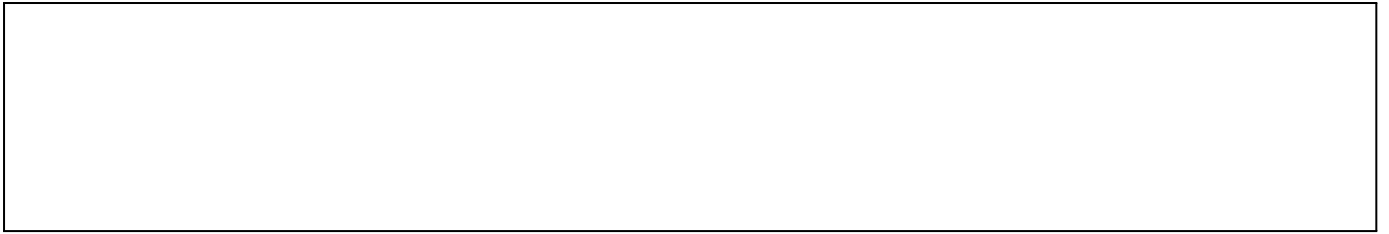
DTL Report Date (Form 7): 13-07-2020

1ST DI Communication with firm on dated: 29-12-2020

Date of Retesting Request of Firm: No Request

Investigation Report Dated: 09-03-2021

PROCEEDINGS & DECISION BY THE COMMITTEE:



Case No. 3

PQCB R-593/2020

(CEO Office Layyah)

ATTENDANCE:

Drug Inspector	<u>Accused Persons involved in subject case</u> 1. M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore through its Managing Director Salman Shahid 2. Salman Shahid Managing Director 3. Hafiz Tariq Mehmood Production Incharge/Warrantor 4. Nuzhat Kausar Mumtaz Quality Control Incharge of M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore
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BRIEF FACTS OF THE CASE

Provincial Inspector of drugs Layyah reported that: -

- His predecessor, on 30-06-2020, inspected the premises of Medicine Store situated at Chief Executive Officer, DHA, Layyah and took samples of four different type of drugs on Form No. 04 for the purpose of test and analysis.
- Following drug sample, after test/ analysis was declared **Substandard** by Government Analyst Drug Testing Laboratory, Multan as detailed below:

Name of drug	Batch no.	Name of manufacturer	DTL Report TRA No. & Date	DTL Test Report Results
Bandages Elastocraft (Cotton Crepe Bandage 7.5cm*4.5m)	72B20	M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore.	01-87001709/DTL 28-08-2020	Analysis with specifications applied: BPC 1973 <u>Description:</u> Cotton crepe bandage of characteristics fabric of plain weave, in one continuous length containing no joints, clean and reasonable free from weaving defects, cotton leaf, and shell having fast edges. (Comply) <u>Warps:</u> Limit: Avg NLT 17/cm Determined: 16.05/cm (Does not Comply) <u>Wefts:</u>

				Limits: Avg NLT 78/10cm Determined: 83.7/10cm (Comply) Weight g/m²: Limit: NLT 140g/m ² Determined: 136.21g/ m ² (Does not Comply) Result: The above sample is Sub-standard on the basis of tests performed...
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iii. Store keeper of Medicine Store situated at Chief Executive Officer, DHA, Layyah provided invoice/ Warranty No. 0840 dated 05-06-2020 issued by M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore as a proof of its purchase.

iv. Warrantor portion and copy of test report was sent to M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore with directions to explain their position and provide requisite information in this regard.

2. Drug Inspector requested for grant of permission for prosecution against the above- accused persons nominated in the instant case who have contravened the provisions of Section 23/27 of the Drugs Act 1976(as amended)/DRAP Act 2012 and Rules framed there under by the way of: -

- a. **Manufacture for sale/ Sale of Substandard Drug**
 - b. **Issuance of false warranty**

3. Show cause notice(s) issued to the accused vide 24-12-2021.

Reply to Show cause Notice:

The firm vide Ref No. 786/0253/2022 Dated 14-01-2022 submitted written reply to Show-Cause Notice stated That:

This is with reference to your Show Cause Notice No. PQCB/R-593/2020 dated 24-12-2021, served to this firm concerning the **(Elastocraft) Cotton Crepe Bandages BPC 7.5cm x 4.5M Batch No.72B20, Mfg. Feb-2020 Exp. Jan- 2025**, sample taken from Medicine Store of Chief Executive Officer, DHA, Layyah and declared sub-standard by the Government Analyst, Punjab DIL Multan vide report No.TRA-01-87001709/DTL dated 28-08.2020 on the basis of Description, Warps and Weight per Unit Area.

It is worthwhile to mention here that the honorable Provincial Quality Control Board, Lahore has already been issued warning to this firm under order No. PQCB/R-357/2020 dated 13.03.2021 with regard the same Batch No.72B20 of the same item (Elastocraft) Cotton Crepe Bandage BPC 7.5cm x 4.5m on account of the Punjab. Hence, we same discrepancies observed by the same DTL Multan understand the case is of similar type/nature and needs to be dropped at your end. A copy of Warning order No. PQCB/R-357/2020 dated 13.03.2021 is attached herewith for your ready reference please.

As far as the sample under reference is concerned, we are reporting here under the details of DTL report No. TRA-01-87001709/DTL dated 28-08-2020 along-with our explanations /comments are given here under for evaluation and kind consideration at your end please

	Tests Performed		Stated Values		Determined/Observed
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	Warp threads/cm		NLT 17/cm= 17.00/cm		16.10/cm =16.05cm
	Weft Threads/10cm		NLT 78/10cm=7.80/cm		83.70/10cm=08.37/cm
			Total=24.80/cm		24.564/cm $\pm$ 5%=25.641/cm Total count almost complies Hence there is no concealment in the threads.
	Weight/m²		NLT 140g/m ²		136.21 $\pm$ 5%=143.02g/m ²

Here it is mentioning that as per Method of testing provided / approved by the Ministry of Health, Government of Pakistan, Islamabad a variation in the threads and weight is allowed $\pm 5\%$. We do understand that if the Thread count complies the specification, then it is understood that weight per unit area is also complies. And there is no question of any shortfall in the weight, hence we confirm the sample under reference is complies the required standards.

We understand it might happen in testing the sample casually and ensure it is up to the required limit. Please observe from the above that other than the above test all necessary parameters (Weft, Width, Length, Elasticity etc.) required under the BPC specification also complies as per DTL Multan vide his report No. TRA-01-87001709/DTL dated 28.08.2020 and confirms it is up to the standards. Hence our submissions are as under: -

We are very much conscious about the quality and quantity of the products and do not compromise on the quality of our product in any case.

It is confident to mention here that we tested the warrantor portion as well as retained sample of the said Batch No.72B20 of Cotton Crepe Bandage BPC 7.5cm x 4.5m at our Quality Control Lab and observe it is of "Standard Quality and there is no such shortfalls in the sample as reported by the Analyst in his report. **A copy of Test Report dated 09-08-2021 performed at our QC Lab is attached herewith for your ready reference.**

It is worthwhile to mention here that the Surgical Bandages (Cotton Crepe Bandage) is meant for external use only and it has many commercial usages other than medical purposes like Cleaning of Machinery, Polishing etc. In the light of above said explanation it is stated that the Product (Medical Device) under reference is complies all test according to the BPC specifications and observations find by the Analyst for declaring sub-standard are unfortunate, ignorable and we understand has no such effect in externally use on human body. Even though if the authority feels it necessary, we are ready to replace the seized stock with fresh stock of standard quality or otherwise forward the sample of the same product (Medical Device) under reference to the NIH for re-testing.

In the light of above said facts it is submitted that we have not contravened the provisions of Section 23/72 of the Drug Act 1976 (as amended) DRAP Act 2012 and Rules framed there under by the way of (a) Manufacturing for sale/Sale of Substandard drug (b) Issuance of false warranty.

Keeping in view the above said explanation it is stated that the product (Medical Device) under reference is complies all test according to the BPC specifications and observations find by the Analyst for declaring sub-standard is unfortunate, which may kindly be ignored and consider our request as under:

- i. Stock under reference may be accepted.

- ii. Allow to return "out of specification" seized stock to us with the conditions of replacement by fresh stock of standard quality to settle this issue at your level.
- iii. Forward the sample of the same product (Medical Device) under reference to the NIH for re-testing purposes.

Thanking you and assuring you our best cooperation for all the time we remain.

Personal Hearing notice(s) issued to accused person(s) on 19-06-2023.

Case is placed before the Board for Decision.

Note:

It is pertinent to mention here that in 236th Board meeting, dated: 15-12-2021, a Product Specific Inspection (PSI) of **M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore**, was marked in cases of similar nature having **same batch numbers**. The inspection was conducted with reference to:

- **Case No. PQCB/R-426/2020**
- **Case No. PQCB/R-427/2020**
- **Case No. PQCB/R-424/2020**

The committee after conducting the Product Specific Inspection (**PSI**) submitted the inspection report vide letter No. DPN/19373/DTL, dated: 17-11-2022. The firm submitted CAPA regarding the recommendations in PSI report and it was placed before the Board in **257th meeting, dated: 07-02-2023**.

The Board after careful perusal of the case record, the report of the product specific inspection and the corrective and preventive action submitted by the firm observed that in compliance to the recommendations by the committee, the firm has taken active measures in terms of improving the quality of raw material and also establish a separate Quality Assurance department to assure the quality of the products manufactured by them. Keeping in view the forgoing facts and the corrective and preventive actions taken by the firm, the Board after due deliberation and detailed discussion, unanimously decided to issue **Warning** to **M/S Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore, Pakistan** with directions to be careful in future.

Summary:

Manufacturing Date: 02-2020

Expiry Date: 01-2025

Sampling Date (Form 4): 30-06-2020

Sent to DTL (Form 6): 30-06-2020

Date of receipt in DTL: 02-07-2020

DTL Report Date (Form 7): 28-08-2020

1ST DI Communication with firm on dated: 19-11-2020

Date of Retesting Request of Firm: No Request

Investigation Report Dated: 01-12-2021

PROCEEDINGS & DECISION BY THE COMMITTEE:

Case No. 4

PQCB R-428/2020

(Tehsil and District Rajanpur)

ATTENDANCE:

Drug Inspector	<u>Accused Persons involved in subject case</u> 1. M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore through its Managing Director Salman Shahid 2. Salman Shahid Managing Director 3. Hafiz Tariq Mehmood Production Incharge/Warrantor 4. Nuzhat Kausar Mumtaz Quality Control Incharge of M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore
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BRIEF FACTS OF THE CASE

Provincial Inspector of drugs Rajanpur reported that:

- His predecessor, on 20-07-2020, inspected the premises of Medicine Store situated at Chief Executive Officer, DHA, Rajanpur and took samples of ten different type of drugs on Form No. 04 for the purpose of test and analysis.
- One out of these ten drug samples, after test/ analysis was declared **Substandard** by Government Analyst Drug Testing Laboratory, Multan as detailed below:

Name of drug	Batch no.	Name of manufacturer	DTL Report TRA No. & Date	DTL Test Report Results
Bandages Elastocraft 10cm*4.5m (Cotton crepe bandage 10cm*4.5m)	73B20	M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore.	TRA No.01-87002057/DTL dated: 28-08-2020	Analysis with specifications applied: BPC 1973 Description: Stated: Cotton crepe bandage of characteristic fabric of plain weave in one continuous length containing no joints, clean and reasonably free from weaving defects, cotton leaf, and shell having fast edges. Determined: <u>Characteristic fabric of plain weave in one continuous length containing no joints, clean but having weaving defects and not so fast edges and poor threads. (Does not comply</u> Warps: Limits: Avg NLT 17/cm

				Determined: 15.45/cm (Does not Comply) <u>Wefts:</u> Limits: Avg NLT 78/10cm Determined: 79.70/10 cm (Comply) <u>Weight g/m² :</u> Limit: 140g/m² Determined: 121.87 g/ m² (Does not Comply) <u>Result:</u> The above sample is Sub-standard on the basis of tests performed...
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- iii. Store keeper of Medicine Store situated at Chief Executive Officer, DHA, Rajanpur provided invoice/ Warranty No. 0888 dated 13-06-2020 issued by M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore as a proof of its purchase.
- iv. Warrantor portion and copy of test report was sent to M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore with directions to explain their position and provide requisite information in this regard.

2. Drug Inspector requested for grant of permission for prosecution against the above- accused persons nominated in the instant case who have contravened the provisions of Section 23/27 of the Drugs Act 1976(as amended)/DRAP Act 2012 and Rules framed there under by the way of: -

- a. **Manufacture for sale/ Sale of Substandard Drug**
b. **Issuance of false warranty**

3. Show cause notice(s) issued to the accused vide 14-04-2021.

Reply to Show cause Notice:

The firm vide Ref No. 786/0732/2021 Dated 21-05-2021 submitted written reply to Show-Cause Notice stated That:

This is with reference to your Show Cause Notice No. PQCB/R-428-2020 dated 14-04-2021, received by us on 17-05-2021, served to this firm concerning the **(Elastocraft) Cotton Crepe Bandages BPC 7.5cm x 4.5M Batch No.73B20, Mfg. Feb-2020 Exp. Jan- 2025**, sample taken from Medicine Store of Chief Executive Officer, DHA, Rajanpur and declared sub-standard by the Government Analyst, Punjab DIL Multan vide report No.TRA-01-87002057/DTL dated 28-08-2020 on the basis of Description, Warps and Weight per Unit Area.

As far as the sample under reference is concerned, we are reporting here under the details of DTL report No. TRA-01-87002057/DTL dated 28-08-2020 along-with our explanations /comments are given here under for evaluation and kind consideration at your end please.

	Tests Performed		Stated Values		Determined/Observed
	Warp threads/cm		NLT 17/cm= 17.00/cm		15.45/cm =15.45cm

	Weft Threads/10cm		NLT 78/10cm=7.80/cm		79.70/10cm=07.97/cm
			Total=24.80/cm		23.42/cm $\pm$ 5%=24.591/cm Total count almost complies Hence there is no concealment in the threads.
	Weight/m²		NLT 140g/m ²		121.87 $\pm$ 5%=127.9635g/m ²

Here it is mentioning that as per Method of testing provided / approved by the Ministry of Health, Government of Pakistan, Islamabad a variation in the threads and weight is allowed $\pm 5\%$. We do understand that if the Thread count complies the specification, then it is understood that weight per unit area is also complies. And there is no question of any shortfall in the weight, hence we confirm the sample under reference is complies the required standards.

We understand it might happen in testing the sample casually and ensure it is up to the required limit. Please observe from the above that other than the above test all necessary parameters (Weft, Width, Length, Elasticity etc.) required under the BPC specification also complies as per DTL Multan vide his report No. TRA-01-87002057/DTL dated 28.08.2020 and confirms it is up to the standards. Hence our submissions are as under: -

We are very much conscious about the quality and quantity of the products and do not compromise on the quality of our product in any case.

It is confident to mention here that we tested the warrantor portion as well as retained sample of the said Batch No.72B20 of Cotton Crepe Bandage BPC 7.5cm x 4.5m at our Quality Control Lab and observe it is of "Standard Quality and there is no such shortfalls in the sample as reported by the Analyst in his report. **A copy of Test Report dated 16-01-2021 performed at our QC Lab is attached herewith for your ready reference.**

It is worthwhile to mention here that the Surgical Bandages (Cotton Crepe Bandage) is meant for external use only and it has many commercial usages other than medical purposes like Cleaning of Machinery, Polishing etc. In the light of above said explanation it is stated that the Product (Medical Device) under reference is complies all test according to the BPC specifications and observations find by the Analyst for declaring sub-standard are unfortunate, ignorable and we understand has no such effect in externally use on human body. Even though if the authority feels it necessary, we are ready to replace the seized stock with fresh stock of standard quality or otherwise forward the sample of the same product (Medical Device) under reference to the NIH for re-testing.

In the light of above said facts it is submitted that we have not contravened the provisions of Section 23/72 of the Drug Act 1976 (as amended) DRAP Act 2012 and Rules framed there under by the way of (a) Manufacturing for sale/Sale of Substandard drug (b) Issuance of false warranty.

Keeping in view the above said explanation it is stated that the product (Medical Device) under reference is complies all test according to the BPC specifications and observations find by the Analyst for declaring sub-standard is unfortunate, which may kindly be ignored and consider our request as under:

- i. Stock under reference may be accepted.
- ii. Allow to return "out of specification" seized stock to us with the conditions of replacement by fresh stock of standard quality to settle this issue at your level.
- iii. Forward the sample of the same product (Medical Device) under reference to the NIH for re-testing purposes.

Thanking you and assuring you our best cooperation for all the time we remain.

Personal Hearing notice(s) issued to accused person(s) on 05-06-2023.

Case is placed before the Board for Decision.

Note:

It is pertinent to mention here that in 236th Board meeting, dated: 15-12-2021, a Product Specific Inspection (PSI) of **M/s Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore**, was marked in cases of similar nature having **same batch numbers**. The inspection was conducted with reference to:

- **Case No. PQCB/R-426/2020**
- **Case No. PQCB/R-427/2020**
- **Case No. PQCB/R-424/2020**

The committee after conducting the Product Specific Inspection (**PSI**) submitted the inspection report vide letter No. DPN/19373/DTL, dated: 17-11-2022. The firm submitted CAPA regarding the recommendations in PSI report and it was placed before the Board in **257th meeting, dated: 07-02-2023**.

The Board after careful perusal of the case record, the report of the product specific inspection and the corrective and preventive action submitted by the firm observed that in compliance to the recommendations by the committee, the firm has taken active measures in terms of improving the quality of raw material and also establish a separate Quality Assurance department to assure the quality of the products manufactured by them. Keeping in view the forgoing facts and the corrective and preventive actions taken by the firm, the Board after due deliberation and detailed discussion, unanimously decided to issue **Warning** to **M/S Cotton Craft Pvt Ltd, Plot No. 407-408, Sundar Industrial Estate, Raiwind Road, Lahore, Pakistan** with directions to be careful in future.

Summary:

Manufacturing Date: 02-2020

Expiry Date:01-2025

Sampling Date (Form 4): 20-07-2020

Sent to DTL (Form 6): 20-07-2020

Date of receipt in DTL: 23-07-2020

DTL Report Date (Form 7): 28-08-2020

1ST DI Communication with firm on dated: 29-12-2020

Date of Retesting Request of Firm: No Request

Investigation Report Dated: 09-03-2021

PROCEEDINGS & DECISION BY THE COMMITTEE:

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ITEM No. 2

SUBSTANDARD REGULAR CASES

Case No. 1

PQCB/ R-438/2021

Tehsil and District Layyah

ATTENDENCE

Secretary DQCB	<u>Accused Persons involved in subject case</u> 1. M/s Macter International Limited F-216, SITE Karachi through its Chief Operating Officer Mujeeb ur Rehman 2. Mujeeb ur Rehman 3. Zeeshan Khan 4. Khalid Irfan 5. Muhammad Muzammil Siddiqui of M/s Macter International Limited F-216, SITE Karachi.
Drug Inspector	

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Layyah reported that: -

- His predecessor, on 03-04-2021, inspected the premises of medicine store of Chief Executive Office (DHA) Layyah and took following drug sample on Form No.04 for the purpose of test/analysis and sent to Drug Testing Laboratory Multan for the purpose of test/analysis.
- Following drug sample after test/analysis was declared as **Substandard** by Government Analyst Drug Testing Laboratory Multan as detailed below:

Name of Drug	Batch No.	Manufacturer	DTL Report TRA No. & Date	DTL Test Report Result
Powder for reconstitution Ultima [Clarithromycin 125mg/5ml]	1003	M/s Macter International Limited F-216, SITE Karachi	01-89003477/DTL Dated: 24-07-2021	Analysis with specifications applied: USP 2020 Description: White to off white granular powder (when reconstituted forms white color suspension), contained in amber colored glass bottle sealed with metallic screw cap, packed in a labeled outer hard carton along with leaflet and plastic spoon. Identification: Clarithromycin identified.

				<u>Assay (Clarithromycin):</u> <table><tr><td>Stated</td><td>125mg/5ml</td></tr><tr><td>Determined</td><td>125.91mg/5ml</td></tr><tr><td>Percentage</td><td>100.73%</td></tr><tr><td>Limit</td><td>90-115%</td></tr></table> <u>pH:</u> <table><tr><td>Stated</td><td>4.0-5.4</td></tr><tr><td>Determined</td><td>5.65</td></tr></table> <u>(Does not comply)</u> <u>Result:</u> The above sample is “Substandard” on the basis of pH Test.	Stated	125mg/5ml	Determined	125.91mg/5ml	Percentage	100.73%	Limit	90-115%	Stated	4.0-5.4	Determined	5.65
Stated	125mg/5ml															
Determined	125.91mg/5ml															
Percentage	100.73%															
Limit	90-115%															
Stated	4.0-5.4															
Determined	5.65															

- iii. Storekeeper Chief Executive Office (DHA) Layyah provided invoice/ warranty 90358088 dated 29-03-2021 issued by M/s Macter International Limited F-216, SITE Karachi as a proof of its purchase.
- iv. Copy of test/analysis report and Warrantor portion was sent to M/s Macter International Limited F-216, SITE Karachi with directions to explain their position and provide requisite information in this regard. In Response, the firm challenged the test/analysis report and requested for re-testing of the above-mentioned drug sample from Appellate Laboratory NIH, Islamabad.
- v. Retesting request was considered in 237th-Meeting of PQCB held on 30-12-2021 in which Board decided to turn down the request.

2. The Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused person(s), who have contravened the provisions of Section 23/27 of the Drugs Act 1976(As amended)/DRAP Act 2012 and Rules framed there under by the way of:

- a. **Manufacture for sale / sale of Substandard drug**
- b. **Issuance of false warranty**

3. Show-cause notice(s) issued to accused person(s) vide 28-06-2022

Personal hearing notice(s) issued to accused person(s) on 19-06-2023.

Case is placed before the board for decision.

Summary:

Manufacturing Date: 03-2021

Expiry Date: 02-2023

Sampling Date (Form 4): 03-04-2021

Sent to DTL (Form 6): 17-04-2021

Date of receipt in DTL: 20-04-2021

DTL Report Date (Form 7): 24-07-2021

1ST DI Communication with firm on dated: 29-07-2021

Date of Retesting Request of Firm: Yes, on 03-08-2021

Fate of Retesting Request: Turned Down in 237th -M dated: 30-12-2021

Investigation Report Dated: 18-05-2022

PREVIOUS PROCEEDINGS & DECISION BY THE BOARD:

253rd meeting held on 29-11-2022

5. Case was considered by the Provincial Quality Control Board, under section 11 of the Drugs Act 1976 in its **253rd meeting** held on **29-11-2022** under the chairmanship of Secretary, Primary & Secondary Healthcare, Department. Mr. Amtiaz Aslam, Secretary DQCB Gujrat and Mr. Zaheer Abbass, Provincial Inspector of Drugs, Tehsil Sarai Alamgir, District Gujrat was present along with the original case record. Among the nominated accused Khalid Irfan (Quality Control Incharge) of M/s Macter International Limited F-216, SITE Karachi, Pakistan appeared before the Board. Firm's representatives pleaded their case upon following arguments:

- i. DTL reports shows a pH increase of almost 0.25 whereas NIH report also confirms a minor pH difference of almost 0.5 in pH of said batches.
- ii. Pharmacopeial limit of pH for active clarithromycin is 8-10 in USP and for that of taste masked granules used by their firm this limit is 4.5-7.0 (approved by DRAP). It also indicates that granules and clarithromycin (active ingredient) are stable up to pH 7 which ultimately is indicative of product's stability at observed pH values of 5.7 in subject sample.
- iii. As far as the clinical effect small difference on basis side has no impact on absorption as the available tablets are at pH 8-10. Buccal cavity pH is more than 6 which can change the pH dose immediately to basic side at 2nd step stomach pH is 1.5-3 and third step in intestine pH is 7 plus. Slightly higher pH does not affect the absorption of drug which is negligible as compare to the high variation in pH during natural absorption process.
- iv. Firm's representatives reiterated that their product is complying the key efficacy parameters of physical description and assay (108.64%) which depicts that a slight increase of pH has not adversely affected the potency and stability of their product.
- v. Firm requested the Board to consider their arguments on sympathetic grounds by ignoring such trivial variation of pH in the subject drug samples and assured to not repeat even this minor variation in future batches.
- vi. There was problem in the raw material. Now the firm reviewed the product and taken remedial measures by improving the formulation of raw material.

6. The Board upon careful perusal of the case record of subject batch and scrutiny of the DTL reports observed that the subject drug samples were declared Substandard from the Drugs Testing Laboratory Faisalabad based on pH, which is slightly higher than the upper permissible limit of 4.0-5.4. Other parameters including the assay and description of the subject samples were well within the official limits. Test results from National Institute of Health, Islamabad of subject drug sample when tested upon firm's own request also showed slight difference.

7. The Board, after due deliberation and detailed discussion, keeping in view the lesser clinical impact of slight pH difference of the subject drug samples, unanimously decided to issue **Warning to M/s Macter international Limited, F-216, S.I.T.E Karachi Pakistan** with directions to be careful in future.

8. Furthermore, the Board showed serious concern over the matter and was of the opinion that in order to dig out the root cause of the variation in pH in the drug sample, the defects in the Production and Quality Control & Assurance for subject drug need to be evaluated. Keeping in view the facts of the case, the Board after due deliberation and discussion unanimously decided to constitute a committee comprising of the following members to conduct **Product Specific Inspection (PSI)** of **M/s Macter international Limited, F-216, S.I.T.E Karachi Pakistan** and submit report for consideration by the Board in rest of the reported cases of Suspension Ultima.

1.	Prof. Dr Sajid Bashir Member PQCB	Convenor
2.	Secretary PQCB	Member

PRODUCT SPECIFIC INSPECTION REPORT OF

M/S MACTER INTERNATIONAL LIMITED F-216, S.I.T.E KARACHI

Member of Inspection Committee:

Prof. Dr. Sajid Bashir (Convener)	Member, Provincial Quality Control Board
Muhammad Shafique Khan Secretary, Provincial Quality Control, Board, Punjab (Member)	Member, Provincial Quality Control Board

Date of Inspection:

Inspection was conducted in reference to PQCB order no. PQCB/R-528/2021 & R-467,468, 469/2021 dated 29-11-2022. Powder for reconstitution Ultima [clarithromycin (as coated granules 27.5%), 125mg/5ml]. Batch no. 1007, 1010, 1011, 1012 were declared from different DTLs of Punjab on the basis of pH test. Furthermore, batches of the subject drug product were also declared substandard on the basis of pH from National Institute of Health, Islamabad. The Board in its 253rd meeting dated 29-11-2022 unanimously decided to direct committee to conduct Product specific inspection of the firm to dig out the root cause of variation in pH. For this purpose, inspection of M/s Macter International Limited F-216 SITE Karachi was conducted on 11-01-2023.

Brief about Manufacturing Unit:

Manufacturing Unit	M/s Macter International Limited
Location/Address	F-216 SITE Karachi, Pakistan
Director Quality Operation	Farooq Mustafa
Senior Manager Quality Control	Khalid Irfan

General Information about the Unit:

M/s Macter International Limited consists of a ground plus 2 floors facility. The facility is well maintained and upgraded time to time as per GMP requirement. The total covered area is about 100,000 square ft.

Detail of Inspection /Observations:

1. The manufacturing unit was inspected on 11-01-2023 for Product specific inspection of Ultima Dry suspension 125mg/5ml. The report of Drug Testing Laboratory and NIH report were discussed with the management/ technical team of the firm. The management presented the Drug Registration Certificate having DRAP registration No. 029793.
2. Firm presented the flow chart of manufacturing of dry suspension Ultima. Total 11 batches were failed by different DTLs (Batch no. 1003-1013). pH difference in the range of 0.11-0.55. As pH difference is closer to upper limit, Batches number 1003, 1004, 1005 and 1006 are passed by some DTLs and also failed by others. Root cause determined was variability of pH in the taste masked granules. In response to query regarding the substandard reports, the representative of the firm submitted that the firm specifically manufactured these batches for Punjab Government and now the firm has no current stock of these batches in warehouse of the firm. The firm's representative briefed that there was problem in the raw material. Now, the firm reviewed the product and taken remedial measures by improving the formulation of raw material. We have already resolved the issue by working with the supplier of granules and we have replaced supplies to many institutions. Trend of last 12 batches showed that now pH is well control in mid of the range.

The following observations were made during inspection

Raw Material Store:

- Raw material store area is properly cleaned & proper demarcation for passed & rejected material was labelled.
- The temperature and humidity charts were displayed and filled accordingly.

- Temperature of the area was 25.4 degrees and log book were maintained.
- Standard Operating Procedures were properly laid down with the help of flow chart.
- Raw-material store was equipped with the electronic digital weighing scale, HVAC Unit.
- Passed material was separately quarantined under proper labeling.
- Firm provided list of approved vendors list of excipients.
- Firm provided that granules of API is registered with DRAP. Moreover API clarithromycin coated granules having material code 10000058 is purchased from Surge Laboratories Pvt Ltd., having pH of granules as below:

Batch No. of API taste masked granules	Manufacture results pH (3.5-7.0)
70688	6.86
71789	5.75

Production:

- The pre-formulation & formulation area is properly designated.
- SOPs of the suspension manufacturing were laid down.
- Flow charts ensuring the processes were laid down.
- List of machines of Production Department in liquid Syrup/suspension section was provided.
- Firm product was manufactured as per SOP laid down and each step was documented in Batch Manufacturing record of specific product.
- Ensure Line clearance during all production activities.

Quality Control & Quality Assurance

- The Quality Control laboratory is well equipped with gas Chromatography, FTIR, HPLC prominence Shimadzu, Spectrophotometer, Shimadzu, Stability Chamber, Stability Chamber, pH meter, Disintegration Apparatus, Dissolution Apparatus, filtration unit, Analytical balance, Moisture Balance, Fribilator test apparatus, Autoclave, Chemicals and glass ware, ting point App., Hygrometers, automatic polarimeter, Karl Fischer, Magnetic stirrer Hot plate, pH meter, climatic chamber, Digital Balance, Analytical Balance, vaccum oven, sieve shaker, refracometer, digital muffle furnace with proper calibration and verification by PCSIR, Karachi. Quality assurance department had hygrometer, calibrated glass ware, calibrated weights, flask shaker, temperature and humidity data loggers.
- SOP for finished product testing was checked and the method for testing was in accordance with the test and method specified in USP Specifications.

Conclusion:

The firm is GMP compliant, the inspection was conducted in detail to address all parameters of manufacture/ Quality control Test to correlate the defect in manufacturing. After thorough and detailed product inspection of the firm and committee members were of the opinion that the problem encountered due to the API raw material. The firm provided CAPA initiation form Doc no. COR/IMS/PP/003-B in in which firm investigate the root cause analysis and took corrective actions

- **Contact existing taste masked granules supplier and request to arrange raw material with low pH** so that the product pH remains in USP limits throughout the shelf life along with their

stability data.

- **Recommended to adjust the pH** to a level in mid of maximum & minimum limits by citric acid. 0.119% citric acid will be added to in the formulation.
- **R & D to review existing formulation and developed revised formulation** with low side pH.
- After corrective action **Supplier provided certificate of analysis of API coated granules** batch no. 87324 with pH 4.41(3.5-7.0).

Formulation after Corrective actions:

Materials	Percentage
Calrithromycin Coated granules 27.5%	15.053%
Ammonium Glycirrihizinate	0.051%
Simethicone C100%F	0.258%
Sucrose (Fine crystals)	80.715%
Saccharin Sodium	0.155%
Sodium benzoate	0.773%
Citric acid Anhydrous	0.119%
Titanium dioxide	1.031%
Guar gum	0.515%
Pineapple powder flavor	1.330%
Total	100%

Recommendations of the Committee:

The firm has already carried out the root cause analysis of the product failure and provided details of SOPs in this regard. Moreover, it is recommended that

1. The firm should **closely monitor the stability studies** of the product after adjusting citric acid to adjust the pH of the product on both accelerated and long-term conditions.
2. The firm should do **trend analysis of pH** after the corrective action implementation.
3. The firm should **revise its standard operating procedures (SOP)** for testing of pH during in-process to ensure the final product compliance with USP.
4. The firm should ensure the **calibration & verification** of the pH measurement system periodically.

5. The firm should ensure the **supply of raw material through approved vendor.**

RESPONSE SUBMITTED BY FIRM IN TERMS OF CORRECTIVE & PREVENTIVE ACTIONS TAKEN

Reply of the firm to Product Specific Inspection Report vide letter No. 1857 dated 08th June, 2023

We would like to explain our position as follows and also submitting evidences as per your recommendations.

- The stability testing of the product is being done to closely monitor the quality of the product on accelerated and long term conditions after the addition of citric acid for pH adjustment and found satisfactory so far till 18 months long term conditions and accelerated conditions too.
- Continuous monitoring of pH trend is being done to assure the quality of the product.
- BMR has been updated for in process testing of pH. Each batch is analyzed at bulk stage for pH during in process to control the quality of the finished product.
- The pH meter is calibrated by PCSIR. Daily in-house calibration and verification also performed as per USP guideline and closely monitor the trend analysis.
- There is only one vendor approved for the active material i.e. Surge Laboratories Pvt. Limited for Clarithromycin taste masked granules.

Hope the above mentioned evidences will fulfill to your all recommendations. We are looking forward to your utmost support in the subject matter from your good office.

COMPARATIVE TABLE OF RECOMMENDATIONS BY COMMITTEE VS ACTIONS TAKEN REGARDING PSI OF SUSPENSION ULTIMA

No.	Recommendations of Committee	CAPA by Firm
1	The firm should closely monitor the stability studies of the product after adjusting citric acid to adjust the pH of the product on both accelerated and long-term conditions.	The stability testing of the product is being done to closely monitor the quality of the product on accelerated and long term conditions after the addition of citric acid for pH adjustment and found satisfactory so far till 18 months long term conditions and accelerated conditions too.
2	The firm should do trend analysis of pH after the corrective action implementation	Continuous monitoring of pH trend is being done to assure the quality of the product.
3	The firm should revise its standard operating procedures (SOP) for testing of pH during in-process to ensure the final product compliance with USP.	BMR has been updated for in process testing of pH. Each batch is analyzed at bulk stage for pH during in process to control the quality of the finished product.

4	The firm should ensure the calibration & verification of the pH measurement system periodically.	The pH meter is calibrated by PCSIR . Daily in-house calibration and verification also performed as per USP guideline and closely monitor the trend analysis.
5	The firm should ensure the supply of raw material through approved vendor .	There is only one vendor approved for the active material i.e. Surge Laboratories Pvt. Limited for Clarithromycin taste masked granules.

Case is placed before the Board for decision.

CURRENT PROCEEDINGS & DECISION BY THE BOARD:

Case No. 2

PQCB/ R-537/2021

Mumtazabad Town, District Multan

ATTENDENCE

Secretary DQCB	<u>Accused Persons involved in subject case</u> 1. M/s Macter International Limited F-216, SITE Karachi through its Chief Operating Officer Mujeeb ur Rehman 2. Mujeeb ur Rehman 3. Zeeshan Khan 4. Khalid Irfan 5. Muhammad Muzammil Siddiqui of M/s Macter International Limited F-216, SITE Karachi.
Drug Inspector	

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Mumtazabad Town, District Multan reported that: -

- His predecessor, on 05-06-2021, inspected the premises of Main Medicine Store, O/o Chief Executive officer (DHA), Multan and took 9 different types of drug samples on Form No.04 and sent to Drug Testing Laboratory Multan for the purpose of test/analysis. The subject drug sample was sent to DTL vide memo no. 96333 dated: 07-06-2021.
- The subject drug sample out of these nine drug samples after test/analysis was declared as **Substandard** by Government Analyst Drug Testing Laboratory Multan as detailed below:

Name of Drug	Batch No.	Manufacturer	DTL Report TRA No. & Date	DTL Test Report Result
Powder for reconstitution Ultima [Clarithromycin 125mg/5ml] Mfg. date: May-2021 Exp. Date: Apr-2023 Regs # 029793	1012	M/s Macter International Limited F-216, SITE Karachi, Pakistan	01-89004481/DTL Dated: 07-08-2021	Analysis with specifications applied: USP 2020 Description: White to off white granular powder (when reconstituted forms white color suspension), contained in amber colored glass bottle sealed with metallic screw cap, packed in a labeled outer hard carton along with leaflet and plastic spoon. Identification: Clarithromycin identified. Assay (Clarithromycin):

					<table><tr><td>Stated</td><td>125mg/5ml</td></tr><tr><td>Determined</td><td>129.31 mg/5ml</td></tr><tr><td>Percentage</td><td>103.45%</td></tr><tr><td>Limit</td><td>90-115%</td></tr></table>	Stated	125mg/5ml	Determined	129.31 mg/5ml	Percentage	103.45%	Limit	90-115%
Stated	125mg/5ml												
Determined	129.31 mg/5ml												
Percentage	103.45%												
Limit	90-115%												

(Complies)

pH:

Stated	4.0-5.4
Determined	5.76

(Does not comply)

Result: The above sample is “**Substandard**” on the basis of **pH Test**.

- iii. Storekeeper Main Medicine Store of O/o Chief Executive officer (DHA), Multan provided invoice/ warranty 90365171 dated 31-05-2021 issued by M/s Macter International Limited F-216, SITE Karachi, Pakistan as a proof of its purchase.
- iv. Copy of test/analysis report and Warrantor portion was sent to M/s Macter International Limited F-216, SITE Karachi, Pakistan with directions to explain their position and provide requisite information in this regard.
- v. In Response, the firm challenged the test/analysis report and requested for re-testing of the above-mentioned drug sample from Appellate Laboratory NIH, Islamabad.
- vi. Pursuant to the request of manufacturer the sample was sent to NIH, Islamabad, from where the sample was declared **Substandard** as detailed below:

Name of drug	Batch No.	Name of manufacturer	NIH Test Report No. & Date	NIH Test Report Results			
Suspension Ulima (Clarithromycin 125mg/5ml)	1012	M/s Macter International Limited F-216, SITE Karachi, Pakistan	054-P/2022 dated: 06-05-2022	Analysis with specifications applied: USP-39 pH: <table><tr><td>Determined</td><td><u>6.0</u>+0.06</td></tr></table>		Determined	<u>6.0</u>+0.06
Determined	<u>6.0</u>+0.06						

				Limit	4.0-5.4
				(Does not comply with USP-39). Result: The sample is of Substandard quality on the basis of tests performed.	

vii. Copy of NIH report was sent to M/s Macter International Limited F-216, SITE Karachi, Pakistan.

2. The Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused person(s), who have contravened the provisions of Section 23/27 of the Drugs Act 1976(As amended)/DRAP Act 2012 and Rules framed there under by the way of:

- a. **Manufacture for sale / sale of Substandard drug**
- b. **Issuance of false warranty**

3. Show-cause notice(s) issued to accused person(s) vide 19-10-2022.

Personal hearing notice(s) issued to accused person(s) on 19-06-2023.

Case is placed before the board for decision.

Summary:

Manufacturing Date: 05-2021

Expiry Date: 04-2023

Sampling Date (Form 4): 05-06-2021

Sent to DTL (Form 6): 07-06-2021

Date of receipt in DTL: 09-06-2021

DTL Report Date (Form 7): 07 - 08 - 2021

1ST DI Communication with firm on dated: 16-08-2021

Date of Retesting Request of Firm: Yes, on 24-08-2021

Fate of Retesting Request: Allowed in 240th -M dated: 15-03-2022

Investigation Report Dated: 02-08-2022

PROCEEDINGS & DECISION BY THE COMMITTEE:

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Case No. 3

PQCB/ R-437/2021

THQ Chowk Sarwar Shaheed, Muzaffargarh

ATTENDENCE

Secretary DQCB	<u>Accused Persons involved in subject case</u> 1. M/s Macter International Limited F-216, SITE Karachi through its Chief Operating Officer Mujeeb ur Rehman 2. Mujeeb ur Rehman 3. Zeeshan Khan 4. Khalid Irfan 5. Muhammad Muzammil Siddiqui of M/s Macter International Limited F-216, SITE Karachi.
Drug Inspector	

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, THQ Chowk Sarwar Shaheed, Muzaffargarh reported that: -

- He, on 20-05-2021, inspected the premises of Main Medicine Store of THQ Level 50 bedded Hospital Chowk Sarwar Shaheed, Tehsil Kot Addu, District Muzaffargarh and took five different types of drug samples on Form No.04 and sent to Drug Testing Laboratory Multan for the purpose of test/analysis.
- One out of these five drug samples after test/analysis was declared as **Substandard** by Government Analyst Drug Testing Laboratory Multan as detailed below:

Name of Drug	Batch No.	Manufacturer	DTL Report TRA No. & Date	DTL Test Report Result		
Powder for reconstitution Ultima [Clarithromycin 125mg/5ml]	1007	M/s Macter International Limited F-216, SITE Karachi	01-89003992/DTL Dated: 24-07-2021	Analysis with specifications applied: USP 2020 Description: White to off white granular powder (when reconstituted forms white color suspension), contained in amber colored glass bottle sealed with metallic screw cap, packed in a labeled outer hard carton along with leaflet and plastic spoon. Identification: Clarithromycin identified. Assay (Clarithromycin): <table><tr><td>Stated</td><td>125mg/5ml</td></tr></table>	Stated	125mg/5ml
Stated	125mg/5ml					

				<table><tr><td>Determined</td><td>133.50mg/5ml</td></tr><tr><td>Percentage</td><td>106.85%</td></tr><tr><td>Limit</td><td>90-115%</td></tr></table>	Determined	133.50mg/5ml	Percentage	106.85%	Limit	90-115%
Determined	133.50mg/5ml									
Percentage	106.85%									
Limit	90-115%									
				<u>pH:</u> <table><tr><td>Stated</td><td>4.0-5.4</td></tr><tr><td>Determined</td><td>5.74</td></tr></table>	Stated	4.0-5.4	Determined	5.74		
Stated	4.0-5.4									
Determined	5.74									
				<u>(Does not comply)</u>						
				<u>Result:</u> The above sample is “Substandard” on the basis of pH Test.						

- iii. Storekeeper Main Medicine Store of THQ Level 50 bedded Hospital Chowk Sarwar Shaheed, Tehsil Kot Addu, District Muzaffargarh provided invoice/ warranty 90361401 dated 28-04-2021 issued by M/s Macter International Limited F-216, SITE Karachi as a proof of its purchase.
- iv. Copy of test/analysis report and Warrantor portion was sent to M/s Macter International Limited F-216, SITE Karachi with directions to explain their position and provide requisite information in this regard. In Response, the firm challenged the test/analysis report and requested for re-testing of the above-mentioned drug sample from Appellate Laboratory NIH, Islamabad.
- v. Pursuant to the request of manufacturer the sample was sent to NIH, Islamabad, from where the sample was declared **Substandard** as detailed below:

Name of drug	Batch No.	Name of manufacturer	NIH Test Report No. & Date	NIH Test Report Results				
Suspension Ulima (Clarithromycin 125mg/5ml)	1007	M/s Macter International Limited F-216, SITE Karachi	064-P/2022 dated: 16-05-2022	Analysis with specifications applied: USP-39 pH: <table><tr><td>Determined</td><td>5.7±0.06</td></tr><tr><td>Limit</td><td>4.0-5.4</td></tr></table> (Does not comply with USP-39). Result: The sample is of Substandard quality on the basis of tests performed.	Determined	5.7±0.06	Limit	4.0-5.4
Determined	5.7±0.06							
Limit	4.0-5.4							

2. The Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused person(s), who have contravened the provisions of Section 23/27 of the Drugs Act 1976(As amended)/DRAP Act 2012 and Rules framed there under by the way of:

- a. **Manufacture for sale / sale of Substandard drug**
- b. **Issuance of false warranty**

3. Show-cause notice(s) issued to accused person(s) vide 12-08-2022.

Personal hearing notice(s) issued to accused person(s) on 19-06-2023.

Case is placed before the board for decision.

Summary:

Manufacturing Date: 04-2021

Expiry Date: 03-2023

Sampling Date (Form 4): 20-05-2021

Sent to DTL (Form 6): 20-05-2021

Date of receipt in DTL: 28-05-2021

DTL Report Date (Form 7): 24-07-2021

1ST DI Communication with firm on dated: 28-07-2021

Date of Retesting Request of Firm: Yes, on 03-08-2021

Fate of Retesting Request: Allowed in 240th -M dated: 15-03-2022

Investigation Report Dated: 18-05-2022

PROCEEDINGS & DECISION BY THE COMMITTEE:

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DISTRICT DERA GHAZI KHAN

PQCB/R-696/2021

Tehsil Dera Ghazi Khan (Urban), District Dera Ghazi Khan

ATTENDANCE:

Secretary DQCB	<u>Accused Persons involved in subject case</u>
Drug Inspector	1. M/s Macter International Limited F-216, S.I.T.E., Karachi-Pakistan through its Chief Operating Officer Mujeeb Ur Rehman 2. Mujeeb Ur Rehman Chief Operating Officer 3. Khalid Irfan Quality Control Incharge 4. Muhammad Zeeshan Khan Production Incharge 5. Muhammad Muzammil Siddiqui Warrantor Of M/s Macter International Limited F-216, S.I.T.E., Karachi-Pakistan.

BRIEF FACTS OF THE CASE

Provincial Inspector of drugs, Tehsil Dera Ghazi Khan (Urban), District Dera Ghazi Khan reported that:-

- i. His Predecessor, on 25-05-2021, inspected the premises of Medicine Store of District Health Office Dera Ghazi Khan and took sample of drug on Form No.04 for the purpose of test/analysis and sent the subject drug sample to Drug Testing Laboratory, Multan vide memorandum No. 0000093926 dated 26-05-2021.
- ii. Following drug sample, after test/analysis, was declared **Substandard** by Government Analyst, Drug Testing Laboratory, **Multan** as detailed below:
 - iii. Store Keeper, Medicine Store of District Health Office Dera Ghazi Khan submitted Invoice/warranty No. 90361408 dated 28-04-2021 issued by M/s Macter International Limited F-216, S.I.T.E., Karachi-Pakistan as a proof of its purchase of the said drug.
 - iv. Warrantor Portion of the drug sample was sent to M/s Macter International Limited F-216, S.I.T.E., Karachi-Pakistan and they were asked to provide requisite information in this regard.
 - v. A copy of test report was sent to M/s Macter International Limited F-216, S.I.T.E., Karachi-Pakistan and they were asked to provide requisite information in this regard.
 - vi. In response, the firm challenged the test/analysis report of the drug sample and requested to re-test the above-mentioned drug sample from Appellate Laboratory, National Institute of Health, Islamabad.
 - vii. Pursuant to firm's retesting request the Provincial Quality Control Board in its 240th meeting held on 15-03-2022 **allowed** to send the drug sample to NIH, Islamabad for retesting from where the sample was declared **Substandard** as detailed below:

Name of drug	Batch No.	Name of manufacturer	DTL Report TRA No. & Date	DTL Test Report Results
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Ultima [When reconstituted as directed each 5 ml contains: Clarithromycin USP...125 mg (As coated granules 27.5%)] Suspension 60 ml.	1007	M/s Macter International Limited F-216, S.I.T.E., Karachi-Pakistan	TRA No. 01-89004053/DTL Dated:-29-07-2021	<u>Result of Test/ Analysis with specifications applied:</u> USP 2020 <u>Description:</u> White to Off white granular powder (when reconstituted forms white color suspension), contained in amber colored glass bottle sealed with metallic screw cap, packed in a labeled outer hard carton along with leaflet and plastic spoon. <u>Identification:</u> Clarithromycin Identified. <u>Assay:</u> <table><tr><th>Stated</th><th>Determined</th><th>Percentage</th><th>Limit</th></tr><tr><td>125 mg/5ml</td><td>128.09 mg/5ml</td><td>102.47%</td><td>90-115%</td></tr></table> (Complies) <u>PH:</u> Sated: 4.0-5.4 Determined: 5.73 (Does Not Comply) <u>RESULT:</u> The above ample is declared <u>Sub-Standard</u>, on the basis of PH Test.	Stated	Determined	Percentage	Limit	125 mg/5ml	128.09 mg/5ml	102.47%	90-115%
Stated	Determined	Percentage	Limit									
125 mg/5ml	128.09 mg/5ml	102.47%	90-115%									
Name of Drug	Batch No.	Name of Manufacturer	NIH Test Report No.	NIH Test Report Result								
Suspension Ultima 60 ml (Clarithromycin 125mg/5ml).	1007	M/s Macter International Ltd. F-216, SITE., Karachi Pakistan	052-P/2022 dated 16-05-2022	<u>PH:</u> Determined: 5.7 ± 0.06 Limit: 4.0-5.4 Does not Comply with USP-39. <u>CONCLUSION:</u> The sample is of <u>Sub-Standard</u> quality on the basis of the test performed.								

vii. The Copy of NIH report was sent to M/s Macter International Limited F-216, S.I.T.E., Karachi-Pakistan.

2. Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused persons who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended) / DRAP Act 2012 and Rules framed there under by the way of: -

- a. Manufacture for sale/sale of the Substandard drug
- b. Issuance of false warranty

3. Show cause Notice (s) issued to the accused person(s) Dated 13-02-2023.

Reply of the firm to show cause notice vide letter no. Ref No. 1814 dated 21-02-2023:

Reference to the letter No. PQCB/R-696/2021 (the "Letter") Dated February 13, 2023, which is received to us on Dated February 18, 2023. In this connection we request that our case kindly be closed on the basis of following facts, as we are quality conscious manufacturer and assure you that in future our product will be fully compliant.

1. Slight difference in pH of 0.33 have no impact on shelf life stability as shown that a stability studies of our product satisfactory, which also support by Drug Testing Laboratory (the "DTL") results.
2. Assay results of all batches are still same as at the initial stage.
3. Shelf life expiry of clarithromycin USP at pH 8-10 is three years see Certificate of Analysis (the "COA") and United States Pharmacopeia (the "USP") monograph
4. Shelf life of granules at pH 4 to 7 is three years as per manufacturer, granules of API is registered with DRAP
5. In use stability studies was conducted for 14 days and found stable Assay results and other parameters were found satisfactory well within good limits.
6. As far as the clinical effect is concerned small difference of pH on basic side has no impact on absorption as the available tablets are at pH 8-10. Buccal cavity pH is more than 6 which can change the pH dose immediately to basic side at 2nd step stomach pH is 1.5 to 3 and third step in intestine pH is 7 plus. Slightly higher pH does not affect the absorption of drug which is negligible as compare to the high variation in pH during natural absorption process.
7. As per discussion with USP officials by mail they don't have privy to the reasoning behind

In the light of above facts our product is not injurious to health and not harmful. We worked with the manufacturer of granules and reached to the conclusion and in future they will provide granules of pH less than 5. Your support is requested in matter which is of trivial nature and has no impact on the having no impact on patient, may be disposed of the case to meet common goal PQCB & Mactar to maintain consistent supply of quality drugs. We are looking forward your utmost support in this regard.

In this context we are enclosing the required information as directed in your letter, i.e, copies of CNICs of technical staff, copy of Drug Manufacturing License, registration certificate and product specification

4. Personal Hearing notice(s) issued to accused person(s) dated 19-06-2023.
5. Case is placed before the Board for Decision

Summary:

- **Manufacturing Date: 04-2021**
- **Expiry Date: 03-2023**
- **Sampling Date (Form 4): 26-05-2021**
- **Sent to DTL (Form 6): 26-05-2021**
- **Date of receipt in DTL: 31-05-2021**
- **DTL Report Date (Form 7): 29-07-2021**
- **Time Extension: NA**
- **1ST DI Communication with firm on dated: 27-09-2021**
- **Date of Retesting Request of Firm: 06-10-2021**
- **Fate of Retesting: Allowed in 240th meeting dated 15-03-2022**
- **Investigation Report Dated: 25-01-2023**

PROCEEDINGS & DECISION BY THE BOARD:

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DISTRICT KHUSHAB

PQCB/R-231/2021Tehsil Naushera, District KhushabATTENDANCE:

Secretary DQCB	<u>Accused Persons involved in subject case</u> 1. M/s Macter International LTD., F-216, S.I.T.E., Karachi-Pakistan through Chief Operating Officer, Mujeeb Ur Rehman 2. Mujeeb Ur Rehman Chief Operating Officer 3. Muhammad Muzammil Siddiqui Warrantor 4. Zeeshan Khan Production Incharge 5. Khalid Irfan Quality Control Incharge of M/s Macter International LTD., F-216, S.I.T.E., Karachi-Pakistan
Drug Inspector	

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Tehsil Naushera, District Khushab reported that: -

- His predecessor, on 21-06-2021 inspected the Medicine Store THQ Hospital Naushera, Tehsil Naushera, District Khushab, took subject drug sample on Form No. 4 for the purpose of test/analysis and sent to Drug Testing Laboratory, Rawalpindi vide memorandum No. 0000098724 dated 21-06-2021.
- Following drug sample, after test/analysis were declared as **Substandard** by Government Analyst, Drug Testing Laboratory, **Rawalpindi** as detailed below: -

Name of Drug	Batch No.	Name of Manufacturer	DTL Report	DTL Test Report Result
Ultima for oral suspension (Clarithromycin 125 mg/5 ml), 60 ml (When reconstituted) Mfg date: Apr-2021 Exp date:	1011	M/s Macter International LTD., F-216, S.I.T.E., Karachi-Pakistan	01-75001740/DTL dated 03-09-2021	Results of test/analysis with specifications applied: USP 2020 <u>PHYSICAL DESCRIPTION:</u> White to off white coloured powder contained in multidose amber coloured glass bottle with affixed label, sealed with aluminium screw cap on which company logo is printed, further packed in outer labelled carton. On reconstitution, off white coloured, slightly viscous suspension formed.

Mar-2023				pH: Limit: 4.0 - 5.4 Determined: 5.77 at 25.1°C (DOES NOT COMPLY) <u>IDENTIFICATION:</u> Clarithromycin Identified. <u>ASSAY OF CLARITHROMYCIN:</u> Stated: 125 mg/ 5mL Determined: 129.792 mg/ 5mL Percentage: 103.83 % Limit: 90.0 – 115 % RESULT: <u>The above sample is ‘</u> <u>‘Substandard’ with respect to pH Test</u> <u>Performed.</u>
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- iii. Storekeeper of Medicine Store THQ Hospital Naushera, Tehsil Naushera, District Khushab provided Invoice/ warranty No. 90364072 dated 26-05-2021 issued by M/s Macter International LTD., F-216, S.I.T.E., Karachi-Pakistan.
- iv. Warrantor Portion and a copy of test report were sent to M/s Macter International LTD., F-216, S.I.T.E., Karachi-Pakistan with directions to provide the requisite information and to explain their position in this regard. In response, the firm challenged the test/analysis report and requested to re-test the above mentioned drug sample from Appellate Laboratory, National Institute of Health, Islamabad.
- v. Pursuant to the request of M/s Macter International LTD., F-216, S.I.T.E., Karachi-Pakistan the retesting request of the subject drug sample was considered in the 244th meeting by the Board held on 31-05-2022 and the board unanimously decided to Turn Down the request by the firm for retesting of the subject drug sample.

2. Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused persons who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended) / DRAP Act 2012 and Rules framed there under by the way of: -

- a. **Manufacture for sale/sale of the Substandard drug**
- b. **Issuance of false warranty**

3. Show cause Notice (s) issued to the accused person(s) Dated 26-10-2022.

Reply of the firm to show cause notice vide letter no. nil dated 03-11-2022:

Reference to the letter No. PQCB /R-231/2021 dated 26-10-2022, which is received to us on 29-10- 2022. In this connection we request that our case kindly be closed on the basis of following facts, as we are quality

conscious manufacturer and assure you that in future our product will be fully compliant

INSHALLAH.

1. Slight difference in pH have no impact on shelf life stability as shown that a) stability studies of our product satisfactory, which also support by DTL results.
2. Assay results of all batches are still same as at the initial stage.
3. Shelf life expiry of clarithromycin USP at pH 8-10 is three years see COA and USP monograph.
4. Shelf life of granules at pH 4 to 7 is three years as per manufacturer, granules of API is registered with DRAP
5. In use stability studies was conducted for 14 days and found stable Assay results and other parameters were found satisfactory well within good limits.
6. As far as the clinical effect small difference on basic side has no impact on absorption as the available tablets are at pH 8-10. Buccal cavity pH is more than 6 which can change the pH dose immediately to basic side at 2 step stomach pH is 1.5 to 3 and third step in intestine pH is 7 plus. Slightly higher pH does not affect the absorption of drug which is negligible as compare to the high variation in pH during natural absorption process.
7. As per discussion with USP officials by mail they don't have privy to the reasoning behind these determination of pH.

In the light of above facts our product is not injurious to health and not harmful. Apart from that we will replace the quantity of ultima suspension on immediate effect. We worked with the manufacturer of granules and reached to the conclusion and in future they will provide granules of pH less than 3. Your support is requested in matter which is of trivial nature and has no impact on the having no impact on patient, may be disposed off the case to meet common goal PQCB & Macter to maintain consistent supply of quality drugs.

4. Personal Hearing notice(s) issued to accused person(s) dated 19-06-2023.
5. Case is placed before the Board for Decision

Summary:

- **Manufacturing Date: 04-2021**
- **Expiry Date: 03-2023**
- **Sampling Date (Form 4): 21-06-2021**
- **Sent to DTL (Form 6): 21-06-2021**
- **Date of receipt in DTL: 07-07-2021**
- **DTL Report Date (Form 7): 03-09-2021**
- **Time Extension: NA**
- **1ST DI Communication with firm on dated: 21-06-2021**
- **Retesting Request of Firm: Yes**
- **Fate of Retesting: Turned down in 244th meeting dated 31-05-2022**
- **Investigation Report Dated: 30-06-2022**

PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 6

PQCB/R-454/2021

Tehsil & District Pakpattan

ATTENDANCE:

Secretary DQCB	<u>Accused Persons involved in subject case:</u> 1. M/s Macter international Limited, F-216, S.I.T.E Karachi through Chief Operating Officer Mujeeb Ur Rehman 2. Mujeeb Ur Rehman Chief Operating Officer 3. Zeeshan Khan Production Incharge 4. Khalid Irfan Quality Control Incharge 5. Muzammil Siddiqui Warrantor of M/s Macter international Limited, F-216, S.I.T.E Karachi
Drug Inspector	

BRIEF FACTS OF THE CASE:

Provincial Inspector of Drugs, Tehsil & District Pakpattan reported that: -

- He, on 07-05-2021 inspected the medicine store CEO DHA Office Pakpattan, and took subject drug sample on Form No. 4 for the purpose of test/analysis and sent to Drug Testing Laboratory, Bahawalpur.
- Following drug sample, after test/analysis was declared as **Substandard** by Government Analyst, Drug Testing Laboratory, **Bahawalpur** as detailed below: -

Name of drug	Batch no.	Name of manufacturer	TRA No & Date	DTL Test Report Results
Suspension Ultima 60ml [Clarithromycin (as coated granules 27.5%, 125mg/5ml, 60ml after reconstitution]	1006	M/s Macter international Limited, F- 216, S.I.T.E Karachi	No. 01- 25007158 dated 03- 07-2021	<u>Results of test/analysis with specifications applied:</u> USP 2020 <u>COMPOSITION:</u> When reconstituted as directed each 5ml contains: Clarithromycin USP.... 125mg (as coated granules 27.5%) <u>DESCRIPTION (MS):</u> White coated granules when reconstituted gives white to off white colored suspension (stated volume: 60m, when reconstituted) <u>pH (USP):</u> <u>Determined:</u> 5.804 Limit: 4.0-5.4

				Does not comply with specs. IDENTIFICATION: Clarithromycin is identified ASSAY: <table border="1"> <thead> <tr> <th>Assay</th><th>Stated</th><th>Found</th><th>Limit</th><th>Percentage</th></tr> </thead> <tbody> <tr> <td>Clarithromycin</td><td>125mg/5ml</td><td>143.43mg/5ml</td><td>90-115%</td><td>114.74%</td></tr> </tbody> </table> RESULT: The sample is Substandard on the basis of pH Test.	Assay	Stated	Found	Limit	Percentage	Clarithromycin	125mg/5ml	143.43mg/5ml	90-115%	114.74%
Assay	Stated	Found	Limit	Percentage										
Clarithromycin	125mg/5ml	143.43mg/5ml	90-115%	114.74%										

- iii. Storekeeper medicine store CEO DHA Pakpattan provided Invoice/ warranty No. 90361397 dated 28-04-2021 issued by M/s Macter international Limited, F-216, S.I.T.E Karachi.
- iv. Warrantor Portion was sent to M/s Macter international Limited, F-216, S.I.T.E Karachi.
- v. A copy of Test/ Analysis report was sent to M/s Macter international Limited, F-216, S.I.T.E Karachi and they were directed to provide requisite information in this regard. In response, Firm challenged the DTL report and requested retesting of the sample from NIH, Islamabad.
- vi. In response, the said request of the firm was considered by the PQCB in its 240th **meeting** dated 15-03-2022. The Board, after discussion, unanimously decided to *Allow* and sent the sample to NIH, Islamabad for retesting. Appellate Laboratory/ NIH Islamabad also declared the sample drug in question as **Substandard** vide Test Report No. 065-P/2022 Dated 16th May, 2022. The detail is as follow: -

Name of drug	Batch no.	Name of manufacturer	NIH Test Report No. & Date	NIH Test Report Results
Suspension Ultima 60ml [Clarithromycin 125mg/5ml]	1006	M/s Macter international Limited, F-216, S.I.T.E Karachi	No. 065-P/2022 dated 16 th May, 2022	pH: Determined: 5.6 ± 0.06 Limit: 4.0-5.4 Does not Comply with USP-39 CONCLUSION: The sample is Substandard quality on the basis of tests performed.

- vii. A copy of Test/ Analysis NIH report was sent to M/s Macter international Limited, F-216, S.I.T.E Karachi Pakistan.

2. Drug Inspector requested to grant permission for prosecution against the above-mentioned accused persons who have contravened the provisions of Section 23/27 of the Drugs Act 1976/DRAP Act 2012 (as amended) and Rules framed there under by the way of: -

- a. **Manufacturing for sale /selling of Substandard Drug**
b. **Issuance of false warranty**

Summary:

Manufacturing Date: 04-2021

Expiry Date: 03-2023

Sampling Date: 07-05-2021

Sent To DTL (Form 6): 08-05-2021

DTL Report Date: 03-07-2021

1ST DI Communication with firm on dated: 12-07-2021

Date of Retesting Request of Firm: 16-07-2021 (NIH substandard on the basis of pH)

Investigation Report Dated: 21-06-2022

3. Show cause notice(s) issued to the accused dated 26-07-2022

Firm's written reply of show-cause notice dated 03-08-2022

With reference to your letter number PQCB /R-454/2021, dated 26-07-2022 received on 01-08-2022 regarding Ultima 125 mg /5ml D/S B. No.1006. Moreover we would like to explain our position as follows.

- NIH report also confirms that pH difference is very minor i.e 0.20. In DTL report pH difference is 0.404. There is difference of 0.204 in results of both labs.
- DTL report shows 114.74 percent potency of active in Batch No. 1006. As per results of DTL, it shows that pH increase of 0.404 has no impact on the stability of drug hence no impact on quality, efficacy and safety.
- This product is taken orally as Sml liquid dose by patient. This 5ml is immediately mixed with 20-100ml gastric juice HCl of pH 1-2 in stomach. So difference of pH in 0.404 in Batch no. 1006 has no impact as drug taken will immediately convert into highly acidic medium.
- Pharmacopeial limit of pH for active clathromycin is 8-10 in USP. It suggests that clathromycin is stable at in pII 5.804 and in finished dry suspension will stable pH 5.804.
- Since we are using taste masked granules. pH limit of taste mask granules 4.5-7.0 (approved in DRAP) as the local source is registered in DRAP. It also indicates that granules and API is stable up to pH7.

We are requesting to PQCB to ignore such trivial difference in pH which has no impact on the quality & efficacy of product and surely not injurious to health. Since we are a quality conscious pharmaceutical company, your support requested in matter which is of trivial nature and have no relevance with the patient may be disposes -off the case instead of retesting, to meet common goal PQCB & Macter to maintain consistent supply of quality drugs.

4. Personal Hearing notice(s) issued to accused person(s)

Case is placed before the Board for Decision

CURRENT PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 7**PQCB/R-771/2021****Tehsil & District Chiniot****ATTENDANCE**

Secretary DQCB	<u>Accused Persons involved in subject case</u>	
Drug Inspector	1. M/s Macter international Limited, F-216, S.I.T.E Karachi through its Chief Operating Officer, Mujeeb Ur Rehman	
	2. Mujeeb Ur Rehman	Chief Operating Officer
	3. Muhammad Zeeshan Khan	Production Incharge
	4. Khalid Irfan	Quality Control Incharge
	5. Muhammad Muzammil Siddiqui	Warrantor
	of M/s Macter international Limited, F-216, S.I.T.E Karachi.	

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Tehsil & District Chiniot reported that: -

- The then drug inspector, on 03-05-2021 inspected the premises of Medicine Store office of the Chief Executive Officer (DHA) District Chiniot, took samples of eight different types of drug samples on Form No. 4 for the purpose of test/analysis and sent the subject drug sample to Drug Testing Laboratory Faisalabad vide memorandum no. 91328 dated 04-05-2021.
- The following drug samples, after test/analyses were declared as **Substandard** by Government Analyst, Drug Testing Laboratory **Faisalabad** as detailed below: -

Name of Drug	Batch No.	Name of Manufacturer	DTL Report	DTL Test Report Result
Suspension. Ultima [When reconstituted as directed each 5ml contains: Clarithromycin USP 125mg (as coated granules 27.5%)] Mfg Date: Apr 2021 Expiry Date: March 2023	1006	M/s Macter international Limited, F-216, S.I.T.E Karachi-Pakistan.	01-68008574/DTL dated 02-07-2021	Results of test/analysis with specifications applied: USP 2021 <u>DESCRIPTION:</u> Off white granular powder (when reconstituted forms white color suspension having pleasant odor), contained in amber colored glass bottle with sealed metallic screw cap, packed in outer hard carton along with leaflet and plastic spoon. <u>IDENTIFICATION:</u> Clarithromycin Identified <u>ASSAY:</u> Stated: 125 mg/ 5ml Determined: 127.674 mg/ 5ml

Regn No.				Percentage: 102.139 % (Complies)
029793				Limit: 90 – 115% (USP 2021)
				pH:
				Limit: 4.0 - 5.4 (USP 2021)
				Determined: 5.73 (Does Not Comply)
				RESULT: Given sample is <u>Sub-Standard</u> , with regards to pH Test.

- iii. Storekeeper of Medicine Store office of the Chief Executive Officer (DHA) District Chiniot, provided invoice/warranty bearing No. 90361178 dated 26-04-2021 issued by M/s Macter international Limited, F-216, S.I.T.E Karachi as a proof of its purchase of the subject drug sample.
- iv. Warrantor portion of subject drug sample was sent to M/s Macter international Limited, F-216, S.I.T.E Karachi.
- v. Copies of Test/ Analyses report was sent to M/s Macter international Limited, F-216, S.I.T.E Karachi with directions to explain their position and provide requisite information in this regard. In response, the firm challenged the test/analysis report and requested to re-test the above-mentioned drug sample from Appellate Laboratory, National Institute of Health, Islamabad.
- vi. Pursuant to the request of M/s Macter international Limited, F-216, S.I.T.E Karachi **the retesting request of the subject drug sample was considered in the 240th-Meeting by the Board held on 15-03-2022, wherein the retesting request of the above-mentioned drug sample was turned down by the Board.**

2. The Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused person(s), who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended), DRAP Act 2012 and Rules framed there under by the way of:

- a. **Manufacture for sale/ Sale of Substandard drug**
- b. **Issuance of false warranty**

3. Show-cause notice(s) issued to accused person(s) dated 29-05-2023

Firm submitted written reply to the show cause notice vide letter no. 1864 Dated 16-06-2023

In this connection we inform you that detailed deliberation have been done with PQCB for the pH control of Ultima 125mg/5ml Dry Suspension. Product Specific Inspection done by PQCB. Their recommendation have been implemented and issue of pH is resolved.

4. Personal hearing notice(s) issued to accused person(s) dated 19-06-2023

5. Case is placed before the Board for decision.

Summary:

Manufacturing Date: March-2021

Expiry Date: Feb-2023

Sampling Date (Form 4): 03-05-2021

Sent to DTL (Form 6): 04-05-2021

Date of receipt in DTL: 06-05-2021

DTL Report Date (Form 7): 02-07-2021

Time Extension: Not Time Barred

1st DI Communication with firm on dated: 12-07-2021

Retesting Request of the Firm: Yes (30-07-2021)

Fate of Retesting Request of the Firm: Turned Down in 240th Meeting dated 15-03-2022

Investigation Report Dated: 24-03-2023

PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 8**PQCB/R-770/2021****Tehsil & District Chiniot****ATTENDANCE**

Secretary DQCB	<u>Accused Persons involved in subject case</u>	
Drug Inspector	1. M/s Macter international Limited, F-216, S.I.T.E Karachi through its Chief Operating Officer, Mujeeb Ur Rehman	
	2. Mujeeb Ur Rehman	Chief Operating Officer
	3. Muhammad Zeeshan Khan	Production Incharge
	4. Khalid Irfan	Quality Control Incharge
	5. Muhammad Muzammil Siddiqui	Warrantor
	of M/s Macter international Limited, F-216, S.I.T.E Karachi.	

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Tehsil & District Chiniot reported that: -

- The then drug inspector, on 03-05-2021 inspected the premises of Medicine Store office of the Chief Executive Officer (DHA) District Chiniot, took samples of eight different types of drug samples on Form No. 4 for the purpose of test/analysis and sent the subject drug sample to Drug Testing Laboratory Faisalabad vide memorandum no. 91327 dated 04-05-2021.
- The following drug samples, after test/analyses were declared as **Substandard** by Government Analyst, Drug Testing Laboratory **Faisalabad** as detailed below: -

Name of Drug	Batch No.	Name of Manufacturer	DTL Report	DTL Test Report Result
Suspension. Ultima [When reconstituted as directed each 5ml contains: Clarithromycin USP 125mg (as coated granules 27.5%)] Mfg Date: March 2021 Expiry Date: Feb 2023 Regn No.	1005	M/s Macter international Limited, F-216, S.I.T.E Karachi-Pakistan.	01-68008573/DTL dated 02-07-2021	Results of test/analysis with specifications applied: USP 2021 DESCRIPTION: Off white granular powder (when reconstituted forms white color suspension having pleasant odor), contained in amber colored glass bottle with sealed metallic screw cap, packed in outer hard carton along with leaflet and plastic spoon. IDENTIFICATION: Clarithromycin Identified ASSAY: Stated: 125 mg/ 5ml Determined: 133.677 mg/ 5ml

029793				Percentage: 106.942 % (Complies) Limit: 90 – 115% (USP 2021) pH: Limit: 4.0 - 5.4 (USP 2021) Determined: 5.64 (Does Not Comply) RESULT: Given sample is <u>Sub-Standard</u> , with regards to pH Test.
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- iii. Storekeeper of Medicine Store office of the Chief Executive Officer (DHA) District Chiniot, provided invoice/warranty bearing No. 90361178 dated 26-04-2021 issued by M/s Macter international Limited, F-216, S.I.T.E Karachi as a proof of its purchase of the subject drug sample.
- iv. Warrantor portion of subject drug sample was sent to M/s Macter international Limited, F-216, S.I.T.E Karachi.
- v. Copies of Test/ Analyses report was sent to M/s Macter international Limited, F-216, S.I.T.E Karachi with directions to explain their position and provide requisite information in this regard. In response, the firm challenged the test/analysis report and requested to re-test the above-mentioned drug sample from Appellate Laboratory, National Institute of Health, Islamabad.
- vi. Pursuant to the request of M/s Macter international Limited, F-216, S.I.T.E Karachi **the retesting request of the subject drug sample was considered in the 240th-Meeting by the Board held on 15-03-2022, wherein the retesting request of the above-mentioned drug sample was turned down by the Board.**

2. The Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused person(s), who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended), DRAP Act 2012 and Rules framed there under by the way of:

- a. **Manufacture for sale/ Sale of Substandard drug**
- b. **Issuance of false warranty**

3. Show-cause notice(s) issued to accused person(s) dated 29-05-2023

Firm submitted written reply to the show cause notice vide letter no. 1864 Dated 16-06-2023

In this connection we inform you that detailed deliberation have been done with PQCB for the pH control of Ultima 125mg/5ml Dry Suspension. Product Specific Inspection done by PQCB. Their recommendation have been implemented and issue of pH is resolved.

4. Personal hearing notice(s) issued to accused person(s) dated 19-06-2023

5. Case is placed before the Board for decision.

Summary:

Manufacturing Date: March-2021

Expiry Date: Feb-2023

Sampling Date (Form 4): 03-05-2021

Sent to DTL (Form 6): 04-05-2021

Date of receipt in DTL: 06-05-2021

DTL Report Date (Form 7): 02-07-2021

Time Extension: Not Time Barred

1st DI Communication with firm on dated: 12-07-2021

Retesting Request of the Firm: Yes (30-07-2021)

Fate of Retesting Request of the Firm: Turned Down in 240th Meeting dated 15-03-2022

Investigation Report Dated: 24-03-2023

PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 9**PQCB/R-769/2021****Tehsil & District Chiniot****ATTENDANCE**

Secretary DQCB	<u>Accused Persons involved in subject case</u>	
Drug Inspector	1. M/s Macter international Limited, F-216, S.I.T.E Karachi through its Chief Operating Officer, Mujeeb Ur Rehman	
	2. Mujeeb Ur Rehman	Chief Operating Officer
	3. Muhammad Zeeshan Khan	Production Incharge
	4. Khalid Irfan	Quality Control Incharge
	5. Muhammad Muzammil Siddiqui	Warrantor
	of M/s Macter international Limited, F-216, S.I.T.E Karachi.	

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Tehsil & District Chiniot reported that: -

- The then drug inspector, on 03-05-2021 inspected the premises of Medicine Store office of the Chief Executive Officer (DHA) District Chiniot, took samples of eight different types of drug samples on Form No. 4 for the purpose of test/analysis and sent the subject drug sample to Drug Testing Laboratory Faisalabad vide memorandum no. 91326 dated 04-05-2021.
- The following drug samples, after test/analyses were declared as **Substandard** by Government Analyst, Drug Testing Laboratory **Faisalabad** as detailed below: -

Name of Drug	Batch No.	Name of Manufacturer	DTL Report	DTL Test Report Result
Suspension. Ultima [When reconstituted as directed each 5ml contains: Clarithromycin USP 125mg (as coated granules 27.5%)] Mfg Date: March 2021 Expiry Date: Feb 2023 Regn No.	1004	M/s Macter international Limited, F-216, S.I.T.E Karachi-Pakistan.	01-68008572/DTL dated 02-07-2021	Results of test/analysis with specifications applied: USP 2021 DESCRIPTION: Off white granular powder (when reconstituted forms white color suspension having pleasant odor), contained in amber colored glass bottle with sealed metallic screw cap, packed in outer hard carton along with leaflet and plastic spoon. IDENTIFICATION: Clarithromycin Identified ASSAY: Stated: 125 mg/ 5ml Determined: 136.321 mg/ 5ml

029793				Percentage: 109.056 % (Complies) Limit: 90 – 115 % (USP 2021) pH: Limit: 4.0 - 5.4 (USP 2021) Determined: 5.62 (Does Not Comply) RESULT: Given sample is <u>Sub-Standard</u> , with regards to pH Test.
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- iii. Storekeeper of Medicine Store office of the Chief Executive Officer (DHA) District Chiniot, provided invoice/warranty bearing No. 90361178 dated 26-04-2021 issued by M/s Macter international Limited, F-216, S.I.T.E Karachi as a proof of its purchase of the subject drug sample.
- iv. Warrantor portion of subject drug sample was sent to M/s Macter international Limited, F-216, S.I.T.E Karachi.
- v. Copies of Test/ Analyses report was sent to M/s Macter international Limited, F-216, S.I.T.E Karachi with directions to explain their position and provide requisite information in this regard. In response, the firm challenged the test/analysis report and requested to re-test the above-mentioned drug sample from Appellate Laboratory, National Institute of Health, Islamabad.
- vi. Pursuant to the request of M/s Macter international Limited, F-216, S.I.T.E Karachi **the retesting request of the subject drug sample was considered in the 240th-Meeting by the Board held on 15-03-2022, wherein the retesting request of the above-mentioned drug sample was turned down by the Board.**

2. The Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused person(s), who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended), DRAP Act 2012 and Rules framed there under by the way of:

- a. **Manufacture for sale/ Sale of Substandard drug**
- b. **Issuance of false warranty**

3. Show-cause notice(s) issued to accused person(s) dated 29-05-2023

Firm submitted written reply to the show cause notice vide letter no. 1864 Dated 16-06-2023

In this connection we inform you that detailed deliberation have been done with PQCB for the pH control of Ultima 125mg/5ml Dry Suspension. Product Specific Inspection done by PQCB. Their recommendation have been implemented and issue of pH is resolved.

4. Personal hearing notice(s) issued to accused person(s) dated 19-06-2023

5. Case is placed before the Board for decision.

Summary:

Manufacturing Date: March-2021

Expiry Date: Feb-2023

Sampling Date (Form 4): 03-05-2021

Sent to DTL (Form 6): 04-05-2021

Date of receipt in DTL: 06-05-2021

DTL Report Date (Form 7): 02-07-2021

Time Extension: Not Time Barred

1st DI Communication with firm on dated: 12-07-2021

Retesting Request of the Firm: Yes (30-07-2021)

Fate of Retesting Request of the Firm: Turned Down in 240th Meeting dated 15-03-2022

Investigation Report Dated: 24-03-2023

PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 10**PQCB/R-624/2021****THQ Hospital Kot Radha Kishan, District Kasur****ATTENDENCE**

Secretary DQCB	<u>Accused Persons involved in subject case</u>
Drug Inspector	1. M/s Macter international Limited, F-216, S.I.T.E Karachi through Chief Operating Officer, Mujeeb Ur Rehman 2. Mujeeb Ur Rehman 3. Zeeshan Khan 4. Khalid Irfan 5. Muzammil Siddiqui Chief Operating Officer Production Incharge Quality Control Incharge Warrantor of M/s Macter international Limited, F-216, S.I.T.E Karachi.

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Tehsil Head Quarter Hospital, Kot Radha Kishan, District Kasur reported that: -

- She, on 07-06-2021 inspected the premises of Main Medicine Store of Tehsil Head Quarter Hospital, Kot Radha Kishan, District Kasur, took sample of subject drug along with other drug sample on Form No. 4 for the purpose of test/analysis and sent to Drug Testing Laboratory Lahore vide memorandum no. 96230 dated 07-06-2021.
- The following drug sample, after test/analysis was declared as **Substandard** by Government Analyst, Drug Testing Laboratory Lahore as detailed below: -

Name of Drug	Batch No.	Name of Manufacturer	DTL Report	DTL Test Report Result
Powder for Suspension. ULTIMA 60ml [Clarithromycin 125mg/5ml] Mfg Date: Apr 2021 Expiry Date: March 2023	1011	M/s Macter international Limited, F-216, S.I.T.E Karachi-Pakistan.	01-73008719/DTL dated 31-07-2021	Results of test/analysis with specifications applied: USP 2021 <u>PHYSICAL DESCRIPTION:</u> WHITE COLOURED GRANULAR POWDER FOR SUSPENSION IN AMBER GLASS BOTTLE WITH A SEALED SCREW CAP AND STOPPER. UPON RECONSTITUTION WITH WATER FORMS WHITE UNIFORM SUSPENSION. <u>pH:</u> Limit: 4.0 - 5.4 Determined: 5.75 at 25.4°C (DOES NOT COMPLY) <u>IDENTIFICATION:</u> The retention time of the

Regn No. 029793				major peak in the sample chromatogram corresponds to the retention time of the major peak in standard chromatogram. (CLARITHROMYCIN IDENTIFIED) <u>ASSAY OF CLARITHROMYCIN:</u> Stated: 125.0 mg/ 5mL Determined: 139.1 mg/ 5mL Percentage: 111.28 % Limit: 90.0 – 115.0 % of stated amount RESULT: The above sample is <u>SUB-STANDARD</u>, on the basis of the pH test performed as per USP.
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- iii. Storekeeper of Main Medicine Store of Tehsil Head Quarter Hospital, Kot Radha Kishan, District Kasur, provided invoice/warranty bearing No. 90364082 dated 25-05-2021 issued by M/s Macter international Limited, F-216, S.I.T.E Karachi as a proof of its purchase.
- iv. Warrantor portion of drug sample was sent to M/s Macter international Limited, F-216, S.I.T.E Karachi.
- v. A copy of Test/ Analysis report was sent to M/s Macter international Limited, F-216, S.I.T.E Karachi with directions to explain their position and provide requisite information in this regard. In response, the firm challenged the test/analysis report and requested to re-test the above-mentioned drug sample from Appellate Laboratory, National Institute of Health, Islamabad.
- vi. Pursuant to the request of M/s Macter international Limited, F-216, S.I.T.E Karachi the retesting request of the subject drug sample was considered in the 240th-M of the Board held on 15-03-2022, retesting request was allowed by the Board and the subject drug sample was sent to NIH, Islamabad, from where the sample was declared as **Sub-standard** as detailed below:

Name of drug	Batch no.	Name of Manufacturer	NIH Report No. & Date	NIH Test Report Results
Suspension Ultima 60ml [Clarithromycin 125mg/5ml]	1011	M/s Macter international Limited, F-216, S.I.T.E Karachi	No. 055-P/2022 dated 6 th May, 2022	Analysis with specifications applied: United States Pharmacopoeia-39 <u>pH:</u> Determined: 6.0 ± 0.06 Limit: 4.0-5.4 Does not Comply with USP-39 <u>CONCLUSION:</u> The sample is of <u>Sub-standard</u> quality on the basis of the tests performed.

- vii. Copy of Test/ Analysis NIH report was sent to M/s Macter international Limited, F-216, S.I.T.E Karachi Pakistan.

2. The Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused person(s), who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended), DRAP Act 2012 and Rules framed there under by the way of:

a. **Manufacture for sale /Sale of Substandard drug**

b. **Issuance of false warranty**

3. Show-cause notice(s) issued to accused person(s) dated 16-03-2022

Firm submitted written reply to the Show Cause Notice vide letter no 1777 dated 15-12-2022

In this connection we request that our case kindly be closed on the basis of following facts, as we are quality conscious manufacturer and assure you that in future our product will be fully compliant.

1. **Slight difference in pH of 0.35** have no impact on shelf life stability as shown that stability studies of our product satisfactory, which also support by Drug Testing Laboratory (the DTL") results.
2. **Assay results of all batches** are still same as at the initial stage.
3. **Shelf life expiry of clarithromycin USP at pH 8-10 is three years** see Certificate of Analysis (the "COA") and United States Pharmacopeia (the "USP) monograph.
4. Shelf life of granules at pH 4 to 7 is three years as per manufacturer, granules of API is registered with DRAP.
5. In use stability studies was conducted for 14 days and found **stable Assay results** and other parameters were found satisfactory well within good limits.
6. As far as the clinical effect **small difference** on basic side has no impact on absorption as the available tablets are at pH 8-10. Buccal cavity pH is more than 6 which can change the pH dose immediately to basic side at 2nd step stomach pH is 1.5 to 3 and third step in intestine pH is 7 plus. Slightly higher pH does not affect the absorption of drug which is negligible as compare to the high variation in pH during natural absorption process.
7. As per discussion with USP officials by mail they don't have privy to the reasoning behind these determination of pH.

In the light of above facts our product is not injurious to heal:' and rot harmful. We worked with the manufacturer of granules and reached to the conclusion and in future they will provide granules of DH less than. Your support is requested in matter which is of trivial nature and has no impact on the having no impact on patient, may be disposed of the case to meet common goal PQCB & Macter to maintain consistent supply of quality drugs. We are looking forward your utmost support in this regard.

4. Personal hearing notice(s) issued to accused person(s) dated 19-06-2023

5. Case is placed before the Board for decision.

Summary:

Manufacturing Date: 04-2021

Expiry Date: 03-2023

Sampling Date (Form 4): 07-06-2021

Sent to DTL (Form 6): 07-06-2021

Date of receipt in DTL: 08-06-2021

DTL Report Date (Form 7): 31-07-2021

Time Extension: Not Time Barred

1st DI Communication with firm on dated: 24-11-2021

Retesting Request of the Firm: Yes (16-08-2021)

Fate of Retesting Request of the Firm: Allowed in 240th Meeting dated 15-03-2022

NIH Test Result: Substandard (Report Date: 06-05-2022)

Investigation Report Dated: 22-10-2022

PROCEEDINGS & DECISION BY THE BOARD:

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DISTRICT DERA GHAZI KHAN

PQCB/R-329/2022Tehsil Dera Ghazi Khan (Urban), District Dera Ghazi KhanATTENDANCE:

Secretary DQCB	<u>Accused Persons involved in subject case</u> 1. M/s Macter International Limited F-216, S.I.T.E., Karachi-Pakistan through its Chief Operating Officer Mujeeb Ur Rehman 2. Mujeeb Ur Rehman Chief Operating Officer 3. Shahid Imtiaz Quality Assurance Manager 4. Khalid Irfan Quality Control Incharge 5. Muhammad Zeeshan Khan Production Incharge 6. Muhammad Muzammil Siddiqui Warrantor Of M/s Macter International Limited F-216, S.I.T.E., Karachi-Pakistan.
Drug Inspector	

BRIEF FACTS OF THE CASE

Provincial Inspector of drugs, Tehsil Dera Ghazi Khan (Urban), District Dera Ghazi Khan reported that:-

- i. He, on 04-01-2022, inspected the premises of Medicine Store, CEO (DHA) office Dera Ghazi Khan and took sample of drug on Form No.04 for the purpose of test/analysis and sent the subject drug sample to Drug Testing Laboratory, Multan vide memorandum No. 0000114921 dated 04-01-2022.
- ii. Following drug sample, after test/analysis, was declared **Substandard** by Government Analyst, Drug Testing Laboratory, **Multan** as detailed below:
- iii. Store Keeper, Medicine Store, CEO (DHA) office Dera Ghazi Khan submitted Invoice/warranty No. 90361407 dated 28-04-2021 issued by M/s Macter International Limited F-216, S.I.T.E., Karachi-Pakistan as a proof of its purchase of the said drug.
- iv. Warrantor Portion of the drug sample was sent to M/s Macter International Limited F-216, S.I.T.E., Karachi-Pakistan and they were asked to provide requisite information in this regard.
- v. A copy of test report was sent to M/s Macter International Limited F-216, S.I.T.E., Karachi-Pakistan and they were asked to provide requisite information in this regard.
- vi. In response, the firm challenged the test/analysis report of the drug sample and requested to re-test the above-mentioned drug sample from Appellate Laboratory, National Institute of Health, Islamabad.
- vii. Pursuant to firm's retesting request the Provincial Quality Control Board in its 246th meeting held on 05-07-2022 after due deliberation and discussion unanimously decided to accept the firm's appeal for withdrawal of the retesting request of the subject drug sample and further directed the Drug Inspector of the concerned area to expedite investigation of the subject case and submit final report for consideration by the Board.

Name of drug	Batch	Name of	DTL Report	DTL Test Report Results
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	No.	manufacturer	TRA No. & Date									
Ultima [Clarithromycin 125mg/5ml (As coated granules 27.5%)] Suspension (After reconstitution) 60 ml. Mfg.date: Apr-2021 Exp. date: Mar-2023 Regn No. 029793	1008	M/s Macter International Limited F- 216, S.I.T.E., Karachi- Pakistan	TRA No. 01- 94001458/DTL Dated:-05-03- 2022	<u>Result of Test/ Analysis with specifications applied:</u> USP 2021 <u>Description:</u> White to Off white granular powder (when reconstituted forms white color suspension), contained in amber colored glass bottle sealed with metallic screw cap, packed in a labeled outer hard carton along with leaflet and plastic spoon. <u>Identification:</u> Clarithromycin Identified. <u>Assay:</u> <table><tr><th>Stated</th><th>Determined</th><th>Percentage</th><th>Limit</th></tr><tr><td>125 mg/5ml</td><td>134.56 mg/5ml</td><td>107.65%</td><td>90-115%</td></tr></table> (Complies) <u>PH:</u> Sated: 4.0-5.4 Determined: 5.85 (Does Not Comply) <u>RESULT:</u> The above ample is declared <u>Sub-Standard</u> , on the basis of <u>PH Test</u> .	Stated	Determined	Percentage	Limit	125 mg/5ml	134.56 mg/5ml	107.65%	90-115%
Stated	Determined	Percentage	Limit									
125 mg/5ml	134.56 mg/5ml	107.65%	90-115%									

2. Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused persons who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended) / DRAP Act 2012 and Rules framed there under by the way of: -

- a. Manufacture for sale/sale of the Substandard drug
- b. Issuance of false warranty

3. Show cause Notice (s) issued to the accused person(s) Dated 13-02-2023.

Reply of the firm to show cause notice vide letter no. Ref No. 1814 dated 21-02-2023:

Reference to the letter No. PQCB/R-329/2022 (the "Letter") Dated February 13, 2023, which is received to us on Dated February 18, 2023. In this connection we request that our case kindly be closed on the basis of following facts, as we are quality conscious manufacturer and assure you that in future our product will be fully compliant.

1. Slight difference in pH of 0.33 have no impact on shelf life stability as shown that a stability studies of our product satisfactory, which also support by Drug Testing Laboratory (the "DTL") results.
2. Assay results of all batches are still same as at the initial stage.
3. Shelf life expiry of clarithromycin USP at pH 8-10 is three years see Certificate of Analysis

(the "COA") and United States Pharmacopeia (the "USP") monograph

4. Shelf life of granules at pH 4 to 7 is three years as per manufacturer, granules of API is registered with DRAP

5. In use stability studies was conducted for 14 days and found stable Assay results and other parameters were found satisfactory well within good limits.

6. As far as the clinical effect is concerned small difference of pH on basic side has no impact on absorption as the available tablets are at pH 8-10. Buccal cavity pH is more than 6 which can change the pH dose immediately to basic side at 2nd step stomach pl is 1.5 to 3 and third step in intestine pll is 7 plus. Slightly higher pH does not affect the absorption of drug which is negligible as compare to the high variation in pH during natural absorption process.

7. As per discussion with USP officials by mail they don't have privy to the reasoning behind

In the light of above facts our product is not injurious to health and not harmful. We worked with the manufacturer of granules and reached to the conclusion and in future they will provide granules of pH less than 5. Your support is requested in matter which is of trivial nature and has no impact on the having no impact on patient, may be disposed of the case to meet common goal PQCB & Macter to maintain consistent supply of quality drugs. We are looking forward your utmost support in this regard.

In this context we are enclosing the required information as directed in your letter, i.e, copies of CNICs of technical staff, copy of Drug Manufacturing License, registration certificate and product specification

4. Personal Hearing notice(s) issued to accused person(s) dated 19-06-2023.

5. Case is placed before the Board for Decision

Summary:

- **Manufacturing Date: 04-2021**
- **Expiry Date: 03-2023**
- **Sampling Date (Form 4): 04-01-2022**
- **Sent to DTL (Form 6): 04-01-2022**
- **Date of receipt in DTL: 10-01-2022**
- **DTL Report Date (Form 7): 05-03-2022**
- **Time Extension: NA**
- **1ST DI Communication with firm on dated: 28-03-2022**
- **Date of Retesting Request of Firm: 04-04-2022**
- **Fate of Retesting: Board decided to accept firm's appeal for withdrawal of retesting request in 246th meeting dated 05-07-2022**
- **Investigation Report Dated: 25-01-2023**

PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 12**PQCB R-689,690,691/2020****Tehsil & District Rahim Yar Khan****ATTENDANCE:**

Secretary DQCB Drug Inspector	<u>Accused Persons involved in subject case:</u> 1. M/s Macter International Limited E-40/A, SITE Karachi through its Chief Operating Officer Mujeeb-ur-Rehman 2. Mujeeb-ur-Rehman Chief Operating Officer 3. Syed Hasnain Raza Kazmi Quality Manager 4. Muhammad Afzal Khan Production Manager 5. Muhammad Shakir Saleem Warrantor of M/s Macter International Limited E-40/A, SITE Karachi.
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BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Tehsil & District Rahim Yar Khan reported that: -

- He, on 22-08-2020 inspected M/s Medicine Store of the District Manager PHFMC District Office, Rahim Yar Khan, and took samples of the following drug samples on Form No. 4 for the purpose of test/analysis and sent to DTL Bahawalpur vide memo no. 0000073875, 0000073876 & 0000073877 dated 22-08-2020.
- Following drug samples, after test/ analysis were declared **Substandard** by Government Analyst, Drug Testing Laboratory, **Bahawalpur** as detailed below:

Sr. No	Name of drug	Batch no.	Name of manufacturer	DTL Report No. & Date	DTL Report Results
	Suspension Co-Amoxi [Amoxicillin as amoxycillin trihydrate: 125mg/5ml, Clavulanic acid as potassium salt: 31.25mg/5ml, 60ml] Mfg. Date: 07-2020	0063	M/s Macter International Limited E-40/A, SITE Karachi.	01-77002257/DTL dated: 22-12-2020	Result Of Test/ Analysis with Specifications Applied: MS/USP 2020 <u>COMPOSITION:</u> When reconstituted as directed each 5ml contains: Amoxycillin as Amoxycillin trihydrate BP....125 Clavulanic acid as Potassium salt BP...31.25mg <u>DESCRIPTION (MS):</u> Light orange to straw color powder in sealed amber glass bottle. Upon reconstitution gives mustard to orange color suspension. (Stated volume: 60ml) (Does not comply with specifications)

1	Exp. Date: 06-2022 Reg. No. 013854				<u>Deliverable Volume (USP):</u> Limit: Avg of 10 NLT 100% Determined: 102.5% <u>pH (USP):</u> Limit.....3.8-6.6 Determined.....7.179 (Does not comply with specifications) <u>IDENTIFICATION (USP)</u> Amoxycillin is identified. Clavulanic acid identified. <u>ASSAY (USP)</u> Amoxycillin Stated 125mg/5ml Determined: 96.89/5ml Percentage: 77.51 % LIMIT: 90-120% Clavulanic acid Stated 31.25mg/5ml Determined: 4.93/5ml Percentage: 15.76 % LIMIT: 90-125% (Does not comply with specifications) <u>RESULT:</u> The sample is <u>Sub-standard</u> on the basis of <u>Physical description, pH test and Assay test.</u>
	Suspension Co-Amoxi [Amoxicillin as amoxycillin trihydrate: 125mg/5ml, Clavulanic acid as potassium salt:	0064	M/s Macter International Limited E-40/A, SITE Karachi.	01-77002258/DTL, dated: 22-12-2020	RESULT OF TEST/ ANALYSIS WITH SPECIFICATIONS APPLIED: MS/USP 2020 <u>COMPOSITION:</u> When reconstituted as directed each 5ml contains: Amoxycillin as Amoxycillin trihydrate BP....125mg

2	31.25mg/5ml, 60ml] Mfg. Date: 07-2020 Exp. Date: 06-2022 Reg. No. 013854				Clavulanic acid as Potassium salt BP...31.25mg <u>DESCRIPTION (MS):</u> Light orange to straw color powder in sealed amber glass bottle. Upon reconstitution gives mustard to orange color suspension. (Stated volume: 60ml) (Does not comply with specifications) <u>Deliverable Volume (USP):</u> Limit: Avg of 10 NLT 100% <u>Determined:</u> 103.83% <u>pH (USP):</u> Limit..... 3.8-6.6 Determined:7.202 (Does not comply with specifications) <u>IDENTIFICATION (USP)</u> Amoxycillin is identified. Clavulanic acid identified. <u>ASSAY (USP)</u> Amoxycillin <u>Stated</u> 125mg/5ml <u>Determined:</u> 78.99/5ml <u>Percentage:</u> 63.19 % LIMIT: 90-120% Clavulanic acid <u>Stated</u> 31.25mg/5ml <u>Determined:</u> 4.90/5ml <u>Percentage:</u> 15.68 % LIMIT: 90-125% (Does not comply with specifications) <u>RESULT:</u> The sample is <u>Sub-standard</u> on the basis of Physical description, pH test and Assay test.
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3	Suspension Co-Amoxi [Amoxicillin as amoxycillin trihydrate: 125mg/5ml, Clavulanic acid as potassium salt: 31.25mg/5ml, 60ml] Mfg. Date: 07-2020 Exp. Date: 06-2022 Reg. No. 013854	0065	M/s Macter International Limited E-40/A, SITE Karachi.	01-77002259/DTL, dated: 22-12-2020	RESULT OF TEST/ ANALYSIS WITH SPECIFICATIONS APPLIED: MS/USP 2020 <u>COMPOSITION:</u> When reconstituted as directed each 5ml contains: Amoxycillin as Amoxycillin trihydrate BP....125 Clavulanic acid as Potassium salt BP...31.25mg <u>DESCRIPTION (MS):</u> Light orange to straw color powder in sealed amber glass bottle. Upon reconstitution gives mustard to orange color suspension. (Stated volume: 60ml) (Does not comply with specifications) <u>Deliverable Volume (USP):</u> Limit: Avg of 10 NLT 100% Determined: 102.3% <u>pH (USP):</u> Limit..... 3.8-6.6 Determined:7.290 (Does not comply with specifications) <u>IDENTIFICATION (USP)</u> Amoxycillin is identified. Clavulanic acid identified. <u>ASSAY (USP)</u> Amoxycillin Stated 125mg/5ml Determined: 104.51/5ml Percentage: 83.61 % LIMIT: 90-120 % Clavulanic acid Stated 31.25mg/5ml Determined: 4.48/5ml Percentage: 14.32%
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					LIMIT: 90-125% (Does not comply with specifications) RESULT: The sample is Sub-standard on the basis of <u>Physical description, pH test and Assay test.</u>
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- iii. M/s Medicine Store of the District Manager PHFMC District Office, Rahim Yar Khan provided invoice/ Warranty No. 90326397 dated 18-07-2020 issued by M/s Macter International Limited E-40/A, SITE Karachi.
- iv. Warrantor Portion of each of the drug sample was sent to M/s Macter International Limited E-40/A, SITE Karachi dated 26-08-2020.
- v. Copies of Test/ Analysis reports were sent to M/s Macter International Limited E-40/A, SITE Karachi and they were directed to provide requisite information in this regard. In response, the firm requested for retesting of sample drug in question from Appellate Laboratory/ NIH Islamabad. **The subject retesting request of the subject drug samples were turned down in 19th Committee meeting of PQCB dated 21-10-2021.**

2. Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused persons who have contravened the provisions of Section 23/27 of the Drugs Act 1976 and Rules framed there under by the way of: --

- i. **Manufacture for Sale / Sale of Substandard Drugs.**
- ii. **Issuance of false warranty.**

Summary: R-689,690,691/2020

Manufacturing Date: 07-2020

Expiry Date: 06-2022

Sampling Date: 22-08-2020

Sent to DTL (Form 6): 22-08-2020

Date of receipt in DTL: 28-08-2020

DTL Report Date: 22-12-2020

Time Barred report: 117days

Time extension: -

1ST DI Communication with firm on dated: 18-01-2021

Date of Retesting Request of Firm: 29-01-2021

Fate of Retesting Request: Turn down in 19-CM dated 21-10-2021

Investigation Report Dated: 29-08-2022

3. Show cause notice(s) issued to the accused persons

Firm submitted Written reply to show cause Notice vide letter vide dated 29-10-2022

We acknowledge the receipt of your letter No. PQCB/P-689,690,69 1 /2020, dated 26-09-2022 received by us on October 24, 2022 for Co-Amoxi (Co-Amoxiclav) DS 156.25mg/5ml B# 0063, 0064, 0065. Moreover we would like to explain our position. Please consider following facts.

1. Batch No. 0063:

- a. DTL Lahore tested B # 0063 as per USP monograph on samples collected from Nankana sahib in which results found satisfactory and our product batch is declared as of standard quality. However, sample of the same B#0063 was declared sub-standard by DTL Bahawalpur on samples collected from Rahim Yar Khan. It clearly indicates that batch is of fine quality. We have observed that DTL Lahore reported satisfactory results of B#0063 after 27days from sample receipt, while DTL Bahawalpur reported unsatisfactory results of same batch **after 3months 23 days from sample** receipt. It seems that at DTL Lahore samples stored under controlled condition. While in DTL Bahawalpur samples might kept at Lab environment for so long under uncontrolled condition as our product is temperature sensitive and should be stored under controlled condition at 25C it can be potential reason for product failure in one of DTL.
- b. Warrantor samples of substandard B#0063 collected from Rahim Yar Khan on 22.08.2020 and reached to us on 21.01.2021 (after 5 months), we have tested samples on 27.01.2021 and found of standard quality.

2. Batch No 0065:

- a. DTL Lahore tested B#0065 twice as per USP monograph on samples collected from different location Sheikhpura and Nankana sahib in both results found satisfactory and our product batch is declared as of standard quality. However, sample of the same B#0065 was declared sub-standard by DTL Bahawalpur on samples collected from Rahim Yar Khan. It clearly indicates that batch is of fine quality. We have observed that DTL Lahore reported satisfactory results of B/0065 after 14 days and 27days respectively from sample receipt, while DTL Bahawalpur reported unsatisfactory results of same batch after 3months 23days from sample receipt. It seems that at DTL Lahore samples stored under controlled condition. While in DTL Bahawalpur samples might kept at Lab environment for so long under uncontrolled condition as our product is temperature sensitive and should be stored under controlled condition at 25C it can be potential reason for product failure in one of DTL.
- b. Warrantor samples of substandard B#0065 collected from Rahim Yar Khan 22.08.2020 and reached to us on 21.01.2021 (after 5months), we have tested samples on 27.01.2021 and found of standard quality.

3. Batch No 0064:

- a. We have observed that DTL Bahawalpur reported unsatisfactory results of B#0064 after 3months 23days from sample receipt. It seems that at DTL Bahawalpur samples might kept at Lab environment for so long under uncontrolled condition as our product is temperature sensitive and should be stored under controlled condition at 25C it can be potential reason for product failure.
- b. Warrantor samples of substandard B#0064 collected from Rahim Yar Khan on 22.08.2020 and reached to us on 21.01.2021 (after 5months), we have tested samples on 27.01 .2021 and found of standard quality.

Moreover, we are sending you annual product review of all the batches of Co-Amoxi DS 156.25mg/5ml that have been manufactured in 2020. Through which you can verify that our product results are consistent.

Case is placed before the Board for Decision

PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 13**PQCB/R-612,613,614, 615/2019****Tehsil & District Rahim Yar Khan****ATTENDENCE**

Secretary DQCB Drug Inspector	<u>Accused Persons involved in subject case</u> 1. P.D.H. Laboratories (Pvt) Ltd. 9.5 Km, Sheikhpura Road, (Khaki) Lahore-Pakistan through its Managing Director, Mian Mohsin Ilyas 2. Mian Mohsin Ilyas Managing Director 3. Muhammad Akhtar Quality Control Manager 4. Abida Dilawar Production Incharge/Warrantor of M/S P.D.H. Laboratories (Pvt) Ltd. 9.5 Km, Sheikhpura Road, Lahore-Pakistan
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BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Tehsil & District Rahim Yar Khan reported that: -

- His predecessor, on 13-06-2019 inspected the Medicine Store of the District Manager PHFMC District Office Gulshan e Ravi Rahim Yar Khan, and took samples of the subject drugs on Form No. 4 for the purpose of test and analysis.
- The drug samples, after test/analysis were declared as **Substandard** by Government Analyst, Drug Testing Laboratory, **Bahawalpur** as detailed below: -

Name of Drug	Batch No.	Name of Manufacturer	DTL Report	DTL Test Report Result
Injection Dolnot [Diclofenac Sodium 75 mg/3 mL]	DT-0958	P.D.H. Laboratories (Pvt.) Ltd., 9.5 Km, Sheikhpura Road, Lahore-Pakistan.	01-65002096/DTL dated: 31Jul 2019	Result of test/ analysis with specifications applied MS/USP 2018 <u>COMPOSITION</u> Each 3ml contains: Diclofenac Sodium75mg <u>DESCRIPTION (MS)</u> Colorless solution in sealed glass ampoule. Visible particulate matter is seen in 06 ampoules out of 20 ampoules with naked eye. (Does not comply with the parenteral specifications). <u>VOLUME:</u>

				Limit: -----3.0-3.2 ml Determined: -----3.0 ml pH: Limit: -----8.0-10.5 Determined: -----8.341 <u>STERILITY:</u> The product is sterile. <u>IDENTIFICATION:</u> _____ Diclofenac Sodium is identified. <u>ASSAY</u> Diclofenac Sodium Stated: 75mg/3ml Determined: 81mg/3ml Percentage 108.002% LIMIT: 90-110% <u>RESULT:</u> The sample is declared <u>Sub-standard</u> on the basis of Physical Test.
Injection Dolnot [Diclofenac Sodium 75 mg/3 mL]	DT-0959	P.D.H. Laboratories (Pvt.) Ltd., 9.5 Km, Sheikhpura Road, Lahore-Pakistan.	01-65002097/DTL dated: 31Jul 2019	Result of test/ analysis with specifications applied MS/USP 2018 COMPOSITION Each 3ml contains: Diclofenac Sodium75mg DESCRIPTION (MS) Colorless solution in sealed glass ampoule. Visible particulate matter is seen in 02 ampoules out of 20 ampoules with naked eye. (Does not comply with the parenteral specifications). VOLUME:

				Limit: -----3.0-3.2 ml Determined: -----3.0 ml pH: Limit: -----8.0-10.5 Determined: -----8.139 STERILITY: The product is sterile. IDENTIFICATION: Diclofenac Sodium is identified. ASSAY Diclofenac Sodium Stated: 75mg/3ml Determined: 77.068mg/3ml Percentage 102.76% LIMIT: 90-110% RESULT: The sample is declared <u>Sub-standard</u> on the basis of Physical Test.
Injection Dolnot [Diclofenac Sodium 75 mg/3 mL]	DT-0960	P.D.H. Laboratories (Pvt.) Ltd., 9.5 Km, Sheikhpura Road, Lahore-Pakistan.	01-65002098/DTL dated: 31Jul 2019	Result of test/ analysis with specifications applied MS/USP 2018 COMPOSITION Each 3ml contains: Diclofenac Sodium75mg DESCRIPTION (MS) Colorless solution in sealed glass ampoule. Visible particulate matter is seen in 06 ampoules out of 20 ampoules with naked eye. (Does not comply with the parenteral specifications). VOLUME:

				Limit: -----3.0-3.2 ml Determined: -----3.0 ml pH: Limit: -----8.0-10.5 Determined: -----8.278 STERILITY: The product is sterile. IDENTIFICATION: Diclofenac Sodium is identified. ASSAY Diclofenac Sodium Stated: 75mg/3ml Determined: 77.99mg/3ml Percentage 103.99% LIMIT: 90-110% RESULT: The sample is declared <u>Sub-standard</u> on the basis of Physical Test.
Injection Dolnot [Diclofenac Sodium 75 mg/3 mL]	DT-0961	P.D.H. Laboratories (Pvt.) Ltd., 9.5 Km, Sheikhpura Road, Lahore-Pakistan.	01-65002099/DTL dated: 06 Aug 2019	Result of test/ analysis with specifications applied MS/USP 2018 COMPOSITION Each 3ml contains: Diclofenac Sodium75mg DESCRIPTION (MS) Colorless solution in sealed glass ampoule. Visible particulate matter is seen in 04 ampoules out of 20 ampoules with naked eye. (Does not comply with the parenteral specifications).

				VOLUME: Limit: -----3.0-3.2 ml Determined: -----3.0 ml pH: Limit: -----8.0-10.5 Determined: -----8.274 STERILITY: The product is sterile. IDENTIFICATION: Diclofenac Sodium is identified. ASSAY Diclofenac Sodium Stated: 75mg/3ml Determined: 74.98mg/3ml Percentage 99.98% LIMIT: 90-110% RESULT: The sample is declared Sub-standard on the basis of Physical Test.
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- iii. The District Manager PHFMC Rahim Yar Khan provided invoice/ warranty bearing No. 2019-05-01336 dated 29-05-2019 issued by M/s P.D.H Laboratories (Pvt.) Ltd. 9.5 Km Sheikhpura Road Lahore.
- iv. Warrantor Portion was sent to M/s P.D.H Laboratories (Pvt.) Ltd. 9.5 Km Sheikhpura Road Lahore.
- v. A copy of Test/ Analysis report was also sent to M/s P.D.H Laboratories (Pvt.) Ltd. 9.5 Km Sheikhpura Road Lahore and they were directed to provide requisite information in this regard.

PREVIOUS PROCEEDINGS REGARDING RE-TESTING REQUEST:

216th Meeting dated 28-12-2019

1. The subject request for retesting of the drug sample was considered by the Provincial Quality Control Board (PQCB) under section 22 of the Drugs Act 1976 in its **216th** meeting held on **28-12-2019**.
2. The Quality Control Manager (Name not mentioned) of the firm appeared before the Board to defend/justify

the firm's position. He said that the firm had not received any warrantor portion to date. The PQCB had dropped a similar case of M/s Trigon Pharma on the basis of warrantor portion not received, and the same may be done in the instant case. Further that the case should be placed in full board instead of a committee constituted by the PQCB, which has no legal standing. Further that the judgment passed by the Honorable High Court in Lasani case is self-evident. Moreover, the firm had not submitted any request for re-testing; instead, their intention was to request to drop the case, as they had not received any warrantor portion.

3. The Board after detailed discussion and deliberations decided that the subject requests for re-testing be **Turn Down** due to following reasons;
 - a. The representative of firm expressed during personal hearing that they were not interested to re-test the sample. Further at this stage the proceedings in the case are according to section 22(4) and 22(5) of Drugs Act i.e. for the retesting of the drug by the Appellate Laboratory.
 - b. The evidence submitted by the firm was not satisfactory (100% optical checking not performed).
 - c. The Board honors the decision of Court of Law and has gone in an Inter-Court Appeal in the mentioned case by the firm representative.
 - d. The case of particulate matter may be life threatening; Particulate matter can result in severe consequences, such as vein irritation, anaphylactic shock, phlebitis, pulmonary emboli, pulmonary granulomas, immune system dysfunction, pulmonary dysfunction, infarction, and death. The Board was of the opinion that it is quite possible that some of the ampoules may contain particles while others do not as it is evident from the evidences submitted by the manufacturer itself. In the circumstances the patient's health will be at risk if the samples would be declared of standard quality by the NIH lab.
4. The Board further decided to direct the Drug Inspector concerned to expedite investigation in subject case and submit final report for consideration by the Board.
5. The Board further directed that:
 - a. Regulatory recall of subject batch of the drug through the firm, monitored by the Chief Drug Controller Office may be done under The Drugs Act 1976 and rules framed thereunder. Recall will be conducted at Level 2 i.e., from market, distributors, hospitals and retailers.
 - b. Provincial Government may advertise Public Awareness Notice through newspaper regarding recall of concerned batches of drug.
 - c. Company will also carry out the comprehensive investigation regarding failure of the drug to comply with specifications, at its own level and submit root cause analysis report.

Firm vide letter no. PDHL/D&RA/20/0702 dated 13-07-2020 submitted documents related to

- i. optical checking of subject batches of Dolnot Injection
- ii. SOP for optical inspection of liquid injections.
- iii. Product recall advertisement.
- iv. Optical checking reports.

2. Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused persons who have contravened the provisions of Section 23/27 of the Drugs Act 1976(as amended)/DRAP Act 2012 and Rules framed there under by the way of: --

- i. **Manufacture for Sale / Sale of Sub-standard Drug.**
- ii. **Issuance of false warranty.**

<u>Summary:</u> <u>R-612/2019</u>	<u>Summary:</u> <u>R-613/2019</u>	<u>Summary:</u> <u>R-614/2019</u>	<u>Summary:</u> <u>R-615/2019</u>
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Manufacturing Date: 02-2019	Manufacturing Date: 05-2019	Manufacturing Date: 05-2019	Manufacturing Date: 05-2019
Expiry Date: 01-2022	Expiry Date: 04-2022	Expiry Date: 04-2022	Expiry Date: 04-2022
Sampling Date: 13-06-2019	Sampling Date: 13-06-2019	Sampling Date: 13-06-2019	Sampling Date: 13-06-2019
Sent to DTL (Form 6): 13-06-2019	Sent to DTL (Form 6): 13-06-2019	Sent to DTL (Form 6): 13-06-2019	Sent to DTL (Form 6): 13-06-2019
Received in DTL: 18-06-2019	Received in DTL: 18-06-2019	Received in DTL: 18-06-2019	Received in DTL: 18-06-2019
DTL Report Date: 31-07-2019	DTL Report Date: 31-07-2019	DTL Report Date: 31-7-2019	DTL Report Date: 06-08-2019
1ST DI Communication with firm on dated: 17-8-2019	1ST DI Communication with firm on dated: 17-8-2019	1ST DI Communication with firm on dated: 17-8-2019	1ST DI Communication with firm on dated: 17-8-2019
Date of Retesting Request of Firm: 29-08-2019	Date of Retesting Request of Firm: 29-08-2019	Date of Retesting Request of Firm: 29-08-2019	Date of Retesting Request of Firm: 29-08-2019
Investigation Report Dated: 19-11-2020	Investigation Report Dated: 19-11-2020	Investigation Report Dated: 19-11-2020	Investigation Report Dated: 19-11-2020

3. Show-cause notice(s) issued to accused person(s) dated 12-01-2021

Firm's Reply of Show cause notice vide letter no. PDHL/D&RA/20/1119 dated 02-02-2021

The following submissions are made

1. That the request for Retesting of all the above samples from the NIH - Appellate Laboratory Islamabad was submitted vide No.PDH.04/S-PQC3-2019/RT Dated 25.11.2019. This request along with evidence in controversion to reports was considered by the PQCB, Punjab, Lahore n is meeting held on 25.11.2019. It was pointed out that Quorum of POCB meeting was not Nevertheless, the company was advised to submit arguments. The issue of Retesting was discussed in detail. The decision of this hearing has never been conveyed to the company. The issuance of SCN without final decision on the issue of Retesting. The copy of Retesting Request Letter No.PDH.04/S-PQCB-2019/RT Dated 25. 11. 2019 may please be taken as part of this reply to SCN This PQCB meeting was unlawful because in violation of the Rule 5 (4) of the Punjab Drug Rules 2007 (Amendment Upto 2017)
2. That Ms PDH Laboratories (Pvt) Ltd 95 Km Sheikhpura Road, (Khaki) Lahore is an ISO 9001- 2015, 14001-201 by encompassing the "Good Manufacturing Practice" (GMP) throughout the process manufacturing, been incorporated with 5 & 18001-2007 Certified company &

guarantee manufacturing of genuine & stable medicines the world's leading Multinational Pharmaceuticals Companies like Farmitalia Carroerba, UCB, in their Hi-tech products. PDH Laboratories (P) Ltd has a vast experience of more than 70 years in the field of manufacturing pharmaceutical products. The doctors actively advise our brands because they trust on the quality and standard of our products. The company never compromises on the quality, which is its corporate vision and organization's culture. We firmly believe in the purity of individual ingredients/items used to manufacture our Products. ZERO DEFECT QUALITY' has been adopted as a part of our QUALITY PHILOSOPHY

3. That prior to release formatting / sale of the batches of all the drugs manufactured the well equipped QC Lab of the company in accordance with approved methods. PDH is determined to contribute towards the health care sector by providing pharmaceuticals of highest quality standards while making them affordable to all human lives. We intend to complo this ambition by exercising true discipline, professionalism & human value Corporate Social Responsibility (CSR) is one of our core values and an integral part of Company's overall vision. Through various ventures in philanthropy, and public awareness, we have historically made significant contributions in the area of corporate social responsibility.

4 That the company has great respect with highest possible level of compliance to all the prevailing low regulating Pharmaceutical Industry and has always worked within the legal framework of the DRAP Act 2012, The Drug Act 1976 and Rules framed thereunder in order to ensure delivery of high quality effective and safe drugs to the patients Regulatory legal advices related to uplifting quality and safety of medicines are always welcome with 100% compliance.

5. That without prejudice to the case and despite having reservation on the legality of proceeding of the case and in-conclusive test/analysis report, the company had agreed to the proposal of Mr. sohail then, AS-DC/VCPOCB, if the company would recall the Batches, there would be no prosecution. The company has already recalled all the batches of inj, DOLNOT (Diclofenac Sodium 75MG/ML).

6. That M/s PDH Laboratories (P.) Ltd. 9.5km Sheikhpura Road, Lahore had supplied in Doint B NO. DT-0958 Inj Dolnot No DT-0959 inj Dolnot B No DT-0960, INJ. Dolnot NO OT-0961 to Medicine Stores of District Manager, PHFMC, Gulshan E Ravi Rahim Yar Khan vide BE Warranty No. 2019-05-01336 Dated 29.05 2019 Subsequently, Di The & Dist Rahim Yar Khan had taken and sent the samples of these drugs to the Government Analyst Drug Testing Laboratory, Bahawapur for the purpose of test / analysis. The Director, DTL, Bpur forwarded the reports of Government Analyst Bahawalpur to De which were subsequent sent to the company.

7. That perusal of the Table 1 shows in a crystal-clear manner that all the four sample of drug Inj. Dolnot B NO. DT-0958 Inj. Dolnot B No. DT-0959 Dolnot B No DT-0960 Inj. Dolnot B. No. DT-0961 are standard quality because the therapeutically active substance Diclofenac Na has been determined as 108.002%, 102.76% 103.99% and 99.98 % within the approved LIMIT: 90-110%. All other tests are also in compliance to the approved standard. A drug could not be declared as substandard when it meets the chemical specification". Reliance on DB Judgment of honorable Lahore High court reported as 19.92 M L D 481. The Government Analyst has declared these sample erroneously substandard on the basis of so called Visible Particulate matter. It appears that Government Analyst, Drug Testing

Laboratory Bahawalpur is unacquainted about the land mark historic judgment of Division Bench of Lahore High court in Intra-Court Appeals Nos. 127 and 128 of 1989, decided on 28th October, 1991reported in 1992 MLD 481 whereby holding that 'A drug could not be declared as substandard when it meets the chemical specifications. The para 6 of this Judgment is crystal clear in this regards. The DB Judgment of Peshawar High court also held that drug could not be declared substandard on the basis of particle and report without protocol was fatally defective 1996 P Cr.L.J 1183 (Peshawar).

That Government Analyst determined that the above sample was up to the Standard Quality as assay of drug was within the standard quality limit. However, he has declared this drug erroneously substandard based on vague expression

Visible Particulate Contamination'

Particulate matter in injections and parenteral infusions consists of extraneous mobile undissolved particles other than gas bubbles, unintentionally present in the solutions. Similarly, products that produce air or gas bubbles when drawn into the sensor may also require microscopic particle count testing. There are basically two tests, light obscuration, which uses light blockage to determine the size and count of particulate matter in the solution and microscopic assay, which is a measurement of un-dissolvable particles or substances present in the solution – usually plastics, metals or dust. There are basically two tests, light obscuration, which uses Light blockage to determine the size and count of particulate matter in the solution; and microscopic assay which is a measurement of un-dissolvable particles or substances present in the solution-usually plastics, Particles of varying sizes have been observed in inject-able drug products, such as visible and sub visible. The particles of 1-50 Micron size are known as sub visible particles and particles of >50 micron are considered as visible particles,

Visible particles are defined as those that can be detected under controlled conditions by the unaided human eye i.e., without supplemental magnification). Identification of the composition of the particulate matter is the first step in characterizing particulate matter risk. Based on this information, particles can be further classified into one of three subcategories. extrinsic, intrinsic, and inherent

a) **Extrinsic** particles are defined as those that are not part of the formulation, package, or process, but are foreign and unexpected. Examples of extrinsic particles include fibers (e.g., cellulous), clothing fragments, hair, rubber, metal, plastic, and paint

b) **Intrinsic** particles are defined as those that arise from sources related to the formulation, packaging, or processes. Examples of intrinsic particle materials include glass, stainless steel, rubber from stoppers, and gasket material

c) **Inherent** particles are defined as materials that are expected from the drug formulation, and thus represent generally accepted characteristic of the product. Examples of inherent matter Proteinaceous aggregates metals or dust.

7. That the crucial question for legality of similar reports was evaluated in depth by honorable Division Bench of honorable Lahore High Court in case of Provincial Quality Control Board v. Irza Pharma reported as 1992 MLD 481. The definitions of "Adulterated drug", Spurious and Substandard Drug as given in Section 3of the Drug Act 1976 were examined. It was held

A That if the samples taken conform to the stated specifications chemically do not fall within the definition of the substandard drugs.

B. That the learned single Judge rightly held the term substandard drug with particles is not known to the Drugs Act, and that is true.

C. There was nothing on the record to show, as to what is the nature of the particles found in the samples, and what are its consequences? (Whether Injurious to health).

D. That Analyst's report in question, when considered within meaning of the definitions of "Adulterated drug" Spurious and Substandard Drug as given in Section 3 of the Drug Act 1976, the drugs tested and reported, fell outside the category of definitions of Substandard Spurious and Adulterated drugs The para 8 of the above Judgement is reproduced as From the aforesaid definition, it is evident that the Law Makers have taken note of the eventualities implications and the nature off the manufacturing of the drugs while making the law. Hence, the law and its intension, as envisaged by the Drugs Act is very sacred and clear. Unfortunately, in our country functionaries

under the law misuse the same, which is nothing but malice in law. Can we allow course to perpetuate so as to leave room for rampant corruption. The obvious answer is in the negative. On the other hand, this Court under its Constitutional jurisdiction, as enjoined by the Constitution has to protect the observance of law as well as the bona

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relevant observations are added as hereunder. -"Under the Constitution of Pakistan, a wholly different state of affairs prevails. Power is expressly given by Article 98 to the Superior Court to probe into the exercise of public power by executive authorities, how high so ever, to determine whether they have acted with lawful authority. The judicial

power is reduced to a nullity if laws are so worded or interpreted that the executive authorities may make what statutory rules they please thereunder and may use this freedom to make themselves the final judges of their own 'satisfaction' for imposing restrains on the enjoyment of the fundamental rights of citizens. Article 2 of the Constitution could be deprived of all its content through this process and the Courts would cease to be guardians of the nation's liberties.

"THE CLINICAL IMPLICATIONS of extraneous particulate matter in injections are determined by many factors, including the size and number of particles, the composition of material, the potential for microbiological contamination, the route of administration, the intended patient population, and the clinical condition of the patient. For example, an otherwise healthy individual receiving a subcutaneous or intramuscular injection containing sterile, inert particulates would likely experience no adverse effect or at worst would develop a small granuloma.

On the other hand, a critically ill premature infant receiving a particle-laden infusion directly through an umbilical catheter might suffer considerable pathophysiologic sequelae.

9. That full protocols the test applied to reach the conclusion and issue Result of disputed drug as substandard have not been given in the Test Report No. 01-57000476 DTL dated 24 March 2020 That Reports of Analyst has to be conclusive and must disclose the tests applied to formulate opinion of Government Analyst. There is always likelihood of errors in Tests! analysis report, which would be of adverse consequence and definitely affects substantial rights of a person. Therefore, the description of the experiment including method evaluating standards /results must be Crystal clear whenever report would be disputed. Reliance on PLD 2003 Lah. The honorable Single Judge relied on these judgments in the reported cases- Gyanendra Nath Mittal v. State AIR 1959 Al 634; S. Dutta and another.

Test Visible Particulates in Injections is intended to be applied to product that has been 100% inspected as part of the manufacturing process. Injections shall be clear and free from visible particulates when examined without magnification (except for optical correction as may be required to establish normal vision) against a black background and against a white background with illumination that at the inspection point has an intensity between 2000 and 3750 lux. This may be achieved through the use of two 15-W fluorescent lamps (e.g., F15/T8). The use of a high-frequency ballast to reduce flicker from the fluorescent lamps is recommended. Higher illumination intensity is recommended for examination of product in containers other than those made from clear glass. The method is described as "Remove any adherent labels from the container and wash and dry the outside. Gently swirl or invert the container, ensuring that air bubbles are not introduced, and observe for about 5 s in front of the white panel. Repeat the procedure in front of the black panel. Record the presence of any particles. Appendix XIII B. Particulate Contamination: Visible Particles. apprehended that Government Analyst did apply this method.

The name of Government Analyst is not mentioned on the reports that raises doubts regarding appointment of Gazette Notified Government Analyst as per requirement of section 16 of the Drug Act 1976.

The honorable Supreme Court has held in case reported as 2019 SCM 930 "Report of the Government Analyst must contain Protocol. The term "protocol has not been defined in the Rules. Its dictionary meaning is "A plan of scientific experiment or other procedure. It is also referred to as the precise method for carrying out or reproducing a given experiment. These definitions are in line with the elaboration of the term "protocol" given in Imam Bakhsh wherein the Court stated the expression protocol to mean an explicit plan of an experiment, procedure or test. It is clarified that "protocol" is, therefore, a recognized standard method or plan for carrying out the test applied to ascertain the nature of the substance under examination No test can take place without a protocol. The

Report of the Government Analyst must show that the test applied was in accordance with a recognized standard protocol. Any test conducted without a protocol loses its reliability. And evidentiary value. Therefore, to serve the purposes of the Act and the Rules, the Report of the Government analyst must contain (i) The Tests Applied (ii) the protocols applied to carry out These Tests (iii) The Result of the tests

10 That without ascertaining the nature, composition, composition and foreign source of particle, it is not possible to ascertain whether particulate matter allegedly observed by the Government Analysis Is injurious to Health as a consequence of degradation product of Diclofenac Na or a Foreign Particle coming from the environment during manufacturing process of injection or is the product of intersection between active and pharmaceutical necessities or some other source. The myths and realities about clinical correlation between alleged visible particulate matter and ADR would be explained before the PQCB if allowed during statutory personal hearing. The presence of particulate matter in injection has never been defended by the company because of Potential as well as Actual Clinical Risk + Harm +ADR. However, misuse of Particulate Matter as a Tool of Victimization is always resisted, opposed and defended.

11. That no Pre-Show Cause Notice (SCN) scrutiny done and SCN issued in violation of rule 5. (3) The Punjab Drugs Rules, 2007 is illegal. This mandatory scrutiny would have done Justice with the applicant who has been dragged in the process of malicious prosecution. The rule reproduced as

"The PQCB shall examine a case referred to it by an Inspector and shall, if an action is proposed to be taken against a person under the Act or the rules issue a show cause notice to the person and provide him an opportunity for hearing before taking the action about the prosecution of the person or recommending suspension or cancellation of his license to the licensing authority."

12. That the author of the SCN has not mentioned date of dispatch/receipt of Warrantor portion in Para-iv due to reason bets known to him. The Warrantor's portion has not been sent to the manufacturer within statutory period of seven days as prescribed under section 19 (3) (iv) of the Drugs Act 1976. The non observance to said procedure is highly doubtful and is an illegality. Recently, the PQCB has unanimously dropped a Caso No POCB R-577-9/2016 related to infusion Dorcip Batch No Dc-075 declared as Adulterated and Substandard by Government Analyst Drug Testing Laboratory Rawalpindi vide OTL Report TRA No. 10777/TL od 22-09-2016. The PQCB had observed that this case was fit for prosecution on the basis of report. However, this case was DROPPED because warrantor portion was not sent to the manufacturer within statutory period as prescribed under Section 19 (3) of the Drug Act 1976.

13. That the para 2 of the SCN is vehemently denied as company has not contravened any provision of the Drug Act 1976/ORAP Act 2012 as evident from the following facts and law

i. The company has contravened section 24/27 of the Drug Ad 1976 (as amended the DRAP act 2012 and Rules framed thereunder. The case is based upon the Conclusive Report of Government Analyst, as sufficient in controversion to this report is available as per requirement of section 22/4 of the Drug Act 1976, 2017 of the Drug Act 1976 is maliciously applied by omitting the specifications, 23(1) (a-I-x, b-h, I0i-ii and (27-1) (27-2), (27-3) and (27-4). The Punjab Amendment in the Drug Act 1976 and DRAP Act 2012 not applicable simultaneously on this case because the Drug Act 1976 which is the part of Schedule VI of DRAP Act 2012 is different from the Drug Act 1976 with Punjab Amendment 2017/2018.

ii. The charge of Issuance of false warranty is based upon misreading of relevant law. The warranty was issued after release of standard quality report by Quality Control Department of the company. The offence of issuance of false warranty is added to enhance punishment with malafide intention.

iii. The application of the Section 27(2) dealing with false warranty is malice in law as well as malice in fact because good and sufficient reason were available as warranty was given after release of medicines by Quality Control Department of the Company. The section 27 (2).(b) is reproduced below

27 (2) whoever himself or by any other person on his

(a) Or

(b) gives to the purchaser a false warranty in respect of any ang sold by him that the drug does not in any way contravene the provisions of section 23 and is not able to prove that, when he gave the warranty, he had good and sufficient reason to believe the same to be true.

14. That the para 3 of the SCN is responded -"The company does not agree with all the names nominated by the Inspector who has acted mechanically while using long handle of Discretion in ascertaining name of Mian Mohsen Ilyas, Managing Director as accused in disrespect the section 11 & 34 of the Drugs Act 1976 and Rule 5 of the Punjab Drug Rules 2007. He is not directly related to the issues under consideration as all routine operations are done without his prior knowledge and consent The Honorable Supreme Court of Pakistan has settled the question of liability related to the company in a case reported as PLD 1978 Supreme Court 193 (Superintendent of Police, Federal Investigation Agency, Lahore and another --Appellants Versus Akhtar Hussain Bhutta-----Respondent). Therefore, it would be difficult to presume that the respondent was guilty of the manufacture of the said substandard drug for and on behalf of the Company, just because he happened to be its Managing Director. Similarly, name of Muhammad Akhtar as Quality Control In-charge has been unlawfully included / ascertained for prosecution by Drug Inspector for the offences of Manufacturing / Sale of Substandard and issuance of False Warranty. Because manufacturing and Quality Control Department are Distinct and independent. The definition of manufacture under section 3 of the Drugs Act 1976 is reproduced below as reference

3(r) "manufacture", in relation to a drug, means all operations involved in the production of the drug, including processing, compounding, formulating, filling, packing, repacking, altering, ornamenting, finishing and labelling with a view to its storage, sale and distribution, but does not include the compounding and dispensing or the packing of any drug in the ordinary course of retail business or on a prescription of a registered medical practitioner or dentist or of a veterinarian and to manufacture' shall be construed accordingly.

The rule 16 (e) of Drugs (Licensing, Registering and Advertising) Rules, 1976 dealing with Conditions for the grant or renewal of licence to manufacture drugs by way of formulation reproduced below

16 (e) The Quality Control Department shall be independent of the manufacturing unit and its Incharge shall be whole time employee of the manufacturer and shall possess a degree in pharmacy, or a degree in science with chemistry or a degree in medicine or pharmacology for pharmacological lasting or a degree in microbiology for microbiological testing and has sufficient experience in testing of drug.

At the end, it is once again requested that PQCB's portions of the above samples may please be sent to Appellate Laboratory, NIH, Islamabad, for appropriate RETSETING as prescribed under section 22 (5) of the Drug Act 1976 by applying approved method of analysis, at the expense of the company. Retesting is a statutory right provided under sections 22(4) & 22(5) of the Drugs Act 1976, and recognized by court. It has been held that the Section 22(5) of the Drugs Act 1976, makes it compulsory for prosecution to send sample to Federal Laboratory for RETESTING. Reliance on 1990 P Cr. L. J. The refusal to send sample for RETESTING is an illegality under all

circumstances and is equivalent to infringement of RIGHT provided under the section 22 of the Drug Act 1976. This RIGHT ensures administration of Justice and Fair Play In the light of above submissions, it is requested that case may please be dropped because it is established that this case is not fit for prosecution without the final conclusive report of Appellate Laboratory established under section 22 (5) of the Drug Act 1976.

4. Personal Hearing notice(s) issued to accused person(s)

Case is placed before the Board for Decision

PREVIOUS PROCEEDINGS & DECISION BY THE BOARD:

5. Case was considered by the Provincial Quality Control Board, under section 11 of the Drugs Act 1976 in its **240th meeting** held on **15-03-2022** under the chairmanship of Secretary Health Primary & Secondary Healthcare Department, Punjab, in the presence of Board members as mentioned above. Mr. Amjad Farooq, Secretary DQCB, Rahim Yar Khan and Mr. Ameer Shahid, Provincial Drug Inspector, Tehsil & District Rahim Yar Khan was present along with the original case record. No one among the nominated accused persons of M/s P.D.H. Laboratories (Pvt.) Ltd., 9.5 Km, Sheikhpura Road, Lahore-Pakistan appeared before the Board.

6. The Board after due deliberation and discussion unanimously decided to **adjourn** the **case** and provide another chance of hearing to the accused in the best interest of justice.

7. Personal Hearing notice(s) issued to accused person(s)

Case is placed before the Board for Decision

CURRENT PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 14

PQCB/R-401/2020

Tehsil Khanpur, District Rahim Yar Khan

ATTENDANCE:

Secretary DQCB Drug Inspector	<u>Accused Persons involved in subject case:</u> 1. M/s P.D.H. Laboratories (Pvt) Ltd. 9.5 Km, Sheikhupura Road, (Khaki) Lahore-Pakistan through its Managing Director, Mohsin Ilyas Sheikh 2. Mohsin Ilyas Sheikh Managing Director 3. Muhammad Akhtar Manager Quality Control 4. Abida Dilawar Production Manager/Warrantor of M/S P.D.H. Laboratories (Pvt) Ltd. 9.5 Km, Sheikhupura Road, Lahore-Pakistan
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BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Tehsil Khanpur, District Rahim Yar Khan reported that:-

- His predecessor, on 23-11-2019 inspected the premises of Medicine Store, Chief Executive Officer, District Health Authority, Government Altaf Hussain Eye Hospital Khanpur and took sample of the subject drug on Form No. 4 for the purpose of test and analysis.
- The drug sample, after test/analysis was declared as **Substandard** by Government Analyst, Drug Testing Laboratory, **Bahawalpur** as detailed below: -
- The Store keeper, Medicine Store Chief Executive Officer, District Health Authority, Government Altaf Hussain Eye Hospital Khanpur provided invoice/ warranty bearing No. 2019-11-00874 dated 20-11-2019 issued by M/s P.D.H. Laboratories (Pvt) Ltd. 9.5 Km, Sheikhupura Road, Lahore-Pakistan.
- Warrantor Portion was sent to M/s P.D.H. Laboratories (Pvt) Ltd. 9.5 Km, Sheikhupura Road, Lahore-Pakistan.
- A copy of Test/ Analysis report was also sent to M/s P.D.H. Laboratories (Pvt) Ltd. 9.5 Km, Sheikhupura Road, Lahore-Pakistan and they were directed to provide requisite information in this regard.

Name of Drug	Batch No.	Name of Manufacturer	DTL Report	DTL Test Report Result
Injection Dolnot [Diclofenac Sodium 75 mg/3 mL]	DT-0968	P.D.H. Laboratories (Pvt.) Ltd., 9.5 Km, Sheikhupura Road, Lahore-Pakistan.	01-65002753/DTL dated: 24 Jan 2020	Result of test/ analysis with specifications applied: MS/USP 2018 COMPOSITION Each 3ml contains: Diclofenac Sodium75mg DESCRIPTION Transparent, colorless to light pale/yellow colored solution. 02 out of 15 ampoules have visible particulate matter seen with

				<i>naked eye.</i> (Does not comply with the parenteral specifications). <u>VOLUME (MS):</u> Limit: -----3.0-3.2 ml Determined: -----3.0 ml <u>pH (MS):</u> Limit: -----8.0-10.5 Determined: -----8.302 <u>STERILITY (USP):</u> The product is sterile. <u>IDENTIFICATION (MS):</u> Diclofenac Sodium is identified. <u>ASSAY (MS)</u> Diclofenac Sodium Stated: 75mg/3ml Determined: 76.9mg/3ml Percentage 102.53% LIMIT: 90-110% <u>RESULT:</u> The sample is declared <u>Sub-standard</u> on the basis of Physical Test.
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2. Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused persons who have contravened the provisions of Section 23/27 of the Drugs Act 1976(as amended)/DRAP Act 2012 and Rules framed there under by the way of: --

- i. **Manufacture for Sale / Sale of Sub-standard Drug.**
- ii. **Issuance of false warranty.**

Summary:

Manufacturing Date: 05-2019

Expiry Date: 04-2022

Sampling Date: 23-11-2019

Sent to DTL (Form 6): 23-11-2019

DTL Report Date: 24-01-2020

1ST DI Communication with firm on dated: 05-12-2020

Date of Retesting Request of Firm: No

Fate of Retesting Request: N/A

Investigation Report Dated: 25-01-2021

3. Show-cause notice(s) issued to accused person(s) dated 10-03-2021

Firm's Reply of Show cause notice vide letter no. PDH. D75-KhP-RYK/401-PQCB/2020 dated 26-3-2021

1. That M's PDH Laboratories (Pvt) Ltd. 9 5 Km Sheikhpura Road, (Khaki Lahore is an ISO 9001 2015, 14001-2015 by encompassing the "Good Manufacturing Practice (GMP) throughout the process manufacturing, been incorporated with ISO 45001:2018 Certified company & guarantee manufacture of genuine & stable medicine the world's leading Multinational Pharmaceuticals Companies like Farmitalia Carloerba, UCB, in their Hi-tech products PDH Laboratories (PVT) LI has a vast experience of more than 70 years in the field of manufacturing pharmaceutical products. The doctors actively advise our brands because they trust on the quality and standard of our products. The company never compromises on the quality, which is its corporate vision and organization's culture. We firmly believe in the purity of individual ingredients / items used to manufacture our Products. ZERO DEFECT QUALITY' has been adopted as a part of our QUALITY PHILOSOPHY. That prior to release for marketing/sale, all the batches of all the drugs manufactured are tested at the well-equipped QCLab of the company in accordance with approved methods. PDH is determined to contribute towards the healthcare sector by providing pharmaceuticals of highest quality standards while making them affordable to all human and animal lives. We intend to accomplish this ambition by exercising true discipline, professionalism & human value. Corporate Social Responsibility (CSR) is one of our core values and an integral part of Company's overall mission. Through various ventures in philanthropy, and public awareness, we have historically made significant contributions in the area of corporate social

responsibility

2. That the company has great respect with highest possible level of compliance to all the prevailing law regulating Pharmaceutical Industry and has always worked within the legal framework of the DRAP Act 2012, The Drug Act 1976 and Rules framed thereunder in order to ensure delivery of high quality effective and safe drugs to the patient Regulatory legal advices related to uplifting quality and safety of medicines are always welcome with 100% compliance

3. That without prejudice to the case and despite having reservation on the legality of proceeding of the case and in- conclusive test/analysis report, the company had agreed to the proposal of Mr. Sohail the then, AS-DC/VC-POCB, if the company would recall the Batches, there would be no prosecution. The company has already recalled all the batches of Inj. DOLNOT (Diclofenac Sodium 75MG/3ML). Evidence already provided to POCB.

4. That report is non-conclusive unlawful as full protocols the test applied to reach the conclusion and Result of disputed drug as substandard have not been given in the Test Report No 01-65002753/DTL, dated 29.08.2019. The approved Method of Analysis that describes the full requirement including appropriate preparation of Samples for Drug and Standard and filters etc, was provided to FQCB.

The honorable Supreme Court has held in case reported as 2019 SCM 930 "Report of the Government Analyst must contain Protocol. The term "protocol has not been defined in the Rules its dictionary Meaning is 'A plan of scientific experiment or other procedure. It is also referred to as the precise method for carrying out or reproducing a given experiment. These definitions are in line with the elaboration of the term "protocol" given in case of Imam Bakhsh wherein the Court stated the expression protocol' to mean an explicit plan of an experiment procedure or lest. It is clarified that protocol" is, therefore, a recognized standard method or plan for carrying out the test applied to ascertain the nature of the substance under examination. No test can take place without a protocol. The Report of the Government Analyst must show that the test applied was in accordance with a recognized standard protocol. Any test conducted without a protocol loses its reliability and evidentiary value. Therefore, to serve the purposes of the Act and the Rules, the Report of the Government Analyst must contain (

The Tests Applied

The Protocols Applied To Carry Out These Tests

fin) The Result Of The Test(s)

The single bench of Lahore High Court has held that Reports of Analyst has to be conclusive and must disclose the tests applied to formulate opinion of Government Analyst. There is always likelihood of errors in Tests / analysis report which would be of adverse consequence and definitely affects substantial rights of a persons. Therefore, the description of the experiment including method evaluating standards / results must be Crystal clear whenever report would be disputed. Reliance on PLD 2003 Lah The honorable Single Judge relied on these judgments in the reported cases Gyanendra Nath Mittal v. State AIR 1959 Al. 634, S. Dutta and another. The DB Judgments of Peshawar High Court and Quetta High Court had also held that report without protocol were fatally defective and unlawful Reliance on 1996 P CILJ 1183 (Peshawar). 115, PLJ 2012 Cr.C. (Quetta) 546 (DB)

5. That perusal of the above pasted report shows in a clear manner that Inj. Dolnot B NO. DT-0968 Injection is standard quality because the therapeutically active substance Diclofenac Na has been determined as, 102.53 %, within the approved LIMIT: 90-110% All other test are also in compliance to the approved standard. A drug could not be declared as substandard when it meets the chemical specification". Reliance on DB Judgment of honorable Lahore High court reported as 19.92 MLD 481. The Government Analyst has declared this sample erroneously substandard on the basis of so called Visible Particulate matter. It appears that Government Analyst, Drug Testing Laboratory Bahawalpur is unacquainted about the land mark historic judgment of Division Bench of Lahore High court in Intra-Court Appeals Nos. 127 and 128 of 1989, decided on 28th October, 1991 reported in 1992 MLD 481 whereby holding that 'A drug could not be declared as substandard when it meets the chemical specification. The para 6 of this Judgment is crystal clear in this regards. The DB Judgment of Peshawar High court also held that drug could not be declared substandard on the basis of partide and report without protocol was fatally defective. 1996 P Cr.L.J 1183 (Peshawar)

6. That Government Analyst determined that the above sample was up to the Standard Quality as assay of drug was within the standard quality limit. However, he has declared this drug erroneously substandard based on vague expression' Visible Particulate Contamination'. Particulate matter in injections and parenteral infusions consists of extraneous mobile undissolved particles other than gas bubbles, unintentionally present in the solutions. Similarly, products that produce air or gas bubbles when drawn into the sensor may also require microscopic particle count testing. There are basically two tests, light obscuration, which uses light blockage to determine the size and count of particulate matter in the solution and microscopic assay, which is a measurement of un-dissolvable particles or substances present in the solution – usually plastics, metals or dust. There are basically two tests, light obscuration, which uses light blockage to determine the size and count of particulate matter in the solution; and microscopic assay which is a measurement of un-dissolvable particles or substances present in the solution-usually plastics, Particles of varying sizes have been observed in inject-able drug products, such as visible and sub visible. The particles of 1-50 Micron size are known as sub visible particles and particles of >50 micron are considered as visible particles, Visible particles are defined as those that can be detected under controlled conditions by the unaided human eye i.e., without supplemental magnification). Identification of the composition of the particulate matter is the first step in characterizing particulate matter risk. Based on this information, particles can be further classified into one of three subcategories. extrinsic, intrinsic, and inherent

a) **Extrinsic** particles are defined as those that are not part of the formulation, package, or process, but are foreign and unexpected. Examples of extrinsic particles include fibers (e.g, cellulous), clothing fragments, hair, rubber, metal, plastic, and paint

b) **Intrinsic** particles are defined as those that arise from sources related to the formulation, packaging, or processes. Examples of intrinsic particle materials include glass, stainless steel, rubber from stoppers, and gasket material

c) **Inherent** particles are defined as materials that are expected from the drug formulation, and thus represent generally accepted characteristic of the product. Examples of inherent matter Proteinaceous aggregates metals or dust.

7. That the crucial question for legality of similar reports was evaluated in depth by honorable Division Bench of honorable Lahore High Court in case of Provincial Quality Control Board v. Irza Pharma reported as 1992 MLD 481. The definitions of "Adulterated drug", Spurious and Substandard Drug as given in Section 3of the Drug Act 1976 were examined. It was held

A That if the samples taken conform to the stated specifications chemically do not fall within the definition of the substandard drugs.

B. That the learned single Judge rightly held the term substandard drug with particles is not known to the Drugs Act, and that is true.

C. There was nothing on the record to show, as to what is the nature of the particles found in the samples, and what are its consequences?

(Whether Injurious to health).

D. That Analyst's report in question, when considered within meaning of the definitions of "Adulterated drug" Spurious and Substandard Drug as given in Section 3 of the Drug Act 1976, the drugs tested and reported, fell outside the category of definitions of Substandard Spurious and Adulterated drugs The para 8 of the above Judgement is reproduced as From the aforesaid definition, it is evident that the Law Makers have taken note of the eventualities implications and the nature off the manufacturing of the drugs while making the law. Hence, the law and its intension, as envisaged by the Drugs Act is very sacred and clear. Unfortunately, in our country functionaries

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relevant observations are added as hereunder. -'Under the Constitution of Pakistan, a wholly different state of affairs prevails. Power is expressly given by Article 98 to the Superior Court to probe into the exercise of public power by executive authorities, how high so ever, to determine whether they have acted with lawful authority. The judicial

power is reduced to a nullity if laws are so worded or interpreted that the executive authorities may make what statutory rules they please thereunder and may use this freedom to make themselves the final judges of their own 'satisfaction' for imposing restrains on the enjoyment of the fundamental rights of citizens. Article 2 of the Constitution could be deprived of all its content through this process and the Courts would cease to be guardians of the nation's liberties.

"THE CLINICAL IMPLICATIONS of extraneous particulate matter in injections are determined by many factors, including the size and number of particles, the composition of material, the potential for microbiological contamination, the route of administration, the intended patient population, and the clinical condition of the patient. For example, an otherwise healthy individual receiving a subcutaneous or intramuscular injection containing sterile, inert particulates would likely experience no adverse effect or at worst would develop a small granuloma.

On the other hand, a critically ill premature infant receiving a particle-laden infusion directly through an umbilical catheter might suffer considerable pathophysiologic sequelae.

TEST VISIBLE PARTICULATES IN INJECTIONS is intended to be applied to product that has been 100% inspected as part of the manufacturing process. Injections shall be clear and free from visible particulates when examined without magnification (except for optical correction as may be required to establish normal vision) against a black background and against a white background with illumination that at the inspection point has an intensity between 2000 and 3750 lux. This may be achieved through the use of two 15-W fluorescent lamps (e.g., F15/T8). The use of a high-frequency ballast to reduce flicker from the fluorescent lamps is recommended Higher illumination intensity is recommended for examination of product in containers other than those made from clear glass. The method is described as "Remove any adherent labels from the container and wash and dry the outside. Gently swirl or invert the container, ensuring that air bubbles are not introduced and observe for about 5 s Infront of the white panel. Repeat the procedure in front of the black panel. Record the presence of any particles. Appendix XIII B. Particulate Contamination: Visible Particles (Ph Eur method 2.9.201t is apprehended that Government Analyst did apply this method. The name of Government Analyst is not mentioned on the reports that raises doubts regarding appointment of Gazette Notified Government Analyst as per requirement of section 16 of the Drug Act 1976.

8. That without ascertaining the nature, composition and foreign source of particle, it is not possible to ascertain whether particulate matter allegedly observed by the Government Analyst is Injurious to Health as a consequence of degradation product of Diclofenac Na or a Foreign Particle coming from the environment during manufacturing process of injection or is the product of interaction between active and pharmaceutical necessities or some other source. The myths and realities about clinical correlation between alleged visible particulate matter and ADR would be explained before the PQCB if allowed during statutory personal hearing. The presence of particulate matter in injection has never been defended by the company because of Potential as well as Actual Clinical Risk + Harm +ADR. However, misuse of Particulate Matter as a Tool of Victimization is always resisted, opposed and defended.

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This mandatory scrutiny would have done Justice with the applicant who has been dragged in the process of malicious prosecution.

The rule reproduced as "The PQCB shall examine a case referred to it by an Inspector and shall, if an action is proposed to be taken against a person under the Act or the rules issue a show cause notice to the person and provide him an opportunity for hearing before taking the action about the prosecution of the person or recommending suspension or cancellation of his license to the licensing authority,

10. That not a single unit of this drug has been used on any patient. It is added that Injection are administered under the supervision of A Professional Health Care Provider who is duty bound to administer clear injectable free from all the particulate matters.

11. There is a need to understand that supply of medicines to the Private market and Public Sector Government Institutions are different. The Sale to private sector does not require any pre testing by lab and purchaser requires to procure medicine under a valid warranty. In government supplies, the manufacturer gives warranty but the medicines are not released for use by the patient until standard quality report received from the competent legal Government Analyst. Furthermore, the manufacturer immediately receives payment while selling drugs to a purchaser in private market whereas the payment in government supplies is subjected to many checks including issuance of Standard Quality Report by the Government Analyst. It is not possible to use any Government Supply Medicine without being tested. The batches manufactured for Government Supplies are for exclusive use of patient coming to government hospitals. No one could use government medicine without the Quality certificate/report.

12. That the para 2 of the SCN is vehemently denied as company has not contravened any provision of the Drug Act 1976 / DRAP Act 2012 as evident from the following facts and law

i. The company has neither contravened section 23/27 of the Drug Act 1976 (as amended) nor the DRAP act 2012 and Rules framed thereunder. The case is based upon the Non-Conclusive Report of Government Analyst as sufficient evidence in controversion to this report is available as per requirement of section 22(4) of the Drug Act 1976. 23/27 of the Drug Act 1976 is maliciously applied by omitting the specific sections. 23(1) (a-I-x, b-h, I0i-ii and (27-1) (27-2), (27-3) and (27-4). The Punjab Amendment in the Drug Act 1976 and DRAP Act 2012 not applicable simultaneously on this case because the Drug Act 1976 which is the part of Schedule VI of DRAP Act 2012 is different from the Drug Act 1976 with Punjab Amendment 2017/2018.

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27 (2) whoever himself or by any other person on his

(a) Or

(b) gives to the purchaser a false warranty in respect of any ang sold by him that the drug does not in any way contravene the provisions of section 23 and is not able to prove that, when he gave the warranty, he had good and sufficient reason to believe the same to be true.

13. That the para 3 of the SCN is responded -"The company does not agree with all the names nominated by the Inspector who has acted mechanically while using long handle of Discretion in ascertaining name of Mian Mohsen Ilyas, Managing Director as accused in disrespect the section 11 & 34 of the Drugs Act 1976 and Rule 5 of the Punjab Drug Rules 2007. He is not directly related to the issues under consideration as all routine operations are done without his prior knowledge and consent The Honorable Supreme Court of Pakistan has settled the question of liability related to the company in a case reported as PLD 1978 Supreme Court 193 (Superintendent of Police, Federal Investigation Agency, Lahore and another --Appellants Versus Akhtar Hussain Bhutta-----Respondent). Therefore, it would be difficult to presume that the respondent was guilty of the manufacture of the said substandard drug for and on behalf of the Company, just because he happened to be its Managing Director. Similarly, name of Muhammad Akhtar as Quality Control In-charge has been unlawfully included / ascertained for prosecution by Drug Inspector for the offences of Manufacturing / Sale of Substandard and issuance of False Warranty. Because manufacturing and Quality Control Department are Distinct and independent. The definition of manufacture under section 3 of the Drugs Act 1976 is reproduced below as reference

3(r) "manufacture", in relation to a drug, means all operations involved in the production of the drug, including processing, compounding, formulating, filling, packing, repacking, altering, ornamenting, finishing and labelling with a view to its storage, sale and distribution, but does not include the compounding and dispensing or the packing of any drug in the ordinary course of retail business or on a prescription of a registered medical practitioner or dentist or of a veterinarian and to manufacture' shall be construed accordingly.

The rule 16 (e) of Drugs (Licensing, Registering and Advertising) Rules, 1976 dealing with Conditions for the grant or renewal of licence to manufacture drugs by way of formulation reproduced below 16 (e) The Quality Control Department shall be independent of the manufacturing unit and is to be a whole time employee of the manufacturer and shall possess a degree in pharmacy, or a degree in science with chemistry or a degree in medicine or pharmacology or pharmacological testing or a degree in microbiology for microbiological testing and has sufficient experience in testing of drug.

14. that the maxim *Acommuni Observantia Non EST Recedendum* (where a thing is provided to be done in a particular manner, has to be done in that manner, and If it has not so done, the same would not be lawful. The maxim is applicable to the present case. It is confirmed with regrets that the special procedure provisions prescribed under sections 11. 18. 19. 22 8 32. 34 of the Drugs Act 1976 and Rule 53 of the Punjab Drug Rules 2007 have not been followed.

Kindly ignore the case, as there would be no likelihood of success of this case in any Court of law. The PQCB is requested to pass speaking order by giving annulled confrontation to the defense of the company. It is now well settled that non-speaking order is to be discouraged and authority is required to give reasons while passing administrative as well as judicial orders. It must supply adequate reasons for the conclusion arrived at and should reflect application of judicious mind by the Judge authority and not to be mechanical or non-speaking. Reliance, in this regard, can be placed upon *Province of Sindh through Secretary Education Government of Sindh Karachi and 3 others vs Miss Salma Bano and others* (2003 SCMR 1126). *Muhammad Farooq Shah v Shakirullah* (2006 SCMR 1657), *Abdul Majeed Zafar and others v Governor of the Punjab through Chief Secretary and others* (2007 SCVR 330). *Umar Din through LRS V. Mst Shakeela bibi and others* (2009 SCMR 29). *Secretary Ministry of Health Government of Pakistan, Islamabad and another v. Dr. Rehana Hameed and others* (2010 SCMR 511), *Government of Pakistan through Director-General Ministry of Interior Islamabad and others v Farheen Rashid* (2011 SCMR 1) and *others v. Messrs MFM Industries Ltd. And others v Federation of Pakistan through Ministry of Commerce and others* (2015 SCMR 1550). The statutory personal hearing may please be given whenever the issue is presented before the PQCB for any interim or Final Order. Additional grounds/viewpoints would be submitted during personal hearing before the PQCB at the time of consideration of this case if confrontation required in response to quire of the honorable PQCB members.

4. Personal Hearing notice(s) issued to accused person(s) dated 04-03-2022

Case is placed before the Board for Decision

PREVIOUS PROCEEDINGS & DECISION BY THE BOARD:

5. Case was considered by the Provincial Quality Control Board, under section 11 of the Drugs Act 1976 in its **240th meeting** held on **15-03-2022** under the chairmanship of Secretary Health Primary & Secondary Healthcare Department, Punjab, in the presence of Board members as mentioned above Mr. Amjad Farooq, Secretary DQCB, Rahim Yar Khan and Mr. Israr Niazi, Provincial Drug Inspector, Tehsil Khanpur, District Rahim Yar Khan was present along with the original case record. No one among the nominated accused persons of M/s P.D.H. Laboratories (Pvt.) Ltd., 9.5 Km, Sheikhpura Road, Lahore-Pakistan appeared before the Board.

6. The Board after due deliberation and discussion unanimously decided to **adjourn** the **case** due to absence of firm and provide another chance of hearing to the accused in the best interest of justice.

7. Personal Hearing notice(s) issued to accused person(s)

Case is placed before the Board for Decision

CURRENT PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 15**PQCB/R-788/2019****Ravi Town, Lahore****ATTENDENCE**

Secretary DQCB	1. M/s Don Valley Pharmaceuticals Pvt. Ltd. 31-KM, Main Ferozepur Road, Lahore, through its Chief Executive Officer, Dr. Shehla Javed Akram.
Drug Inspector	2. Dr. Shehla Javed Akram Chief Executive Officer. 3. Muhammad Yamin Production Manager/Warrantor. 4. Zia ul Haq Quality Control In-Charge Of M/s Don Valley Pharmaceuticals Pvt. Ltd. 31-KM, Main Ferozepur Road, Lahore.

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Ravi Town, Lahore reported that:-

- His predecessor, on 22-05-2019, inspected the premises of Main Medicine Store, Government Said Mitha Hospital, Said Mitha Bazar, Lahore and took sample of Tablet Ulsin, Batch no. 7916, manufactured by M/s Don Valley Pharmaceuticals Pvt. Ltd. 31-KM, Main Ferozepur Road, Lahore vide on Form 4 for the purpose of test/analysis.
- The sample was forwarded to Drug Testing Laboratory Lahore vide Memo number 19 DI/RT dated 23-05-2019 for test/analysis.
- The following drug sample, after test/analysis was declared as **Substandard** by Government Analyst, Drug Testing Laboratory Punjab, Lahore as detailed below: -

Name of Drug	Batch No.	Name of Manufacturer	DTL Report	DTL Test Report Result
Tablet Ulsin 40mg [Famotidine USP 40mg] Mfg. Date: 04-2019 Exp. Date: 04-2021 Reg # 021518	7961	M/s Don Valley Pharmaceuticals Pvt. Ltd. 31-KM, Main Ferozepur Road, Lahore	01-129004634/ DTL dated: 23 Aug 2019	Result of test/ analysis with specifications applied: USP 2018 <u>PHYSICAL DESCRIPTION:</u> Green coloured elliptical tablets “D.V” engraved on one side in green blister packing of Unit 10. <u>WEIGHT VARIATION:</u> Sample meets acceptance criteria for uniformity of mass or weight. Limit $\pm$ 7.5% of 102 mg (Average weight=103.2mg) <u>IDENTIFICATION:</u> The retention time of the major peak in the sample chromatogram corresponds to the

retention time of the major peak in standard chromatogram (Famotidine identified).

ASSAY:

Stated: 40mg/Tab

Determined: 41.96 mg/capsule

Percentage 104.9%

Limit: 90-110%

DISSOLUTION TEST: Does not comply with the USP Specifications as detailed below:

Tolerance Limit: NLT 80% (Q) of the labelled amount of famotidine is dissolved.

S1: Each unit is NLT Q+5%

S2: Average of 12 units (S1+S2) is $\geq$ Q, and no unit is $<$ Q-15%

S3: Average of 24 units (S1+S2=S3) is $\geq$ Q, NMT two units are $<$ Q-15%, and no unit is $<$ Q-25%

LEVEL	NUMBER TESTED	ACCEPTANCE CRITERIA						REMARKS
1	6	Each individual unit should NLT 85% (Q+5%)						Does not comply
		1	2	3	4	5	6	
Determined (%)		22.4	25.9	22.8	21.3	25.4	19.9	

The sample fails to comply the dissolution test, performed as per USP, as all 6 units showed release less than Q -25% (i.e. 55%) and remained intact at the bottom of vessels after dissolution at S1. Hence, not proceeded to S2 and S3

.RESULT:

The above sample is SUB-STANDARD on the basis of DISSOLUTION TEST performed as per USP.

- iv. The Store Keeper, Main Medicine Store, Government Said Mitha Hospital, Said Mitha Bazar, Lahore provided Invoice No. 3018 dated 08-05-2019 issued by M/S IS Enterprises 229-A New Sample Road, Railway Colony, Mughal Pura, Lahore, who in turn provided invoice/warranty bearing No. 1905-12859 dated 08-05-2019 issued by M/s Don Valley Pharmaceuticals Pvt. Ltd. 31-KM, Main Ferozepur Road, Lahore.
- v. The Warrantor portion was sent M/S M/S IS Enterprises 229-A New Sample Road, Railway

Colony, Mughal Pura, Lahore.

vi. A copy of test/analysis report was sent to M/S Don Valley Pharmaceuticals and they were asked to provide requisite information in this regard.

2. Drug Inspector requested for grant of permission for prosecution against the accused persons nominated in the instant case who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended) and Rules framed there under by the way of: -

- i. **Manufacturing for Sale /Selling of Substandard drug**
- ii. **Issuance of false warranty**

3. Showcause was issued to accused person(s) dated 27.02.2023.

Reply of the Firm to the Show Cause Notice:

Reply to the Show Cause Notice bearing reference No. PQCB/R-788/2019 dated 27-02-2023.

1. This is in response to the Show Cause Notice bearing reference No. POCB/R- 788/2019 dated 27-02-2023 wherein your good office has instructed M/s Don Valley Pharmaceuticals ("Don Valley") to show cause as to why any legal action, including but not limited to initiation of prosecution before the Honourable Drug Court and the cancellation/suspension of the Drug Manufacturing License, Drug Sale License along with the registration of the Drug, may not be taken against Don Valley and its concerned officials for allegedly contravening the provisions of the Drug laws and the rules framed thereunder.

2. Firstly, at the outset, Don Valley does not agree with the findings of the Government Analyst Drug Testing Laboratory, Lahore rendered vide TRA No. 01-129004634/DTL dated 23-08-2019 (DTL Report") where under its product, namely, Tablet Ulsin 40mg Batch No. 7961 ("Product") has allegedly been declared as "substandard" on the basis of the result of the Dissolution Test. In view thereof, Don Valley seeks to refute the inaccurate findings of the Government Analyst, inter alia, on the following grounds:

i. A perusal of the DTL Reports reveals that the Government Analyst has failed to mention the testing protocols employed to test the Product. As such, the variation is likely to have occurred due to several reasons including but not limited to a non-calibrated apparatus used at the time of testing. It is a matter of fact that a non-calibrated dissolution apparatus causes significant fluctuations in the temperature and RPM of the apparatus resulting in inaccurate and incorrect findings in relation to the dissolution of the Product.

ii. In addition to the foregoing, it may also be noted that no evidence has been brought on record to substantiate the fact that the pH of the phosphate buffer was maintained properly by the Government Analyst. More so, the DTL Report is completely silent vis-à-vis the condition of the media solution used to test the Product. The quality and/or condition of the media solution has a direct and substantial bearing on the dissolution of the Product.

iii. Even otherwise, all tests carried out by the quality control department of Don Valley at the time of the release of the Product are in compliance with the parameters defined under the United States Pharmacopeia. More importantly, a thorough investigation has also been conducted on the retention samples and in-process batches wherein it has transpired that the same are of standard quality. Accordingly, the findings rendered by the Government Analyst are defective and incapable of being relied upon.

3. Notwithstanding the foregoing and despite the complete innocence of the Don Valley and its concerned officials in the subject case, please note the following information and documents as per your requirement:

- i. Shehla Javed Akram (Chief Executive Officer).
- ii. Muhammad Yamin (Production In charge/Warrantor)

- iii. Zia-ul-Haq (Quality Control In-charge)
- iv. Drug Manufacturing License.
- v. Drug Registration Certificate.
- 4. Accordingly, it is submitted that Don Valley and its concerned officials have not contravened the provisions of the Drug Laws and the rules framed thereunder as has been alleged in the Show Cause Notice under reply. As reiterated earlier, the findings rendered by the Government Analyst are incorrect, defective and without any merit. Therefore, it shall be against the tenets of justice to rely upon such findings and initiate any subsequent proceedings against Don Valley and/or its concerned officials on the basis of the
- 5. In view of the foregoing, it is very kindly requested that the Show Cause Notice under reply and all subsequent proceedings may be withdrawn in the interest of justice and the case be consigned to record

4. Personal Hearing notice(s) issued to accused person(s) dated 19.06.2023.

Case is placed before the Board.

Summary:

Manufacturing Date: 04-2019

Expiry Date: 04-2021

Sampling Date: 22-05-2019

Sent to DTL (Form 6): 23-05-2019

Date of receipt in DTL: 23-05-2019

DTL Report Date: 23-08-2019

Time Extension: Granted in 210-M

| 1ST DI Communication with firm on dated: 22-07-2020 **|**

Date of Retesting Request of Firm: N/A

Fate of Retesting Request: -N/A

| Investigation Report Dated: 01-11-2022 **|**

**CURRENT PROCEEDINGS AND
DECISION OF THE BOARD**

Case No. 16**PQCB/ R-540/2018****Jehanian, Khanewal****ATTENDENCE**

Secretary DQCB	<u>Accused Persons involved in subject case</u> 1. M/s Don Valley Pharmaceuticals, 31-Km Main Ferozepur Road, Lahore , through its Chief Executive Officer Dr. Shehla Javed Akram 2. Dr. Shehla Javed Akram 3. Shabana Kashif W/o Kashif Islam Sheikh 4. Tariq Mehmood 5. Muhammad Yamin of M/s Don Valley Pharmaceuticals, 31-Km Main Ferozepur Road, Lahore.
Drug Inspector	

BRIEF FACTS OF THE CASE

Provincial Inspector of drugs Tehsil Jehanian, District Khanewal reported that: -

- His predecessor, on 31-10-2017, inspected the business premises of M/s Khalil Pharmacy, Main Bazar Thatta Sadiq Abad Tehsil Jehanian and took sample of below mentioned drugs on Form No. 04 for the purpose of test and analysis.
- The drug sample, after test/ analysis was declared **Substandard** by Government Analyst Drug Testing Laboratory, Multan as detailed below:

Name of drug	Batch no.	Name of manufacturer	DTL Report TRA No. & Date	DTL Test Report Results							
Film coated Tablet, Dyramid (Ofloxacin 200mg)	5635	M/s Don Valley Pharmaceuticals, 31-Km Main Ferozepur Road, Lahore	TRA No.01-17000576/DTL dated: 19-02-2018	Analysis with specifications applied: USP 2017							
				<u>Dissolution Test</u>							
				Does not comply with specifications as described below:							
				Tolerance limit: NLT 80% (Q) of the labelled amount of Ofloxacin dissolved							
				Level	No. Tested	Acceptance Criteria					
						Each Unit Should not less than Q+5%					
				S1	6	Unit 1	Unit 2	Unit 3	Unit 4	Unit 5	Unit 6
				Determined		40.11	34.24	36.41	37.72	35.54	38.59

%age							
S2	Average of 12 units (S1+S2) is equal to or greater than Q, and no unit is less than Q-15%.						
	6	Unit 1	Unit 2	Unit 3	Unit 4	Unit 5	Unit 5
Determined %age		24.78	23.69	25.87	23.37	23.69	82.94
S3	Average of 24 units (S1+S2+S3) is equal to or greater than Q, and NMT 2 Units are less than Q-15% and no unit is less than Q-25%						
	6	Unit 1	Unit 2	Unit 3	Unit 4	Unit 5	Unit 5
Determined %age		24.35	26.19	87.17	26.41	26.41	25.33
	6	Unit 7	Unit 8	Unit 9	Unit 10	Unit 11	Unit 12
Determined %age		22.83	22.72	23.26	24.56	24.78	24.89
Assay (Ofloxacin)							
Stated				200mg/Tab			
Determined				205.36mg/Tab			
Percentage				102.68%			
Limit				90%-110%			
Result: The above sample is Sub-standard on the basis of dissolution.							

iii. M/s Khalil Pharmacy, Main Bazar Thatta Sadiq Abad Tehsil Jahanian provided invoice/ Warranty No. 971 dated 20-10-2017 issued by M/s Rayyan Pharma, Medicine Market Town Hall Multan as a

proof of its purchase.

- iv. Warrantor portion was sent to M/s Rayyan Pharma, Medicine Market Town Hall Multan with directions to explain their position in this regard.
- v. M/s Rayyan Pharma, Medicine Market Town Hall Multan provided invoice/warranty No. 1709-8641 dated 19-09-2017 issued by M/s Don Valley Pharmaceuticals, 31-Km Main Ferozepur Road, Lahore as a proof of its purchase.

2. The Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused person(s), who have contravened the provisions of Section 23/27 of the Drugs Act 1976(As amended)/DRAP Act 2012 and Rules framed there under by the way of:

- a. **Manufacture for sale / sale of Substandard drug**
- b. **Issuance of false warranty**

3. Show-cause notice(s) issued to accused person(s) vide 17-05-2021

Reply of the Firm to Show-Cause Notice:

With reference to your Letter No. PQCB/R-540/2018 dated 17/05/2021, received by us on 24/05/2021. It is to inform that your office Letter No. PQCB/R-540/2018 dated 17/05/2021 was somehow mixed with other documents due to the negligence of our staff that's why couldn't reply timely; as soon as we found the letter we are replying. Moreover, it is to inform that we didn't receive any such letter or report from the provincial inspector of drugs in which Dymamid Tablet (our product) B#5635 was declared as substandard and it is informed that batch is already expired since August, 2019. So, we request you to please dispose of this case.

4. Personal hearing notice(s) issued to accused person(s) on 17-03-2022.

PREVIOUS PROCEEDINGS OF THE CASE:

PQCB's 241st meeting held on 31-03-2022:

5. Case was considered by the Provincial Quality Control Board, under section 11 of the Drugs Act 1976 in its **241st meeting held on 31-03-2022** under the Chairmanship of Secretary Primary & Secondary Healthcare Department, Punjab. Mr. Junaid Mahmood Secretary DQCB District Khanewal and Shehroze Khan Drug Inspector Tehsil Jehanian were present. No one among the nominated accused were present however, Imran Abbass (Area Sales Manager) appeared before the Board on the behalf of M/s Don Valley Pharmaceuticals, 31-Km Main Ferozepur Road, Lahore and requested to adjourn the case.
6. Secretary PQCB apprised the Board that request for adjournment has been received in subject case from the Firm due to non-availability of their technical staff i.e Shabana Kashif (Production Incahrge) and Dr. Shehla Javed Akram is not present in Lahore on 31-03-2022. The Board after discussion decided to **adjourn the case** on the request of the firm. The Board further decided to provide another but final opportunity of personal hearing to the accused persons.
7. Personal hearing notice(s) issued to accused person(s) on 30-08-2022.

PQCB's 250th meeting held on 22-09-2022:

8. Case was considered by the Provincial Quality Control Board, under section 11 of the Drugs Act 1976 in its **250th meeting held on 22-09-2022** under the Chairmanship of Secretary Primary and Secondary Healthcare Department, Punjab. Mr. M Anwar ul Haq Member DQCB, District Khanewal

and Mr. Shehroze Khan Drug Inspector Tehsil Jahanian, District Khanewal were present along with original case record. No one among the nominated accused, of **M/s Don Valley Pharmaceuticals, 31-Km Main Ferozepur Road, Lahore**, was present. However, Mr. Shoib Safdar, counsel of the firm along with M Ishfaq (Quality Control Manager) and M. Imran (Sales Manager) on behalf of **M/s Don Valley Pharmaceuticals, 31-Km Main Ferozepur Road, Lahore**, were present. Technical representatives of the firm told the board that the technical staff has been changed and they were unable to produce any authority letter by the firm to attend the meeting at the time of hearing.

9. In view of the preceding facts, the Board after due deliberation and detailed discussion unanimously decided to **Adjourn the case** due to absence of accused technical staff of the firm. The board further decided to provide another but final opportunity of personal hearing to the accused persons.

Personal hearing notice(s) issued to accused person(s) on 19-06-2023.

Case is placed before the board for decision.

Summary:

Manufacturing Date: 08-2017

Expiry Date: 08-2019

Sampling Date (Form 4): 31-10-2017

Sent to DTL (Form 6): 31-10-2017

Date of receipt in DTL: 10-11-2017

DTL Report Date (Form 7): 19-02-2018

1ST DI Communication with firm on dated: 09-05-2018

Date of Retesting Request of Firm: No request

Investigation Report Dated: 16-04-2021

PROCEEDINGS & DECISION BY THE COMMITTEE:

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Case No. 17**PQCB/R-382/2021****Tehsil Pattoki, District Kasur****ATTENDENCE**

Secretary DQCB Drug Inspector	<u>Accused Persons involved in subject case</u> 1. M/s Donvalley Pharmaceuticals (Pvt) Limited 31-Km Main Ferozpur Road, Lahore Pakistan through its Chief Executive Officer, Dr. Shehla Javed Akram 2. Dr. Shehla Javed Akram Chief Executive Officer 3. Shabana Kashif Production Incharge 4. Tariq Mehmood Quality Control Incharge 5. Muhammad Yamin Warrantor Of M/s Donvalley Pharmaceuticals (Pvt) Limited 31-Km Main Ferozpur Road, Lahore-Pakistan.
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BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Tehsil Pattoki, District Kasur reported that: -

- His predecessor, on 15-12-2020, inspected the business premises of M/s Al-Madina Pharmacy Allama Iqbal Road, Tehsil Pattoki, District Kasur and took following subject drug sample on Form No.04 for the purpose of test/analysis and sent to Drug Testing Laboratory Lahore.
- The subject drug sample after test/analysis was declared as **Substandard** by Government Analyst Drug Testing Laboratory **Lahore**, as detailed below:

Name of Drug	Batch No.	Name of Manufacturer	DTL Report No. & Date	DTL Test Report Result
Tablet. Pensulid [Nimesulide B.P. 100mg]	EY-20-007	M/S DONVALLEY Pharmaceuticals (Pvt.) Limited, 31 km, Main Ferozepur Road, Lahore- Pakistan.	01- 73006957/DTL dated 04-02-2021	Analysis with Specifications Applied: MS <u>PHYSICAL CHARACTERISTICS:</u> YELLOW ROUND BICONVEX TABLET, PLAIN FROM BOTH SIDES IN ALU ALU PACK OF 10 UNITS. <u>AVERAGE WEIGHT:</u> This sample meets the MS acceptance criteria of average weight (316 mg $\pm$ 5%) with average weight of 310.5 mg. <u>IDENTIFICATION:</u> The retention time of the major peak in the sample chromatogram corresponds to the retention time of the major peak in standard chromatogram. (NIMESULIDE IDENTIFIED) <u>ASSAY OF Nimesulide:</u> Stated: 100 mg/ Tab Determined: 94.60 mg/ Tab

					Percentage:	94.6%
					Limit:	90.0% - 110.0% of the label claim
					<u>DISSOLUTION TEST:</u> Does not comply with the MS Specifications as detailed below:-	
					Tolerance Limit: NLT 80.0% after 60 minutes.	
					For S1: Each unit is not less than Q + 5%	
					For S2: Average of 12 units (S1+S2) is equal to or greater than Q, and no unit is less than Q – 15%	
					For S3: Average of 24 units (S1 + S2 + S3) is equal to or greater than Q, not more than 2 units are less than Q – 15%, and no unit is less than Q – 25%	

- iii. Proprietor of M/s Al-Madina Pharmacy Allama Iqbal Road, Tehsil Pattoki, District Kasur provided warranty bearing No. 20647 dated 28-11-2020 issued by M/s Umair Traders, Rehman Plaza, Railway Road, Kasur as a proof of its purchase.
- iv. M/s Umair Traders, Rehman Plaza, Railway Road Kasur, in-turn provided warranty bearing No. 2011-17171 dated 19-11-2020 issued by M/s Donvalley Pharmaceuticals (Pvt) Limited 31-Km Main Ferozpur Road, Lahore-Pakistan as a proof of its purchase.
- v. Warrantor portion of drug sample was sent to M/s Umair Traders Rehman Plaza, Railway Road Kasur -Pakistan.
- vi. A copy of test/analysis report was sent to M/s Donvalley Pharmaceuticals (Pvt) Limited 31-Km Main Ferozpur Road, Lahore-Pakistan with directions to explain their position and provide requisite information in this regard.

2. The Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused person(s), who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended), DRAP Act 2012 and Rules framed there under by the way of:

a. **Manufacture for sale /Sale of Substandard drug**

b. **Issuance of false warranty**

3. Show-cause notice(s) issued to accused person(s) dated 16-03-2022

Firm submitted written reply to the Show Cause Notice vide letter no PENSULID/DV/11/04/22 dated 11-04-2022

*In such regards, we wish to state the following That till to date no warrantor/manufacturer portion had received from concerned drug inspector after taking the samples against the requirement of section 19 (3) (ii) of Drug Act, 1976. The test report has passed the sample on all other tests declared on the report including physical description, weight variation. Assay of Pensulid 100mg Tablet BP (Nimesulide) Batch # EY-20-007. After receiving the DTL report we initiate investigation and **it was identified that DTL Lahore tested the product using the old Method of analysis. The method was changed in July 2020** and the information and method has also been sent to provincial Inspector of Drugs tehsil Pattoki District Kasur vide letter No PENSULID/DV/037-2021 dated 25th June 2021 product and the method was sent to DTL Punjab. The samples of different batches has also been picked by Drug Inspector and sent to different drug testing Laboratories of Punjab for testing purpose the results were found satisfactory.*

*While testing Product Pensulid 100mg Tablet BP (Nimesulide) Batch # EY-20-07 **DTL Lahore did not request us for provision of new dissolution method and DTL Lahore use the old method which lead to substandard of the product. we have retested our retained samples of the said batch all parameters were found within the specification.** This indicates the Product Pensulid 100mg Tablet BP (Nimesulide) Batch# EY-20-07 is of standard quality. In these circumstances it is apparent that there is no need, cause or justification for any further action in the matter and request the case may be closed.*

Furthermore, firm verified the names of the accused persons mentioned in the Show Cause Notice:

1. Chief Executive Officer (Dr. Shehla Javed Akram)
2. Production in charge/Warrantor (Muhammad Yamin)
3. Quality Control In charge (Tariq Mehmood)

7. Personal hearing notice(s) issued to accused person(s) dated 19-06-2023

8. Case is placed before the Board for decision.

Summary:

Manufacturing Date: 11-2020

Expiry Date: 11-2022

Sampling Date (Form 4): 15-12-2020

Sent to DTL (Form 6): 15-12-2020

Date of receipt in DTL: 16-12-2020

DTL Report Date (Form 7): 04-02-2021

Time Extension: Not Time Barred

1st DI Communication with firm on dated: 06-04-2021

Firm's Reply to DI's First Intimation: 25-06-2021

2nd DI Communication with firm on dated: 16-08-2021

Firm's Reply to DI's Second Intimation: 24-08-2021 (Intention for Retesting)

Retesting Request of Firm: Firm showed intention for retesting in response to 2nd letter by Drug Inspector.

Investigation Report Dated: 16-12-2021

PROCEEDINGS & DECISION BY THE BOARD:

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THQ Hospital Wazirabad, District Gujranwala

ATTENDENCE

Secretary DQCB Drug Inspector	<u>Accused Persons involved in subject case</u> 1. M/S Jassh Pharmaceuticals, Farooq Industrial Estate, 20 km Ferozpur Road, Lahore through its Managing Director Hassan Jamil 2. Hassan Jamil Managing Director 3. Jamil Asghar Rana Production Incharge 4. Rehana Tabassum Quality Control Manager 5. Muhammad Naeem Akhtar Warrantor/ Quality Assurance Officer of M/S Jassh Pharmaceuticals, Farooq Industrial Estate, 20 km Ferozpur Road, Lahore.
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BRIEF FACTS OF THE CASE:

Provincial Inspector of drugs THQ Hospital Wazirabad, District Gujranwala reported that:-

- He, on 19-02-2020, inspected the premises of Anjuman Behboode Mareezan (Regd) THQ Hospital Gujranwala and took sample of a drug on Form No.04 for the purpose of test/analysis and send to Drug Testing Laboratory Lahore.
- The drug sample, after test/analysis, was declared **Substandard** by Government Analyst, Drug Testing Laboratory, Gujranwala Division **Faisalabad** as detailed below:

Name of Drug	Batch No.	Name of Manufacturer	DTL Report TRA No. & Date	DTL Test Report Result
Carbosol Haemodialysis Concentrate	1910237	M/S Jassh Pharmaceuticals, Farooq Industrial Estate, 20 km Ferozpur Road, Lahore	TRA No. 01-68002687/DTL dated:20-04-2022	Analysis with specifications applied: BP 2020 Physical Description: Colorless liquid contained in plastic bottle of four litres capacity sealed with plastic cap and bicarbonate powder separately in polythene bag. Identification (BP 2020): Sodium, Chloride, Acetate, Sodium Bicarbonate and Dextrose are identified. Assay (BP 2020):

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iii. Finance Secretary Anjuman Behboode Mareezan (Regd) THQ Hospital Gujranwala, provided invoice/ warranty No. 624 dated 08-10-2019 issued by Tariq Mehmood (Warrantor) of M/S Passia Pharma Medicine/Distributor/ wholeseller, Faiz Plaza Commissioner Road, opp. Allama Iqbal Hospital Sialkot as a proof of its purchase of the said drug.

iv. Warrantor portion of the drug sample was sent to M/S Passia Pharma Medicine/Distributor/ wholeseller, Faiz Plaza Commissioner Road, opp. Allama Iqbal Hospital Sialkot who inturn provided invoice/ warranty no. 1433-B dated 08-10-2019 issued by M/S Jassh Pharmaceuticals, Farooq Industrial Estate, 20 km Ferozpur Road, Lahore as a proof of purchase of the said drug.

v. A copy of test report of the drug sample was sent to M/S Jassh Pharmaceuticals, Farooq Industrial Estate, 20 km Ferozpur Road, Lahore with directions to provide the requisite information and to explain their position in this regard.

2. In this way You have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended) / DRAP Act 2012 and Rules framed there under by the way of:-

i. **Manufacture for sale / Sale of Sub-standard Drug**

ii. **Issuance of false warranty.**

3. Show cause notice issued to the accused(s) persons dated 21-07-2020.

FIRM REPLY TO SHOW CAUSE NOTICE:

4. M/S Jassh Pharmaceuticals, Farooq Industrial Estate, 20 km Ferozpur Road, Lahore submitted written reply stating that:

- i). JASSH Pharma is a manufacturer of haemodialysis concentrate solution, since 2006, under manufacturing license number 000601
- ii). There were 1250 canes (Units) produced against the batch number 1910237, and all stock was delivered to THQ Hospital Wazirabad, District Gujranwala. We respect and consider PQCB as final decision as always and ready to re-call the said batch and replace with equal new stock.
- iii). Carbosol Haemodialysis Concentrate is not a drug and pharmacologically inactive because of its mechanism of action it is a solution for haemodialysis machines, the solution is used only to replace water and electrolytes to serve as a exchange medium for use during hemodialysis", hence falls under category of medical devices (medical devices rules 2017).
- iv). The determined quantity of acetate by the government analyst vide DTL reports no; TRA NO 01-68002687/DTL dated 20.04.2020 (Acetate 4.1094m.mol/L) is well within range (2.5m.mol/L to 10.0m.mol/L) set for the haemodialysis concentrate solutions by British pharmacopeia, health Canada etc. (Copy attached).
- v). The identified substance i.e., acetate is a micro-ingredient, and not affect the quality of haemodialysis concentrate solution, because haemodialysis concentrate solution function on the principle of sodium potassium pump, sodium potassium chlorides and glucose are its major components that are all within range determined by the government analyst vide DTL reports no; TRA NO 01-68002687/DTL dated 20.04.2020.
- vi). Acetic acid one of the ingredients of haemodialysis solutions, that is only source of acetates in this solution, which is mainly used to acidifying the haemodialysis solution and to maintain its pH only..
In government tenders for haemodialysis solutions and dialysis centers demands from us acetates 5m.mol because their dialysis machines parameters set for higher acidic dialysis solution i.e. acetates 5.0m.mol/ Many other national and international brands are available with the range of acetates NMT 10 m.mol/L, we were already applied for the "approval of post registration variations" case submitted to DRAP dated 20, July 2018.
- vii). There were two batches (Batch No. 1910235 and 1910237) supplied to THQ Hospital Wazirabad, both batches were manufactured against our current, approved manufacturing procedure, i.e. there was no change in master formula or manufacturing procedure, though assay of acetate for batch no. 1910237 declared high, by government analyst and 1910235 found satisfactory (**Copy of batch production records attached**).

Conclusion:

In the light of above narrated parameters, it is justified that:

1. Carbosol is not a drug.
2. Acetate is a micro-ingredient in dialysis solutions and not affects the quality of product,
3. The value of acetates, 4.1094m.mol/L is well within range (2.5m.mol/L to 10.0m.mol/L) set by B.P, E.P etc.
4. Carbosol haemodialysis concentrate is a solution for haemodialysis machines, hence design as per dialysis machines (Fresenius, Torry etc.) parameters that is up to 5.0m.mol/l for acetates.
5. Ready to re-call the said batch and replace with equal new stock.

4. Personal hearing notice(s) issued to accused person(s) dated 26-07-2022

PROCEEDINGS & DECISION BY THE BOARD:

5. Case was considered by the Provincial Quality Control Board, under section 11 of the Drugs Act 1976 in its **248th meeting** held on **04-08-2022** under the chairmanship of Secretary Primary & Secondary Healthcare Department, Government of Punjab. Ms. Sonia Arshad Secretary DQCB District Gujranwala and Mr. Shahryar Khan Afridi THQ Hospital Wazirabad, District Gujranwala was present along with original case record. Among nominated accused persons Rehana Tabassum (Quality Control Manager)

and Muhammad Naeem Akhtar (Warrantor/ Quality assurance Officer) appeared before the Board on behalf of **M/S Jassh Pharmaceuticals, Farooq Industrial Estate, 20 km Ferozepur Road, Lahore** and submitted before the Board that the firm has no previous history of substandard products and this is only substandard report of the firm. They endorsed the arguments as already submitted by them in response to show-cause notice issued to them. They requested for lenient view.

6. The Board after careful perusal of the case record observed that the subject drug sample has been declared substandard from Drug Testing Laboratory, Faisalabad, on the basis of assay of Acetate. The assay was found to be 136.98%, whereas the limit was 95-105%. The Board was of considerate view that in the given case, the root cause analysis of the defect must be evaluated. Keeping in view the facts of the case, the Board after due deliberation and discussion unanimously decided to **pend the case** and constitute the committee comprising of the following members for product specific inspection of **M/S Jassh Pharmaceuticals, Farooq Industrial Estate, 20 km Ferozepur Road, Lahore** and submit report for consideration by the Board.

Dr. Mehmood Ahmad (Member PQCB)	Convener
Dr. Munawar Hayat (Director DTL, Lahore.)	Member

Product specific inspection report of M/S Jassh Pharmaceuticals, Farooq Industrial Estate, 20 km Ferozepur Road, Lahore

Members of inspection Committee:

Prof. Dr. Mehmood Ahmad	Professor of Pharmacy Member PQCB	Convener
Dr Muhammad Munawar Hayat	Director, Drug Testing Laboratory, Lahore	Member

Date of Inspection:
20-12-2022

Inspection was conducted with reference to PQCB order No. PQCB/R-67/2020, Dated 21-10-2022.
Brief of the Case:

Carbosol Hemodialysis concentrate, Batch No. 1910237, Declared as Sub-standard by Drug testing laboratory, Faisalabad on Acetate test (136.98%), Test report No. 01-68002687/DTL, Dated 20-04-2022.

The case was considered before PQCB case no.43/M-248.

Premises:

The design and layout of manufacturing unit was good, neat, clean, proper and facilitate organized working.

The sanitation condition of the building was found satisfactory.

- The manufacturing area was having proper doors and control of humidity.
- Main Raw material store of the firm was separate and segregated for flammable store.
- List of equipment (Annex-A) but not having potentiometer.

As sample was declared substandard by DTL on acetate concentration / assay (136.98%) by potentiometric titration as per method given in Ph. Eur. (Annex-B).

Technical Staff of Firm:

Jamil Asghar Rana, CEO

Najma Babar, Production In charge

Kashaf Nazir, QC In charge (Annex-C)

Detail of Product from Master Batch Record (BMR: Annex-D)		
1.	Name of Product	Carbosol Haemodialysis Concentrate
2.	Batch No.	1910237
3.	Medical Device License No.	ELM-0037 (Annex-E)
4.	Enlistment Number	MD-MR-000162
5.	Batch Size	5000 Litres
6.	Tank Size	8000 Litres
7.	pH	2.5
8.	Ingredients as per BMR	Magnesium chloride, Potassium chloride, Sodium chloride, Calcium Chloride, Dextrose monohydrate Glacial Acetic acid Sodium bicarbonate (Part-B)
9.	Date of Manufacture	04-10-2019
10.	Expiry Date	04-10-2022
11.	Theoretical Yield	98-102%

12.	Pack Size	4 Litres/ cane
13.	Finished Product Loss	0.64%

Quality Control Department

- Potentiometer was not available at the time of inspection in QC Lab, which is required for testing of acetate as per Ph. Eur.
- The Quality Control laboratory was properly equipped (List of equipment's Annex-A).
- Sufficient quality control SOPs. / Checks were present to control the quality of product.
- The measuring glass and cylinders were not calibrated by ISO certified firm.
- The QC lab was not having FTIR.
- The stability chambers were functional
- Karl fisher apparatus / reagent is not available.
- Testing method mentioned on label is Eur. Ph. (Annex-F), but not fully followed by the firm (Annex-G).

Detail of Inspection / Observations:

The findings of the panel are as follows:

- The analysis of Carbosol Hemodialysis Concentrate 4000 ers was not as per Eur. Ph. Monograph.
- Potentiometer was not present at the time of inspection in QC Lab, which is required for testing of acetate.
- Acetate analysis by simple Titration with wrong calculations which is not official as per Eur. Ph.
- Testing method mentioned on label is Eur. Ph. (Annex-F), But not fully followed by the firm (Annex-G).
- Karl fisher apparatus / reagent is not available.
- No method verification protocol or data was available.

Conclusion:

In view of the observations of the panel mentioned in detail above, scrutiny of the documents provided by the firm at the time of inspection, the worth of documents shown to the panel and the personnel met during the inspection, the panel conclude that the firm had not conducted the proper testing of Carbosol Hemodialysis Concentrate as per monograph of Ph. Eur.
The report is submitted for final decision by the Board.

Product Specific Inspection Report of the firm was conveyed vide letter dated 20-04-2023.

M/s Jassh Pharmaceuticals Submitted CAPA Report vide Ref. No. JP/QA/230502 dated 24-05-2023.

Following are the CAPA against the minor findings and observations (Major) of the inspection Committee

Sr. No.	Findings and observations of the inspection committee				Corrective and preventive actions taken by Jassh Pharma				
	Report Ref.	Issue		Issue rating	Reason/ Justification	CAPA	Target Date	Status	Evidence
1	1.5 & 2.1	Issues related to instrument	a. List of equipment (Annex-A) but not having	Major	As per Eu. Pharmacopeia apparatus for potentiationmetric	Automatic potentiometer has been arranged		Done	Annex I

			potentiometer. b. Potentiometer was not available at the time of inspection in QC Lab, which is required for testing of acetate as per Ph. Eur.		titration is an electronic device which comprises a voltmeter allowing reading in the millivolt and simply consist of an electrode attached with a digital device.				
					At the time of inspection Acetates were detected by method that is based on the aforementioned principle i.e. potentiometric titration but with pH meter that has ability to give reading in mVol. Ref. SOP # JP/QC/SOP/031				
2.	2.2 & 2.9	Issues related to analytical testing	The analysis of Carbosol Haemodialysis Concentrate 4000 litres was not as per Eur. Ph. monograph	Major	All test were performed as per Pharmacopeia having complete recommended instrumentation except acetates that were performed by Potentiometer.	As now QC has been equipped with potentiometer so this discrepancy has been rectified and the test methods for Carbosol HAemodialysis Concentrate have been updated as per Pharmacopeia. SOP # JP/QC/FG/C0201		Done	Ann
3	2.10	Issues related to documentation	Testing method mentioned on label is Eur. Ph., but not fully followed by the firm.	Major	All test were performed as per Pharmacopeia having complete recommended	Test methods for carbosol Haemodialysis Concentrate have been updated as		Done	

					instrumentation except acetates that were performed by Potentiometer.	per Pharmacopeia. SOP# JP/QC/FG/C0201		
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Following are the CAPA against the minor findings and observations (Minor) of the inspection Committee

Sr. No.	Findings and observations of the inspection committee				Corrective and preventive actions taken by Jassh Pharma				
	Report Ref.	Issue		Issue rating	Reason/ Justification	CAPA	Target Date	Status	Evidence
1.	2.5	Issues related to calibration	The measuring glass and cylinder were not calibrated by ISO certified firm.	Minor	Firm has contract with third party (Pakistan Scientific International) for calibration, in-house calibration as well performed by QA Department	Although the party shows its registration and business with Pharma industry but not registered through ISO hence we have decided to contract with new calibrating party,	30 th June 2023	In-Process	None
2.	2.6	Issues related to Instrumentation	The QC lab was not having FTIR	Minor	As per pharmacopeia, not required for any of raw materials used for the manufacturing of dialysis solutions, as these are all inorganic salts and FTIR is required for the identification of organic compounds	FTIR not required, not recommended by Pharmacopeia, as the type of raw materials used in manufacturing cannot be identified by FTIR		Done	BP monograph for all RM used in carbosol HD, i.e. 1 sodium chloride 2 potassium chloride 3. Magnesium chloride 4. Calcium chloride

3.	2.8	Issues related to Instrumentation	Karl Fischer apparatus/reagent is not available	Minor	As per pharmacopeia, not required for any of raw materials used for the manufacturing of dialysis solutions	Not required, not recommended by Pharmacopeia, as the type of raw materials used in manufacturing of dialysis solution do not require Karl Fischer apparatus. Moreover potentiometer that we have in lab can be modified as Karl Fischer when required, by changing its vessel and burette.	Done
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Personnel Hearing notice(s) issued to accused person(s).

Summary:

Manufacturing Date: 10-2019

Expiry Date: 09-2022

Sampling Date (Form 4): 19-02-2020

Sent to DTL (Form 6): 20-02-2020

Date of receipt in DTL: 20-02-2020

DTL Report Date: 20-04-2020

Time Extension: N/A

1ST DI Communication with firm on dated: 19-05-2020

Date of Retesting Request of Firm: Nil

Date of retesting Request: N/A

Investigation Report Dated: 11-06-2020

Case is placed before the Board for Decision.

CURRENT PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 19

PQCB/R-568/2018

Aroop Town, District Gujranwala

ATTENDENCE

Secretary DQCB	<u>Accused Persons involved in subject case</u> 1. M/S Star Laboratories Pvt. Ltd. 23-km, Multan Road, Lahore through its Chief Executive Officer Muhammad Israr H. Malik 2. Muhammad Israr H. Malik 3. Ubaid Mahmood Khan 4. Asifa Asghar 5. Sameer Ashfaq of M/S Star Laboratories Pvt. Ltd. 23-km, Multan Road, Lahore.
Drug Inspector	

BRIEF FACTS OF THE CASE

Provincial Inspector of drugs Aroop Town, District Gujranwala reported that:-

- His Predecessor, on 15-05-2018, inspected the premises of Director Livestock, Gujranwala and took sample of seven different types of drugs on Form No.04 for the purpose of test/analysis and sent the sample to Drug Testing Laboratory, Faisalabad.
- Three out of twelve drug samples, after test/analysis, were declared **Substandard** by Government Analyst, Drug Testing Laboratory, **Multan** as detailed below:

Name of drug	Batch No.	Name of manufacturer	DTL Report TRA No. & Date	DTL Test Report Results
Injection PRED CPM 50ML [Prednisolone 10 mg, Chlorpheniramine Maleate 4mg]	VD-254	M/S Star Laboratories Pvt. Ltd. 23-km, Multan Road, Lahore.	TRA No. 01-56000651/DTL Dated: 03-07-2018	Analysis with specifications applied: Manufacturer's Specifications Description: Milky liquid in glass vial sealed with rubber stopper and Aluminum seal. Assay: Prednisolone Stated: 10 mg/ ml Determined: 0.756 mg/ml Percentage: 7.564% (Does not comply)

				Limit: 90-110% Chlorpheniramine Maleate Stated: 4 mg/ml Determined: 3.99 mg/ml Percentage: 99.88% (Complies) Limit: 90-110% Sterility: Confirms to sterility RESULT: The above sample is “ Substandard ” on the basis of tests performed.
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- iii. Director Livestock, Gujranwala, provided invoice/ warranty/ no. 87 dated 16-02-2018 issued by M/S Star Laboratories Pvt. Ltd. 23-km, Multan Road, Lahore as a proof of its purchase of the said drug.
- iv. Warrantor portion of the drug sample was sent to M/S Star Laboratories Pvt. Ltd. 23-km, Multan Road, Lahore.
- v. A copy of test report of the drug sample was sent **to** M/S Star Laboratories Pvt. Ltd. 23-km, Multan Road, Lahore with directions to provide the requisite information and to explain their position in this regard. In response, firm requested for re-test/ analysis of their drug sample from Appellate Laboratory, National Institute of Health Sciences, Islamabad.
- vi. Pursuant to their request, the PQCB portion of the drug samples were sent to Appellate Laboratory, National Institute of Health Sciences, Islamabad for the purpose of retest/ analysis. These drug samples were declared **Substandard** from National Institute of Health Sciences, Islamabad as detailed below:

Name of drug	Batch No.	Name of manufacturer	NIH Report No. & Date	DTL Test Report Results
PRED CPM Injectable Suspension Veterinary	VD-254	M/S Star Laboratories Pvt. Ltd., Animal Healthcare Division 23-km, Multan Road, Lahore.	06-P/2019 dated 14 th March, 2019	Analysis with specifications applied: Manufacturer's Specifications Description: Segregated suspension having the particles settle on the base and the remaining solution is light milky which contained in amber colored labelled glass vial with grey flip off. (Does not comply

with manufacturer specification which states that PRED CPM injectable suspension is white to almost white color suspension free from extraneous matter filled in amber glass vial).

Identification:

Prednisolone acetate and Chlorpheniramine Maleate identified.

Volume:

Determined: 50ml

Limit: 50ml

Complies with the volume stated on label.

pH:

Determined: 4.60

Limit: 5.0-7.5

Does not comply with manufacturer specification

Sterility Test:

Sterile (Complies with manufacturers specifications)

Bacterial Endotoxin test:

Complies with manufacturer specifications

Assay:

	Stated	Found	Limit	Percentage
Prednisolone as acetate	10 mg/ml	4.34mg/ml	90-110%	43.40%
Chlorpheniramine Maleate	4mg/ml	3.6 mg/ml	90-110%	90.0%

Does not comply with manufacturer specification.

RESULT:

The sample is of “**Substandard**” quality on the basis of tests performed.

vii. A copy of NIH test report of the drug sample was sent to M/S Star Laboratories Pvt. Ltd. 23-km, Multan Road, Lahore with directions to provide the requisite information and to explain their

position in this regard.

2. Drug Inspector requested for grant of permission for prosecution against the accused persons nominated in the instant case who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended) and Rules framed there under by the way of: -

- a. **Manufacture for sale/ Sale of Substandard Drug.**
- b. **Issuance of false warranty.**

3. Show-cause was issued to accused person(s) vide dated 26-08-2022.

REPLY OF FIRM IN RESPONSE TO SHOWCAUSE NOTICE:

M/S Star Laboratories Pvt. Ltd., Animal Healthcare Division 23-km, Multan Road, Lahore submitted written reply stating that:

Respected Sir,

It is submitted that Pred CPM Batch No. 254 was supplied against Government Supply order at 5 different locations i-e.

- | | | |
|------------------------|----------------------|---------------------|
| <i>1. Muzzafargarh</i> | <i>2. Gujranwala</i> | <i>3. D.G. Khan</i> |
| <i>4. Multan</i> | <i>5. Sargodha</i> | |

Sample of above mentioned locations were sent for testing to DTL Multan, out of 5 samples, two samples i-e Multan & Sargodha were declared of standard quality while remaining 3 could not pass quality test.

Out of these 3 cases, one case i-e of DG Khan supplied portion has been forwarded to Drug Court Multan by PQCB for prosecution.

Sir since all three samples under consideration are of same product, same batch and from same origin and same testing laboratory, therefore you are hereby requested to please club all three reports

- 1. Multan TRA 01-56000651 dated: 03-07-2018 (Gujranwala)*
 - 2. Multan TRA 01-60002502 dated: 03-07-2018 (DG Khan)*
 - 3. Multan TRA 01-56000888 dated: 03-07-2018 (Muzzafargarh)*
- and proceed as a single case.*

Star Laboratories (Pvt.) Ltd strongly hope that your good self will consider our request.

Furthermore QC testing method/ record, alongwith other relevant documents are also attached as desired please.

Thanking you in anticipation and assuring our full cooperation

Personnel Hearing notice(s) issued to accused person(s).

Summary:

Manufacturing Date: 03-2018

Expiry Date: 03-2020

Sampling Date (Form 4): 15-05-2018

Sent to DTL (Form 6): 16-05-2018

Date of receipt in DTL: 21-05-2018

DTL Report Date: 03-07-2018

Time Extension: N/A

1ST DI Communication with firm on dated: 03-09-2018

Date of Retesting Request of Firm: 26-09-2018

Fate of retesting Request: Allowed (NIH Substandard)

Investigation Report Dated: 06-07-2022

Case is placed before the Board for Decision.

CURRENT PROCEEDINGS & DECISION BY THE BOARD:

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PQCB/R-726/2019

ATTENDANCE:

Secretary DQCB	<u>Accused Persons involved in subject case</u> 1. M/s Gallop water Sciences, 404-Sunder Industrial Estate, Raiwind Lahore-Pakistan, through its MD Ashfaq Ahmad Mehar 2. Ashfaq Ahmad Mehar Managing Director 3. Muhammad Khalil Quality Control Manager / Warrantor 4. Nazar Abbas Production Manager Of M/s Gallop Water Sciences, 404- Sunder Industrial Estate, Lahore-Pakistan
Drug Inspector	

Provincial Inspector of Drugs, Sheikh Zayed Hospital, Rahim Yar Khan reported that: -

- i. He, on 08-04-2019 inspected the M/s Central Pharmacy (Main Medicine Store) Sheikh Zayed Hospital Rahim Yar Khan and took sample of drug sample on Form No. 4 for the purpose of test and analysis.
- ii. Following drug sample, after test/analysis was declared as **Substandard** by Government Analyst, Drug Testing Laboratory, **Bahawalpur** as detailed below: -

Name of Drug	Batch No.	Name of Manufacturer	DTL Report	DTL Test Report Result
Infusion Gee-sol NS 0.9% w/v [Sodium Chloride 0.9 gm/100ml, 1000ml]	9C063	M/s Gallop Water Sciences, 404-Sunder Industrial Estate, Lahore-Pakistan	01-250003368/DTL dated: 03 June 2019	Result of test/ analysis with specifications applied: USP 2018 <u>COMPOSITION:</u> Sodium chloride 0.9gm/100ml, 1000ml <u>DESCRIPTION:</u> Colorless liquid in translucent plastic sealed bottle for IV infusion. Stated volume: 1000ml) <u>EXTRACTABLE VOLUME:</u> Determined: 1040ml Limit: NLT nominal 1000ml Does not comply with specifications <u>pH:</u> Determined: 6.000

				Limit; 6.0-7.5 <u>STERILITY:</u> The product is sterile. <u>ASSAY: NaCl</u> Stated: 0.9%wv Determined 0.9266%w/v Percentage 102.96% Limit: 95-105% <u>RESULT:</u> The sample is Sub-Standard on the basis of Physical Test i.e., Extractable volume Test.
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- iii. M/s Central Pharmacy (Main Medicine store) Sheikh Zayed Hospital Rahim Yar Khan provided invoice/warranty No. SOB-0001059 dated 19-3-2019 issued by M/s Faisal Pharma Muhammad Colony, 326/B, XI, Bahawalpur.
- iv. Warrantor Portion was sent to M/s Faisal Pharma Muhammad Colony, 326/B, XI, Bahawalpur.
- v. M/s Faisal Pharma Muhammad Colony, 326/B, XI, Bahawalpur provided invoice/warranty No. 18-01-0261 dated 18-3-2019 issued by M/s Gallop Water Sciences, 404- Sunder Industrial Estate, Lahore-Pakistan.
- vi. A copy of Test/ Analysis report was also sent to M/s Gallop Water Sciences, 404- Sunder Industrial Estate, Lahore-Pakistan and they were directed to provide requisite information in this regard.

2. Drug Inspector requested for grant of permission of prosecution against above mentioned accused persons who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended) / DRAP Act 2012 and Rules framed there under by the way of:

- i. **Manufacture for Sale / Sale of Substandard Drug**
- ii. **Issuance of false warranty**

Previous Proceeding:

The subject retesting request was considered in 213 meeting dated 15-11-2019. The firm requested to withdraw the application for retesting request of the subject sample from NIH. The Board approved the withdraw request of the firm.

3. Show cause notice(s) issued to the accused dated 17-12-2021

Firm submitted written reply of Show cause vide letter Ref: GWS/1-2022 dated 05-1-2022:

We the management of M/s Gallop Water Sciences hereby take opportunity to submit the "CURRENT STATUS" mentioned below:

1- We the representative of M/s Gallop Water Sciences appeared before the honourable members of the PQCB on 15-11-2019. 2-We have formally submitted (with reply letter in response to the PQCB Letter for submission of Evidence) the following detailed record at PQCB. Complete Batch Analysis Report (Physical & Chemical Analysis) Including, Calculations, Specifications, Method of Analysis with limits, Details of

IPQC tests performed on the subject batch and Test Performed/Results of QC retention sample/ warrantor portion of drug sample bearing the same batch number.

According to DTL report GEE- SOL NS 1000 ml (NORMAL SALINE 0.9%) Batch# 9C063

- The composition ok (Sodium Chloride 0.900g/100ml.1000ml
- Assay is 102.96% - (Limit is 95-105%).
- pH is 6.000 - (Limit is 6.0-7.5)
- The Sterility (Product is sterile) of the product: Complies the specifications
- EXTRACTABLE VOLUME:1040 ML (Limit: NLT Nominal Volume 1000 ML does not comply the specifications.)

It is worth mentioning here that the filled volume as per specification should be NOT LESS THAN 1000 MIL" and our product Complies the standard specifications.

Finally, we have checked the filled volume of the warrantor portion & retained samples and found them within the prescribed specifications.

3- At Gallop Water Sciences, Large volume Parenteral- (LVP- INFUSIONS) are filled on Automatic filling machine Weiler from USA- (Latest technology of Blow, Fill & Seal (BFS).

No Manual operation is conducted whereas the automatic machines have the filling precision / accuracy, However, we don't entirely rely only on the automatic machine's operation. Our Production department is continuously visualizing & monitoring the filled volume which is counter checked by the Quality Assurance Department Inspectors independently. All these activities of in process checking are recorded regularly.

Moreover, considering the filled volume on higher side throughout the batch is not practical, possible & feasible as the balance volume will definitely affect the manufacturing yield of the batch which is normal in this case i.e., 97.4%. We the Management of Gallop Water Sciences have previously challenged the report TRA No# 01-250003368/DTL Dated, June, 03, 2019 by the DRUGS TESTING LABORATORY Bahawalpur

It is worth mentioning here that we have requested the honourable members to take a lenient view (keeping in view the nature of the case) and drop the proceeding against the company.

During previous hearing of the case, we have been told the unavailability of the investigation report.

Now after more than two years of gap, (when the product has been expired, and it is of no use for anyone else), we have received a letter from your honour advising to submit the attested copies of all relevant documents, Copy of DML, Product Registration letter, the Names of the concerned professionals. Please find the same 1-Mr. Nazar Abbas. Manager Production CNIC: 32202- 8162342-9 2-Mr. Muhammad Khalil. Manager Q C & Warrantor CNIC:35202-2387229-9 3-Ashfaq Ahmed G.M Plant & Managing Director CNIC: 35202-3705859-1 Hoping to fulfill the requirements. We hereby request you to please drop the proceeding against the company at this stage.

4. Personal Hearing notice(s) issued to accused person(s) dated 15-2-2022

Case is placed before the Board for Decision

PROCEEDINGS & DECISION BY THE BOARD:

5. Case was considered by the Provincial Quality Control Board, under section 11 of the Drugs Act 1976 in its **239th meeting** held on **24-02-2022** under the chairmanship of Secretary Health Primary & Secondary Healthcare Department, Punjab, in the presence of Board members as mentioned above. Mr. Amjad Farooq, Secretary DQCB, Rahim Yar Khan and Mr. Ilyas Ahmed, Provincial Inspector of Drugs,

Sheikh Zayed Hospital Rahim Yar Khan was present along with the original case record. Among the nominated accused persons Ashfaq Mehar (Managing Director) of M/s Gallop Water Sciences, 404- Sunder Industrial Estate, Lahore-Pakistan appeared before the Board. He submitted that there was 2-5% of relaxation present in volume filling according to pharmacopoeia, whereas, filled volume as per specification should be Not less than 1000 ml and their product complies the standard specifications. They have checked the filled volume of the warrantor portion & retained samples and found it within the prescribed specifications. He added that Large volume parenteral (LVPs) are filled on Automatic filling machines which are calibrated and validated. He further submitted that considering the filled volume on slightly higher side throughout the batch is not practical and feasible as the manufacturing yield of the batch which is normal in this case i.e., 97.4%. The Assay of the NaCl was 103% which is within the limits. The product has been already expired. So, he requested to drop the proceedings against the company.

6. The Board after keen perusal of the case record and DTL report observed that the extractable volume as per report of the Government Analyst was found out to be 1040ml and after application of 2% of relaxation according to Pharmacopoeia the volume should be 1020ml i.e., 20ml is in excess. This shows that either the firm is not performing inprocess quality control test or the filling machines are not calibrated. The Board was of the considerate view that in order to dig out the root cause of this defect, the Production and Quality Control & Quality Assurance processes needs to be evaluated. Considering the forgoing facts, the Board after due deliberation and discussion decided to **pend** the case and constituted a committee comprising of the followings members in order to conduct Product Specific Inspection (PSI) of all large volume parenteral of the **M/s Gallop Water Sciences, 404-Sunder Industrial Estate, Lahore-Pakistan** with directions to committee to submit detailed inspections report for further consideration and decision by the Board.

1.	Prof. Dr Mehmood	Convener
2	Prof. Dr Jamshed	Member
3.	Secretary PQCB	Member

7 Committee submitted PSI report received in office of PQCB dated 05-05-2023

PRODUCT SPECIFIC INSPECTION REPORT OF M/S GALLOP WATER SCIENCES, 404-SUNDAR INDUSTRIAL ESTATE, LAHORE, PAKISTAN.

Panel Members:

Prof. Dr. Mehmood Ahmad

Prof. Dr. Muhammad Jamshaid

Sidra Saghir (Government Analyst)

Date of Inspection: 10-01-2023

Inspection was conducted with reference to Order dated 20-10-2022, and 24-02-2022 in Case No.11/M-251 and No. 09/M-239th respectively.

Drugs:

1. Injection Gee Water for Injection 5mL, Batch No. 21AA016, Manufacturing date: 01-2021, and Expiry date: 12-2022 declared Substandard on the basis of Oxidizable substances from DTL Faisalabad, vide test report no. 01-65000282/DTL dated 17-05-2021.
2. Infusion Gee sol NS 0.9%w/v (Sodium chloride 0.9gm/100mL, 1000mL), Batch No. 9C063, Manufacturing date: 03-2019, and Expiry date: 02-2021 declared Substandard on the basis of Extractable volume from DTL Bahawalpur, vide test report no. 01-250003368/DTL dated 03-06-2019.

Premises:

Total area: 73,494 square feet and covered area of 61,163 square feet comprising of Production, Warehouses, Quality Control, Quality Assurance, Research and Development, Engineering, Water Treatment Plant, Head office, HR & Admin Department.

Type of Products manufactured at site:

Large Volume Parenteral (L.V.P), Small Volume Parenteral (S.V.P), Ampoules in LDPE prepared aseptically and Ampoules sterilized terminally. 23 registered products, all are injectables.

Staff:

Designation	Person Name
Production Manager	Mr. Ahmad Kamal Mosa
GM Quality control	Mr. Muhammad Khalil

Batch processing record of specific product:

1. Injection Gee. Water for Injection 5mL

- a. BMR record: available
- b. Testing method: record available (TOC analyzer is in-use by the company, and company is of the view that we rely only on TOC test, and not on oxidizable test, however **QC report bearing oxidizable substances test is presented in BMR record provided by Manufacturer.**)
- c. Filling machine was automated, and regular volume checking record was available in BMR.

Observations:

- a. Calibration certificate of filling machine, and autoclaves are checked and found satisfactory.

- b. Operational Qualification report, Performance Qualification report of Bottle filling and sealing machine are available and found satisfactory.
- c. Record of products supplied in Govt supply is provided and no fail sample of respective products is found afterwards.
- d. Validation schedule of autoclaves, mixer tanks, automatic BFS machine is available and found satisfactory.
- e. SOP, Manual and Calibration/Validation record and schedule of TOC analyzer is available and found satisfactory.
- f. Record of Preventive maintenance for water treatment plant is available and satisfactory.
- g. DML and GMP reports are available and found satisfactory.
- h. Filling Capacity of BFS for LVP is 1000 bottle/hour, SVP is 1500 bottle /hour and of ampoules is 8000 ampoules/hour.
- a. Annual shut down and complete maintenance procedure is done by the company.
- j. RO plant has a capacity of 3000L/hour, with 2000/L for water for injection, and a storage capacity of 10000L.
- k. **SOP for QC testing of Gee-H₂O 5mL is provided which covers TOC test but not oxidizable substances test, however water treatment plant verification/validation record again contains test report bearing oxidizable substances test.**
- ax. %RSD of sample run 4 times in TOC analyzer is done and then sample reading is taken.

Findings:

- i. Curtains in Dispensing room should be overlapped.
- ii. Optical checking is done by a single person only.
- iii. Segregation of area for optical checking and dispatch should be done as there is single hall for both operations.
- iv. Pass through windows are available for material transfer from one section to other and some of them are not working properly, as there is gap when completely closed, and some were not closing properly.

Conclusion:

The above-mentioned findings must be rectified/improved by the manufacturer.

Oxidizable substances test is not removed by USP, and is still part of monograph of sterile water for injection USP. The test results are available in BMR record.

The report is submitted to the honorable Board for final decision

8. PSI report was sent to M/s Gallop Water Science vide letter dated 12-05-2023

9. In response Firm submitted **CAPA** vide letter Ref: GWS/PQCB/6-23 dated 09-06-2023 received in office of PQCB dated 12-05-2023

"CORRECTIVE AND PREVENTIVE ACTIONS" (CAPA)

We have been advised to submit our response regarding "CORRECTIVE AND PREVENTIVE ACTIONS" (CAPA) taken in lieu of the observations made by the Honorable Members of the Inspection committee, constituted by PQCB (with reference to order dated 20-10-2022 and 24-02-

2022 in case No.11/M-251 and No .09/M-239th respectively.)

We are highly thankful to PQCB for constituting the panel for Product Specific inspection. We also highly appreciate the respected members of Inspection team for identification of the problems and also guiding our qualified staff for the rectification of problems and methodology for its improvement.

We have managed to rectify/ complete all the findings mentioned in the report its true spirit for all the tasks pointed out by the worthy members.

A complete and detailed report of CAPA is also being enclosed as advised.

We assure you Sir, that the management and the technical staff are committed to follow cGMP compliance.

We the members of QA/ QC Gallop Water Sciences also assure you that we will be strictly following cGLP, CGDP & cGSP.

We also assure your honor to adopt both the tests required for Oxidizable substances simultaneously as per USP monograph, as advised by the worthy members of the Panel.

We the management of M/S Gallop Water Sciences would like to request your honour and the Honorable members of PQCB to drop the cases for the following products (under Observations) against the company.

1. Injection Gee- H2O 5ml (Water for Injection) Batch # 21AA016 Manufacturing date: 01-2021 and Expiry Date 12-2022 declared substandard by DTL Faisalabad, vide test report # 01-65000282/DTL dated 17-05-2021
2. Infusion Gee-Sol NS 0.9% w/v (Sodium Chloride 0.9 gm/100ml, 1000 mL) Batch# 9C 063, Manufacturing date 03-2019 and Expiry date: 02-2021 declared Substandard on the basis of extractable volume from DTL Bahawalpur, vide test report # 01-250003368/DTL dated 03-06-2019.

CAPA Report for PSI of Gallop Water Science by Panel Members of PQCB on 10-01-2023

S. No	CAPA #	Observations	Corrective/preventive Action	Phase I Compliance date	CAPA Effectiveness Remarks
Warehouse					
1	CAPA/23-001	Curtains in dispensing room should be overlapped	Curtains installed as advised by panel of inspection	Till June 07 th , 2023	Done
Production					
2	CAPA/23-002	Optical checking is	Optical checking staff, increased up to four	Till June 07 th , 2023	Done

		done by a single person only.	members & they are on training now a days.		
3	CAPA/23-003	Segregation of area for optical checking and dispatch should be done as there is single hall for both operations.	Separators have been placed for proper segregation in optical checking & Packing area	Till June 07 th , 2023	Done
4	CAPA/23-004	Pass through windows are available for material transfer from one section to other and some of them are not working properly, as there is gap when completely closed, and some were not closing properly.	Maintenance required. Job order initiated immediately. Engineering department committed to perform it within a week.	Till June 07 th , 2023	Maintenance Done

10. Personal Hearing notice(s) issued to accused person(s)

Case is placed before the Board for Decision

CURRENT PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 21**PQCB/R-54/2023****Services Hospital, Lahore****ATTENDENCE**

Secretary DQCB	<u>Accused Persons involved in subject case</u> 1. M/s Bosch Pharmaceuticals Pvt Ltd., Sector 23 Korangi Industrial Area Karachi, Pakistan through its Managing Director Sheikh Mohiuddin Chawla. 2. Sheikh Mohiuddin Chawla Managing Director/ Warrantor 3. Amir Shadmani Production Incharge 4. Imran Ali Qureshi Quality Control Incharge Of M/s Bosch Pharmaceuticals Pvt Ltd., Sector 23 Korangi Industrial Area Karachi, Pakistan.
Drug Inspector	

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Services Hospital, Lahore reported that:

- He, on 26-01-2023, inspected the premises of medicine store of Services Hospital, Lahore, and took following drug sample on Form No. 04 for the purpose of test/analysis and sent to DTL, Lahore vides memorandum no. 155243 dated 26-01-2023.
- Following drug samples after test/analysis were declared as **Substandard** by Government Analyst Drug Testing Laboratory **Lahore**, as detailed below:

Name of Drug	Batch No.	Name of Manufacturer	DTL Report TRA No. & Date	DTL Test Report Result
Infusion Izilon 400mg/250ml [Each 250ml vial contains: Moxifloxacin Hydrochloride eq to Moxifloxacin 400mg] Mfg date: 01-2023 Exp. Date:	IL230046	M/S Bosch Pharmaceuticals Pvt Ltd., Sector 23 Korangi Industrial Area Karachi-Pakistan	01-177004382/DTL Dated 09-04-2023	Analysis with specifications applied: MS <u>DESCRIPTION:</u> Greenish yellow colored liquid in transparent glass infusion bottle with rubber stopper, aluminum seal and green colored flip off cover, label pasted on bottle. Claimed volume: 250ml <u>pH:</u> Determined: 4.6 at 24.6°C Limit: 4.1-4.6 at 25°C <u>FILLED VOLUME:</u> LIMIT: 250-260ml Determined: 245ml Does not comply

12-2024				<u>IDENTIFICATION:</u> The retention time of major peak in the sample chromatogram corresponds to the retention time of the major peak in standard chromatogram. (Moxifloxacin HCl identified) <u>ASSAY:</u> Moxifloxacin Stated 400mg/250ml Determined 425.68 mg/250ml Percentage 106.42% Limit 90-115% <u>STERILITY:</u> The product is sterile. <u>BACTERIAL ENDOTOXIN:</u> the product complies the limit of NMT 0.87EU/mg <u>RESULT:</u> The sample is <u>Substandard</u> on the basis of filled volume performed as per MS
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- iii. Store keeper Services Hospital, Lahore provided Invoice/Warranty No. 2322010099 dated 20-01-2023 issued by M/S Bosch Pharmaceuticals Pvt Ltd., Sector 23 Korangi Industrial Area Karachi-Pakistan as a proof of its purchase.
- iv. Warrantor portion of drug sample was sent to M/S Bosch Pharmaceuticals Pvt Ltd., Sector 23 Korangi Industrial Area Karachi-Pakistan.
- v. A Copy of test/analysis report was sent to M/S Bosch Pharmaceuticals Pvt Ltd., Sector 23 Korangi Industrial Area Karachi-Pakistan with directions to explain their position and provide requisite information in this regard.

2. Drug Inspector requested for grant of permission of prosecution against above mentioned accused persons who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended) / DRAP Act 2012 and Rules framed there under by the way of:

- i. **Manufacture for sale/ sale of Substandard drug**
- ii. **Issuance of false invoice/warranty**

Summary:

Manufacturing Date: 01-2023

Expiry Date: 12-2024

Sampling Date: 26-01-2023

Sent to DTL (Form 6): 26-01-2023

Date of receipt in DTL: 26-01-2023

DTL Report Date: 09-04-2023 (74 days-Time Barred report)

Time extension granted: 259-M dated 18-04-2023

1ST DI Communication with firm on dated: 17-4-2023

Date of Retesting Request of Firm: No

Investigation Report Dated: 10-05-2023

3. Show-cause notice(s) issued to the accused dated 07-06-2023

Firm submitted reply of Show cause vide letter Ref No. SCMR&Os/221-223/130623/A dated 13-06-2023

With reference to your letter No. PQCB/R-54/2023, dated 07-06-2023, addressing to Pharmaceuticals (Pvt.) Ltd. Karachi, Chief Executive Officer, Production Incharge. Quality Control Incharge and Warrantor regarding above cited subject received on 12-06-2023 against test report No. TRA # 01-177004382/DTL, Lahore dated 09-04-2023, purporting to declare sample of Infusion Izilon 400 mg / 250 ml, Bateh No. IL230046, as Sub-standard by the Government Analyst Drug Testing Laboratory, Lahlhore. Drug was supplied to Services Hospital Lahore against invoice No. 2322010099, dated 20-01-2023, with total quantity 1738 bottles.

As required, we submit our explanation as follows: -

That we have submitted our explanation through letter Ref. No. Ref: sCMRA&OS221-223 /28042023, dated: April 28, 2023, received in the office of the Drug Inspector Services Hospital, Lahore on 02-05-2023.

i) That the only reason of sub-standard is filled volume of infusion which is 245 ml against limits of 250 - 260 ml. However, all other tests like Physical description, pH, Identification, Assay of Moxifloxacin, Sterility and Bacterial Endotoxin tests are complies with the specification.

ii) The target filled volume is 255 ml whereas limit is 250- 260 ml according to the U.S.P chapter <697> CONTAINER CONTENT FOR INJECTIONS. It is clearly mentioned in the said chapter that "**Alternatively the volume of the content in ml may be calculated as the mass, in g, divided by density**" Each container of an injection is filled with a volume in slight excess of the labeled size" or the volume that is to be withdrawn. The excess volume recommended in the accompanying table are usually sufficient to permit withdrawal and administration of the labeled volumes.

iii) That the stated result is probably a deviation and error of reading or physical mishandling of the testing methodology and thus cannot be accepted as a normal out of specification (OOS) result without through investigation and rechecks etc.

iv) That despite the test report of DTL, Lahore, we have as an abundant precaution rechecked / retested our reference laboratory sample and warrantor portion for the test of filled volume and have found the same with in the specified limits of 250 ml to 260 ml and of Standard Quality.

v) We attach herewith the readings (In process sheet) of test report of filled volume carried out by us at the time of filling and on warrantor portion dated 28-04-2023 which clear the doubt of filled volume and quality of the drug.

vi) That in view of the undeniable and established fact of the test reports of DTL, Lahore being incompetent and

inaccurate as regards to test performed, there is no basis, justification or propriety in declaring the samples sub-standard; or, for any further proceedings or actions in such regards.

In the circumstances, we request the Honorable Board to kindly withdraw your notice forthwith and formally closed the case.

4. Personal Hearing notice(s) issued to accused person(s)

Case is placed before the Board for Decision

PROCEEDINGS & DECISION BY THE BOARD:

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PQCB/R-695/2020

ATTENDANCE

BRIEF FACTS OF THE CASE

- i. His predecessor, on 29-01-2020, inspected the business premises of M/s Qammar Medical Store, situated at Near Shairwala Choubara, Tehsil Bhowana, District Chiniot, took following drug sample on Form No.04 for the purpose of test/analysis and sent to Drug Testing Laboratory Faisalabad vide memorandum no. 57400 dated 31-01-2020
- ii. The following drug sample after test/analysis was declared as **Substandard** by Government Analyst Drug Testing Laboratory **Faisalabad**, as detailed below:

Name of drug	Batch no.	Name of manufacturer	DTL Report No. & Date
Sustained/ Extended Release Tablet. Cyclofen-SR [each tablet contains: Diclofenac Sodium 100mg] Mfg Date Expiry Date Regn No. Dec 2018 Dec 2020 054592	TA1071	M/S Danas Pharmaceuticals (Pvt.) Ltd., , 312-Industrial Triangle, Kahuta Road, Islamabad-Pakistan.	01-68002425/DTL dated 30-03-2020
DTL Test Report Results			

Analysis with specifications applied: USP 2019**DETAIL RESULT OF TEST/ANALYSIS:**

DESCRIPTION: Pink colored, round shape biconvex tablets contained in ALU-PVC blister of 10's packed in outer hard carton.

IDENTIFICATION: Diclofenac sodium is identified.

ASSAY:

Stated: 100 mg/ Tablet **Determined:** 101.613 mg/ Tablet **Percentage:** 101.613% (Complies) Limit: 90 – 110 % (USP 2019)

DISSOLUTION TEST: Does not comply with the USP 2019 Test 2 as detailed below:

Tolerance Limit: The percentage of the labeled amount of diclofenac sodium dissolved at the times specified conform to the amount dissolved stated in table below

LEVEL	NUMBER TESTED	ACCEPTANCE CRITERIA						AVERAGE	REMARKS
L ₁	6	No individual value lies outside each of the stated ranges and no individual value is less than the stated amount at the final test time.						L ₁	Does Not Comply
TIME	AMOUNT DISSOLVED	UNIT 1	UNIT 2	UNIT 3	UNIT 4	UNIT 5	UNIT 6		
1 st Hour	NMT 28%	72.77%	69.74%	47.91%	64.00%	51.63%	66.47%		
2 nd Hour	20 – 40%	84.13%	79.63%	67.37%	74.80%	79.86%	80.87%		Does Not Comply
4 th Hour	35 – 60%	81.77%	79.97%	81.88%	82.45%	83.23%	82.22%		Does Not Comply
6 th Hour	50 – 80%	84.69%	81.43%	84.58%	84.81%	84.81%	84.81%		Does Not Comply
10 th Hour	NLT 65%	86.72%	88.63%	85.14%	85.26%	89.76%	85.26%		Complies
L ₂	6	The average value of the 12 units (L ₁ +L ₂) lies within each of the stated ranges and is NLT the stated amount at the final test time; none is more than 10% labeled content outside each of the stated ranges; and none is >10% of the labeled content below the stated amount at the final test time.						L ₁ + L ₂	

	TIME	AMOUNT DISSOLVED	UNIT 7	UNIT 8	UNIT 9	UNIT 10	UNIT 11	UNIT 12	55.32%	
	1 st Hour	NMT 28%	50.98%	51.82%	41.60%	45.38%	52.80%	48.74%	68.01%	Does Not Comply
	2 nd Hour	20 – 40%	60.22%	59.10%	62.60%	50.84%	56.16%	60.50%	78.89%	Does Not Comply
	4 th Hour	35 – 60%	75.07%	74.51%	84.45%	67.93%	74.93%	78.29%		Does Not Comply
	6 th Hour	50 – 80%	99.72%	98.46%	99.44%	102.10%	99.16%	82.77%	90.56%	Does Not Comply
	10 th Hour	NLT 65%	104.76%	105.32%	109.38%	104.76%	103.92%	102.52%	95.95%	Complies
	L3	12	The average value of the 24 units (L1+L2+L3) lies within each of the stated ranges and is NLT the stated amount at the final test time; NMT 2 of the 24 units are more than 10% of labeled content outside each of the stated ranges; NMT 2 of the 24 units are >10% of labeled content below the stated amount at the final test time; and none of the units are >20% of labeled content outside each of the stated ranges or >20% of the labeled content below the stated amount at the final test time.						L ₁ + L ₂ +L ₃	
	TIME	AMOUNT DISSOLVED	UNIT 13	UNIT 14	UNIT 15	UNIT 16	UNIT 17	UNIT 18		
	1 st Hour	NMT 28%	52.04%	73.98%	54.57%	53.45%	51.20%	51.48%		
	2 nd Hour	20 – 40%	68.07%	79.89%	66.11%	54.85%	64.56%	67.37%		
	4 th Hour	35 – 60%	84.67%	84.25%	87.63%	70.33%	85.52%	85.66%		
	6 th Hour	50 – 80%	101.97%	103.66%	102.11%	95.36%	98.17%	91.00%		
	10 th Hour	NLT 65%	107.18%	108.86%	106.19%	102.53%	105.07%	106.19%		
	TIME	AMOUNT DISSOLVED	UNIT 19	UNIT 20	UNIT 21	UNIT 22	UNIT 23	UNIT 24		

1 st Hour	NMT 28%	67.50%	78.73%	58.62%	77.60%	79.85%	58.18%	59.21%	Does Not Comply
2 nd Hour	20 – 40%	81.09%	85.02%	66.15%	87.60%	87.82%	67.83%	70.52%	Does Not Comply
4 th Hour	35 – 60%	90.18%	86.81%	80.30%	90.07%	88.95%	90.18%	82.14%	Does Not Comply
6 th Hour	50 – 80%	92.20%	88.05%	84.68%	90.97%	91.42%	91.19%	92.40%	Does Not Comply
10 th Hour	NLT 65%	99.73%	90.30%	85.02%	91.98%	92.32%	92.20%	97.46%	Complies

RESULT: The above sample is **Sub-Standard** on the basis of Dissolution Test.

- iii. Proprietor of M/s Qammar Medical Store, situated at Near Shairwala Choubara, Tehsil Bhowana, District Chiniot provided invoice/warranty bearing No. 2006 dated 15-05-2019 issued by M/s Akram Traders, situated at Yousaf Shah Road Jhang Sadar as a proof of its purchase.
- iv. Warrantor portion of drug sample was sent to M/s Akram Traders, situated at Yousaf Shah Road Jhang Sadar.
- v. A copy of test/analysis report was sent to M/s Akram Traders, situated at Yousaf Shah Road Jhang Sadar with directions to explain their position and provide requisite information in this regard. M/s Akram Traders, situated at Yousaf Shah Road Jhang Sadar, provided invoice/warranty bearing No. 28517 dated 13-02-2019 issued by M/s Harmain Traders situated at First Floor, Al Hayat Medicine Market Namak Mandi Peshawar as a proof of its purchase.
- vi. A copy of test/analysis report was sent to M/s Harmain Traders situated at First Floor, Al Hayat Medicine Market Namak Mandi Peshawar with directions to explain their position and provide requisite information in this regard. M/s Harmain Traders situated at First Floor, Al Hayat Medicine Market Namak Mandi Peshawar, finally provided invoice/warranty bearing No. WAR-HT-01 dated 21-01-2019 issued by M/s Danas Pharmaceuticals (Pvt.) Ltd., 312-Industrial Triangle, Kahuta Road, Islamabad-Pakistan as a proof of its purchase.
- vii. A copy of test/analysis report was sent to M/S Danas Pharmaceuticals (Pvt.) Ltd., 312-Industrial Triangle, Kahuta Road, Islamabad-Pakistan with directions to explain their position and provide requisite information in this regard. In response, the firm challenged the test/analysis report of the drug sample and requested to re-test the above-mentioned drug sample from Appellate Laboratory, National Institute of Health, Islamabad.
- viii. **Pursuant to firm's retesting request the Provincial Quality Control Board in its 222nd meeting held on 15-07-2020 allowed to send the drug sample to NIH, Islamabad for retesting, from where the sample was declared Substandard as detailed below:**

Name of Drug	Batch No.	Name of Manufacturer	NIH Test Report No.	NIH Test Report Result
Cyclofen SR 100 Tablets	TA1071	M/s Danas Pharmaceuticals (Pvt.) Ltd., 312-	0136-P/2020 dated 09-10-2020	Analysis with specifications applied: United States Pharmacopoeia-39

	Industrial Triangle, Kahuta Road, Islamabad-Pakistan.	<u>DESCRIPTION:</u> Pink colored, circular, biconvex, coated tablets packed in blister packing further contained in an outer carton. <u>IDENTIFICATION:</u> Diclofenac sodium identified. <u>WEIGHT VARIATION:</u> Complies with USP-39. <u>DISSOLUTION TEST:</u> <table><tr><td></td><td>Determined</td><td>Limit</td></tr><tr><td>After 1 hour</td><td>58.77%</td><td>Not more than 28%</td></tr><tr><td>After 2 hours</td><td>79.92%</td><td>20 – 40%</td></tr><tr><td>After 4 hours</td><td>82.35%</td><td>35 – 60%</td></tr><tr><td>After 6 hours</td><td>90.67%</td><td>50 – 80%</td></tr><tr><td></td><td colspan="2">Does not comply with USP-39</td></tr></table> <u>ASSAY:</u> <table><tr><td>Assay</td><td>Stated</td><td>Found</td><td>Limit</td><td>Percentage</td></tr><tr><td>Diclofenac sodium</td><td>100mg/ Tablet</td><td>106.25mg/ Tablet</td><td>90-110%</td><td>106.25%</td></tr><tr><td colspan="5">Complies with USP-39.</td></tr></table> <u>CONCLUSION:</u> The sample is of <u>Sub-Standard</u> quality on the basis of the tests performed.		Determined	Limit	After 1 hour	58.77%	Not more than 28%	After 2 hours	79.92%	20 – 40%	After 4 hours	82.35%	35 – 60%	After 6 hours	90.67%	50 – 80%		Does not comply with USP-39		Assay	Stated	Found	Limit	Percentage	Diclofenac sodium	100mg/ Tablet	106.25mg/ Tablet	90-110%	106.25%	Complies with USP-39.				
	Determined	Limit																																	
After 1 hour	58.77%	Not more than 28%																																	
After 2 hours	79.92%	20 – 40%																																	
After 4 hours	82.35%	35 – 60%																																	
After 6 hours	90.67%	50 – 80%																																	
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Assay	Stated	Found	Limit	Percentage																															
Diclofenac sodium	100mg/ Tablet	106.25mg/ Tablet	90-110%	106.25%																															
Complies with USP-39.																																			

2. The Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused person(s), who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended), DRAP Act 2012 and Rules framed there under by the way of:

M/s Danas Pharmaceuticals (Pvt.) Ltd., 312-Industrial Triangle, Kahuta Road, Islamabad-Pakistan	a. Manufacture for sale/ Sale of Substandard drug b. Issuance of false warranty
M/s Harmain Traders situated at First Floor, Al Hayat Medicine Market Namak Mandi	a. Distribution for sale/ Sale of Substandard drug b. Issuance of false warranty

Peshawar	
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3. Show-cause notice(s) issued to accused person(s) dated 08-12-2022
4. Personal hearing notice(s) issued to accused person(s) dated 19-06-2023
5. Case is placed before the Board for decision.

Summary:

Manufacturing Date: Dec-2018

Expiry Date: Dec-2020

Sampling Date (Form 4): 29-01-2020

Sent to DTL (Form 6): 31-01-2020

Date of receipt in DTL: 06-02-2020

DTL Report Date (Form 7): 30-03-2020

Time Extension: Not Time Barred

1st DI Communication with firm on dated: 13-04-2020

Retesting Request of the Firm: Yes (21-04-2020)

Fate of Retesting Request of the Firm: Allowed in 222nd Meeting dated 15-07-2020

NIH Test Result: Substandard (Report Date: 09-10-2020)

Investigation Report Dated: 17-09-2022

PROCEEDINGS & DECISION BY THE BOARD:

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PQCB/R-113/2020

ATTENDANCE

BRIEF FACTS OF THE CASE

- i. Her predecessor, on 28-11-2019, inspected the premises of Main Medicine Store of Lahore General Hospital, Lahore, took sample of below-mentioned drug on Form-4 for the purpose of test/analysis and sent the sample to Drug Testing Laboratory, Lahore vide memorandum no. 52584 dated 28-11-2019.
- ii. The subject drug sample after test/ analysis was declared **Substandard** by Government Analyst, Drug Testing Laboratory, **Lahore** as detailed below:

Name of Drug	Batch No.	Name of Manufacturer	DTL Report No. & Date	DTL Test Report Result
Infusion. ZEESOL-NS [SODIUM CHLORIDE 0.9%] Mfg Date Oct 2019 Expiry Date: Sep 2022	910405	M/S Shazeb Pharmaceutical Industries Limited Hazara Trunk Road, Sarai Gadaee Distt Haripur, KPK, Pakistan.	01- 147000303/DTL Dated 24-01- 2020	Analysis with specifications applied: BP 2019 <u>PHYSICAL DESCRIPTION:</u> COLOURLESS LIQUID FOR INFUSION IN TRANSPARENT SEALED PLASTIC INFUSION BOTTLE WITH NO LEAKAGE. CLAIMED VOLUME = 1000 ML <u>pH:</u> Limits: 4.5 – 7.0 Determined: 5.83 (MS) <u>ASSAY OF SODIUM CHLORIDE</u>

Regn No. 016609																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																	
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- iii. Store keeper of Main Medicine Store of Lahore General Hospital, Lahore provided invoice/warranty no. 0520 dated 26-11-2019 issued by M/s Shazeb Pharmaceutical Industries Limited Hazara Trunk Road, Sarai Gadaee District Haripur, KPK, Pakistan as a proof of its purchase.
- iv. Warrantor portion of the drug sample was sent to M/s Shazeb Pharmaceutical Industries Limited Hazara Trunk Road, Sarai Gadaee District Haripur, KPK, Pakistan.
- v. A copy of test report was sent to M/s Shazeb Pharmaceutical Industries Limited Hazara Trunk Road, Sarai Gadaee District Haripur, KPK, Pakistan with directions to explain their position and provide requisite information in this regard. In response, the firm challenged the test/analysis report and requested to re-test the above mentioned drug sample from Appellate Laboratory, National Institute of Health, Islamabad.
- vi. Pursuant to the request of M/s Shazeb Pharmaceutical Industries Limited Hazara Trunk Road, Sarai Gadaee District Haripur, KPK, Pakistan the retesting request of the subject drug sample

was considered in the 16th Committee Meeting of the Board held on 16-06-2021 and the subject drug sample was sent to NIH, Islamabad, from where the sample was declared **Sub-standard** as detailed below:

Name of Drug	Batch No.	Name of Manufacturer	NIH Report No.	NIH Test Report Result										
Zeesol-NS Infusion	910405	M/s Shazeb Pharmaceutical Industries Limited Hazara Trunk Road, Sarai Gadaee District Haripur, KPK, Pakistan.	No.0251-P/2021 dated 12-08-2021	Analysis with specifications applied: British Pharmacopoeia-2017 DESCRIPTION: Clear colourless liquid contained in labelled translucent plastic infusion bottle. IDENTIFICATION: Sodium chloride identified. VOLUME: Determined: 1000ml Limit: 1000ml Complies with volume stated on the label. STERILITY TEST: Sterile. Complies with B.P-2017. BACTERIAL ENDOTOXIN TEST: Free from Bacterial Endotoxins Complies with B.P-2017. ASSAY: <table border="1"> <thead> <tr> <th>Assay</th><th>Stated</th><th>Found</th><th>Limit</th><th>Percentage</th></tr> </thead> <tbody> <tr> <td>Sodium Chloride</td><td>9gm/1000ml</td><td>7.205g/1000ml</td><td>95-105%</td><td>80.062%</td></tr> </tbody> </table> Does not comply with B.P-2017. Result: The sample is of Sub-Standard quality on the basis of the tests performed.	Assay	Stated	Found	Limit	Percentage	Sodium Chloride	9gm/1000ml	7.205g/1000ml	95-105%	80.062%
Assay	Stated	Found	Limit	Percentage										
Sodium Chloride	9gm/1000ml	7.205g/1000ml	95-105%	80.062%										

2. The Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused person(s), who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended), DRAP Act 2012 and Rules framed there under by the way of:

- Manufacture for sale /Sale of Substandard drug**
- Issuance of false warranty**

3. Show-cause notice(s) issued to accused person(s) dated 08-12-2022
4. Personal hearing notice(s) issued to accused person(s) dated 19-06-2023
5. Case is placed before the Board for decision.

Summary:

Manufacturing Date: Oct-2019

Expiry Date: Sep-2022

Sampling Date (Form 4): 28-11-2019

Sent to DTL (Form 6): 28-11-2019

Date of receipt in DTL: 29-11-2019

DTL Report Date (Form 7): 24-01-2020

Time Extension: Not Time Barred

1st DI Communication with firm on dated: 12-02-2020

Retesting Request of the Firm: Yes (25-02-2020)

Fate of Retesting Request of the Firm: Allowed in 16th Committee Meeting dated 16-06-2021

NIH Test Result: Substandard (Report Date: 12-08-2021)

Investigation Report Dated: 16-11-2022

PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 24**PQCB/R-715/2020****Tehsil Phalia, District Mandi Bahauddin****ATTENDANCE**

Secretary DQCB	<u>Accused Persons involved in subject case</u>
Drug Inspector	1. M/s Trigon Pharmaceuticals (Pvt) Ltd., 8-km Thokar Raiwind Road, Raiwind Lahore-Pakistan through its Chief Executive Officer, Muhammad Safdar. 2. Muhammad Safdar Chief Executive Officer 3. Imran Mehmood Production Manager 4. Muhammad Umer Quality Control Manager/Warrantor of M/s Trigon Pharmaceuticals (Pvt) Ltd., 8-km Thokar Raiwind Road, Raiwind Lahore-Pakistan.

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Tehsil Phalia, District Mandi Bahauddin reported that: -

- His predecessor, on 18-03-2020, inspected the business premises of M/s Faizan Medical Store, Old Gujrat Road near Allied Bank Phalia, District Mandi Bahauddin, took following drug sample on Form No.04 for the purpose of test/analysis and sent to Drugs Testing Laboratory Faisalabad vide memorandum no. 61461 dated 24-03-2020
- The sample after test/analysis was declared as **Substandard** by Government Analyst Drug Testing Laboratory **Faisalabad**, as detailed below:

Name of Drug	Batch No.	Name of Manufacturer	DTL Report No. & Date	DTL Test Report Result
Suspension. Fenober 90ml [Each 5ml contains: Ibuprofen 100mg] Mfg Date: Dec 2019 Expiry Date: Nov 2021	FR-006	M/S Trigon Pharmaceuticals (Pvt) Ltd., 8-km Thoker Raiwind Road, Raiwind Lahore-Pakistan.	01-68003642/ DTL Dated 03-06-2020	Analysis with specifications applied: USP 2019 <u>DESCRIPTION:</u> Orange colored suspension with fruity smell filled in amber colored plastic bottle sealed with white colored metallic cap packed in hard outer carton. <u>IDENTIFICATION:</u> Ibuprofen identified. <u>ASSAY:</u> Stated: 100 mg/ 5ml Determined: 46.434 mg/ 5ml Percentage: 46.434% (Does Not Comply) Limit: 90–110 % (USP 2019)

Regn No. 042738				pH: Stated: 3.6 – 4.6 (USP 2019) Determined: 4.28 (Complies) RESULT: <u>Given sample is Sub-Standard.</u> <u>with regards to Assay.</u>
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- iii. M/s Faizan Medical Store, Old Gujrat Road near Allied Bank Phalia, District Mandi Bahauddin provided invoice/ warranty bearing No. 13730 dated 16-03-2020 issued by M/s Ali Medicine Distributor, Wapda Colony, Mandi Bahauddin as a proof of its purchase.
- iv. Warrantor portion of drug sample and a copy of test/analysis report was sent to M/s Ali Medicine Distributor, Wapda Colony, Mandi Bahauddin who provided invoice/warranty bearing no. WR/03/22 dated 11-03-2020 issued by M/s Trigon Pharmaceuticals (Pvt) Ltd., 8-km Thokar Raiwind Road, Lahore-Pakistan as a proof of its purchase.
- v. A copy of test/analysis report was sent to M/S Trigon Pharmaceuticals (Pvt) Ltd., 8-km Thokar Raiwind Road, Lahore-Pakistan with directions to explain their position and provide requisite information in this regard.

2. The Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused person(s), who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended), DRAP Act 2012 and Rules framed there under by the way of:

a. **Manufacture for sale /Sale of Substandard drug**

b. **Issuance of false warranty**

3. Show-cause notice(s) issued to accused person(s) dated 09-01-2023
4. Personal hearing notice(s) issued to accused person(s) dated 19-06-2023
5. Case is placed before the Board for decision.

Summary:

Manufacturing Date: Dec-2019

Expiry Date: Nov-2021

Sampling Date (Form 4): 18-03-2020

Sent to DTL (Form 6): 24-03-2020

Date of receipt in DTL: 08-04-2020

DTL Report Date (Form 7): 03-06-2020

Time Extension: Not Time Barred

DI Communication with firm on dated: 18-12-2020

Retesting Request of Firm: NA

Investigation Report Dated: 14-11-2022

PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 25

PQCB/R-771/2019

Tehsil Phalia, District Mandi Bahauddin

ATTENDENCE

Secretary DQCB	<u>Accused Persons involved in subject case</u>
Drug Inspector	1. M/s Venus Pharma, 23-Km, Multan Road, Lahore-Pakistan through its Managing Partner, Pervaiz Iqbal Siddique 2. Pervaiz Iqbal Siddique Managing Partner/ Warrantor 3. Malik Muhammad Asif Production Incharge 4. Adnan Tahir Quality Control Incharge of M/s Venus Pharma, 23-Km, Multan Road, Lahore-Pakistan.

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Tehsil Phalia & District Mandi Bahauddin reported that: -

- His predecessor, on 28-08-2019, inspected the business premises of M/s Faizan Medical Store, old Gujrat Road near Allied Bank Phalia, District Mandi Bahauddin, took following drug sample on Form No.04 for the purpose of test/analysis and sent to Drug Testing Laboratory Faisalabad vide memorandum no. 47962 dated 31-08-2019.
- The subject drug sample after test/analysis was declared as **Substandard** by Government Analyst Drug Testing Laboratory **Faisalabad**, as detailed below:

Name of Drug	Batch No.	Name of Manufacturer	TRA No. & Date	DTL Test Report Result										
Injection. Threebion [Each 3ml contains: Vitamin B1 (Thiamine HCl)100mg, Vitamin B6 (Pyridoxine HCl) ... 100mg, Vitamin B12 (Cyanocobalamin) 1000 mcg]	H-23919	M/s Venus Pharma, 23-Km, Multan Road, Lahore-Pakistan.	01-71000020/DTL dated: 01-11- 2019	Analysis with specifications applied: MS DESCRIPTION: Clear, red color solution, filled in amber colored glass vials, packed in outer hard carton. IDENTIFICATION: Thiamine HCl, Pyridoxine HCl and Cyanocobalamin Identified. ASSAY: <table><tr><th>Generic</th><th>Stated Potency</th><th>Determined Potency</th><th>Percentage</th><th>Reference Limit (MS)</th></tr><tr><td>Pyridoxine HCl</td><td>100mg/ 3ml</td><td>109.585 mg/ 3ml</td><td>109.585%</td><td>90-120%</td></tr></table>	Generic	Stated Potency	Determined Potency	Percentage	Reference Limit (MS)	Pyridoxine HCl	100mg/ 3ml	109.585 mg/ 3ml	109.585%	90-120%
Generic	Stated Potency	Determined Potency	Percentage	Reference Limit (MS)										
Pyridoxine HCl	100mg/ 3ml	109.585 mg/ 3ml	109.585%	90-120%										

Expiry Date: July-2021	Regn No. 012088					Thiamine HCl	100mg/ 3ml	57.482 mg/ 3ml	57.482%	90-120%
						Cyanocobalamin	1000 mcg/ 3ml	3726.420 mcg/ 3ml	372.642 %	90-120%
<u>pH:</u>										
Limit: 3.6 - 4.5 (Manufacturer's Specifications)										
Determined: 3.67 (Complies)										
<u>AVERAGE VOLUME OF AMPOULE (EXTRACTABLE VOLUME)</u>										
Stated: 3ml + 0.2 ml (Manufacturer's Specifications)										
Determined: 3.00ml (Average of 5 ampoules)										
Complies										
<u>STERILITY:</u>										
Stated: Must be Sterile (Manufacturer's Specifications)										
Determined: Sterile (Complies)										
<u>RESULT:</u> <u>Given sample is Sub-Standard with regards to Assay.</u>										

- iii. Faizan Medical Store, old Gujrat Road near Allied Bank Phalia, District Mandi Bahauddin provided invoice/ warranty bearing No. 16127 dated 21-08-2019 issued by M/s M.S. Distributors & Pharmacy Gujrat-Pakistan as a proof of its purchase.
- iv. A copy of test/analysis report was sent to M/s M.S. Distributors & Pharmacy Gujrat-Pakistan who in-turn provided invoice/ warranty bearing No. 263 dated 07-08-2019 issued by M/s Venus Pharma, 23-Km, Multan Road, Lahore-Pakistan as a proof of its purchase.
- v. Warrantor portion of drug sample was sent to M/s M.S. Distributors & Pharmacy Gujrat-Pakistan.
- vi. A copy of test/analysis report was sent to M/s Venus Pharma, 23-Km, Multan Road, Lahore-Pakistan with directions to explain their position and provide requisite information in this regard. In response, the firm challenged the test/analysis report of the drug sample and requested to re-test the above-mentioned drug sample from Appellate Laboratory, National Institute of Health, Islamabad.

Previous Proceedings & Decision by the Board:

13th Committee Meeting dated 28-10-2020

2. The subject request for retesting of the drug sample was considered by the committee of Provincial Quality Control Board (PQCB) under section 22 of the Drugs Act 1976 in its 13th meeting held on 28-10-2020. Counsel of the firm, Sheikh Muhammad Nawaz appeared before the Committee of PQCB. Secretary PQCB apprised the Committee that the DTL test report was conveyed by drug inspector to the firm vide letter no. 83/DDC/PHL dated 08-07-2020 received by the firm dated:11-07-2020 and the firm requested for retesting of the drug in PQCB vide letter no VP.20/DI/PHALIA dated 22-07-2020

3. In view of the above, the committee after keen and thorough scrutiny of the record observed that the Drug Inspector conveyed the DTL report vide letter no. 83/DDC/PHL dated: 08-07-2020 which was received by the firm dated 11-07-2020 (as stated by the firm in its request for retesting) and the firm requested for retesting of the drug sample vide letter no. VP.20/DI/PHALIA dated 22-07-2020 i.e. **after a lapse of 11 days** whereas, according to Section 22(4) of the Drugs Act 1976, as amended **the firm is bound to file its request for retesting of their drug sample within stipulated time of 10 days**. Keeping in view the foregoing fact, the Committee after due deliberation unanimously decided to **turn down** the subject request for retesting of the drug sample. The committee further decided to direct the Drug Inspector concerned to expedite investigation in subject case and submit final report, bearing complete names and addresses of the accused persons involved in the subject case at the earliest, for consideration by the Board.

4. The Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused person(s), who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended), DRAP Act 2012 and Rules framed there under by the way of:

a. **Manufacture for sale /Sale of Substandard drug**

b. **Issuance of false warranty**

5. Show-cause notice(s) issued to accused person(s) dated 28-10-2022
6. Personal hearing notice(s) issued to accused person(s) dated 19-06-2023
7. Case is placed before the Board for decision.

Summary:

Manufacturing Date: July-2019

Expiry Date: July-2021

Sampling Date (Form 4): 28-08-2019

Sent to DTL (Form 6): 31-08-2019

Date of receipt in DTL: 03-09-2019

DTL Report Date (Form 7): 01-11-2019

Time Extension: Not Time Barred (Reporting Days: 60)

DI Communication with firm on dated: 08-07-2020

Retesting Request of Firm: Yes (22-07-2020)

Fate of Retesting Request: Turned Down in 13th Committee Meeting dated 28-10-2020

Investigation Report Dated: 14-09-2022

PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 26**PQCB/ R-790/2019****Sir Ganga Ram Hospital****ATTENDENCE**

Secretary DQCB	1. M/s Hafiz Pharma Industry, G.T. Road (Ghania) Kamoke District Gujranwala through its Managing Director/Warrantor, H. Abdul Rahman.
Drug Inspector	2. H. Abdul Rahman Managing Director/Warrantor 3. Hassan Warraich Quality Control Incharge 4. Akhtar Hussain Production Incharge Of M/s Hafiz Pharma Industry, G.T. Road (Ghania) Kamoke District Gujranwala

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Ganga Ram Hospital, Lahore reported that:-

- His predecessor, on 28-01-2019 inspected the business premises of Medicine Store, Sir Ganga Ram Hospital, Lahore, took samples of Cotton Bandage (Bandage of Dressing 6.5cmx6m) Batch No. 745, manufactured by M/s Hafiz Pharma Industry, G.T. Road (Ghania), Kamoke District Gujranwala on Form No. 4 for the purpose of test and analysis and sent to Drug Testing Laboratory Punjab, Lahore vide memo No. 00000027066 Dated 28-01-2019.
- The following drug sample, after test/analysis was declared as **Substandard** by Government Analyst, Drug Testing Laboratory Punjab, Lahore as detailed below: -

Name of Drug	Batch No.	Name of Manufacturer	DTL Report	DTL Test Report Result
Cotton bandage [Bandage For Dressing 6.5 cm*6M] Mfg. Date: 01-2018 Exp. Date: 01-2021 Reg # 070085	745	M/S Hafiz Pharma Industry, G.T. Road (Ghania) Kamoke District Gujranwala	01-129002678/ DTL dated: 15 Mar 2019	Result of test/ analysis with specifications applied: BPC 1973 <u>PHYSICAL DESCRIPTION:</u> COTTON CLOTH OF PLAIN WEAVE, BLEACHED TO A GOOD WHITE, IN ONE CONTINUOUS LENGTH CONTAINING NO JOINS, EDGES ARE EVENLY CUT AND REASONABLY FREE FROM LOOSE THREADS. IT IS CLEAN AND FREE FROM WEAVING DEFECTS, LEAF AND SHELL. CLAIMED SIZE= 6M X 6.5CM <u>WARPS</u> LIMIT: Average 17.1/cm DETERMINED: 20/cm

				<u>WEFTS:</u> LIMIT: Average 10.7/cm DETERMINED: 12.8/cm <u>LENGTH:</u> LIMIT: Average: $\pm 5\%$ of 6m DETERMINED: 6.0m <u>WIDTH:</u> LIMIT: $+5\%$ of 6.5 cm DETERMINED: 6.6cm <u>WEIGHT per unit area:</u> LIMIT: Average 71 g/m² DETERMINED: 67.8 g/m² <u>(NOT COMPLIES)</u> <u>RESULT:</u> The above sample is <u>SUB-STANDARD</u> on the basis of Weight per unit area, as per BPC.
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- iii. The Storekeeper, Medicine Store, Sir Ganga Ram Hospital, Lahore provided warranty/invoice No. 130 dated 21-01-2019 issued by M/s Hafiz Pharma Industry, G.T. Road (Ghania), Kamoke District Gujranwala
- iv. Warrantor Portion was sent to M/s Hafiz Pharma Industry, G.T. Road (Ghania), Kamoke District Gujranwala
- v. A copy of Test/ Analysis reports was sent to M/s Hafiz Pharma Industry, G.T. Road (Ghania), Kamoke District Gujranwala. With directions to provide requisite information in this regard. In response, the firm challenged the report and requested for re-testing of the sample by Appellate Laboratory, National Institute of Health (NIH), Islamabad.
- vi. Pursuant to the retesting request of the firm, sample was sent to Appellate Laboratory, National Institute of Health (NIH), Islamabad from where the sample was declared misbranded and substandard.

Name of Drug	Batch No.	Name of Manufacturer	Test Report No.	Details of Result of Test/analysis (With protocols of test applied)
SURGEON BANDAGE FOR DRESSING 100% COTTON	745	M/S Hafiz Pharma Industry, G.T. Road (Ghania) Kamoke District Gujranwala	0199-P/2019 dated: 23 rd September 2019	Reference: BPC 1973 <u>DESCRIPTION:</u> Off white cotton cloth, bleached not to a good white. The edges are cut evenly to the warp threads. The bandage is uniform throughout the length but have loose threads. The bandage is wrapped in printed paper further contained in polythene bag. (Does not comply with

				official pharmacopoeia which states that cotton cloth of plain weave bleached to good white in one continuous length containing no joints, clean and reasonably free from weaving defects, lead and shells. The edges are evenly cut parallel with the warp threads and are reasonably free from loose threads). <u>IDENTIFICATION:</u> Cotton fibre identified. <u>SIZE:</u> 5.85m x 6cm Complies with the size stated on the label. <u>THREAD PER STATED LENGTH:</u> <u>i- Warp:</u> <u>DETERMINED:</u> 17.33 threads/cm <u>LIMIT:</u> Average 17.1 threads/cm <u>ii- Weft:</u> <u>DETERMINED:</u> 11.2 threads/cm <u>LIMIT:</u> Average 10.7 threads/cm Complies with BPC 1973 <u>WEIGHT PER UNIT AREA:</u> <u>DETERMINED:</u> 76.16 gm/m² <u>LIMIT:</u> 17.0gm/m² Complies with BPC 1973 <u>FOREIGN MATTER:</u> <u>DETERMINED:</u> 1.32% <u>LIMIT:</u> Not more than 1.5% Complies with BPC 1973 <u>REMARKS:</u> Reference of pharmacopeia, registration Number, Licence Number, Batch Number and Date of expiry is not mentioned on the immediate pack which is violation of Printing and Labelling Rules of Drugs Act 1976. <u>CONCLUSION:</u> The above sample is MISBRANDED and SUB-STANDARD quality on the basis of tests performed.
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2. Drug Inspector requested for grant of permission for prosecution against the accused persons nominated in the instant case who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended) and Rules framed there under by the way of:

- i. **Manufacture for Sale/Sale of Substandard and Misbranded Drug.**
- ii. **Issuance of false warranty.**

3. Showcause was issued to accused person(s) dated 26.04.2023.

Reply of the Firm to the Show Cause Notice:

REPLY TO THE SHOW-CAUSE NOTICE

Kindly refer to your letter No. PQCB/R-790/2019, dated 26-04-2023 received on 11-05-2023 on the subject cited above.

1. That M/s Hafiz Pharma Industry is one of the leading and trusted national Pharmaceutical Companies in the field of surgical dressings, having valid drug manufacturing license, best known for its high quality absorbent cotton, bandages, gauze etc., which are fully compliant with Drugs Act 1976 and Rules framed thereunder. Its firm's commitment to quality and adherence to high standards/ cGMP guidelines to meet the high expectations of the patients as well as Health care providers.
2. That we have been supplying the same products to various prestigious institutions in Pakistan as well as market without any complaint and our products have been declared of standard quality by various Drug Testing laboratories in Pakistan.
3. That our product Cotton Bandage (Bandage for dressing 6.5 cmx 6 M) Batch No. 745 was declared substandard on the basis of weight per unit area (determined 67.8 g/m² against the 71g/m² average Limit) by Drugs Testing Laboratory Lahore, whereas, NIH in its report determined weight per unit area as 76.16 g/m² and declared it complying with B.P.C-1973 specifications. It shows that contravention detected by DTL Lahore have been declared null and void by NIH Islamabad. Reports of both Laboratories are at 180 degree and make the results highly doubtful.
4. That the warps and wefts were declared within Pharmacopeia limits by both the Laboratories
and it is understood that when warps and wefts are within the limits of BPC then technically the weight per unit area cannot be out of specifications.
5. Moreover, report of DTL Lahore declared our product of standard quality with respect to Physical specifications which is reproduced as below:
"Cotton cloth of plain weave, bleached to a good white in one continuous length containing no joins edges, edges are evenly cut and reasonably free from loose Threads, it is clean and free from weaving defects, leaf and shell".
Unfortunately, NIH Islamabad gave the opposite report in the Description and declared our product misbranded and substandard on the basis of physical tests, It is beyond comprehension when a product is within physical specifications, how come another Laboratory declares it contrary to that report. It shows personal bias and subjective approach of the analyst which is not representative of the whole stock of stores supplied by us. Contradictions of the reports make the whole proceeding of testing doubtful and entitle us to benefit of doubt.
6. That it is held in various judgments of High Court that Physical appearance is not part of standard of sample and any such minor variation is remediable as acknowledged in number Office of judgments like; 1984 P.Cr. L.J 1580. & 1985 P.Cr.L.J 2064
7. That according to Drugs Act 1976 the objection of Misbranded and physical description are remediable and it has nothing to do with the quality of our product. The section 18(1)(f) of Drugs Act 1976 is reproduced below:
"Provided that where the contravention is such which can be remedied, the stocks shall not be seized upon undertaking in writing of the person not to sell drug without remedying the defect, under intimation to the Board concerned"

8. That we have taken measures to further improve cutting of bandages by Cutter and overall manufacturing process in order to ensure Quality by design (QbD). However, as a goodwill gesture we have provided the replacement stock with Batch No. 839 & Invoice No. 168. The replacement stock having batch no. 839 is tested by DTL Lahore and declared of standard quality dated 17.04.2020.
9. That we have remedied the apparent defect of the stock in the Ganga Ram Hospital Lahore to be used in the hospital as precautionary measure for the benefit of the patients and avoid loss to government exchequer.

4. Personal Hearing notice(s) issued to accused person(s) dated 19.06.2023.

Case is placed before the Board.

Summary:

Manufacturing Date: 01-2018

Expiry Date: 01-2021

Sampling Date: 28-01-2019

Sent to DTL (Form 6): 28-01-2019

Date of receipt in DTL: 31-01-2019

DTL Report Date: 15-03-2019

Time Extension: N/A

| 1ST DI Communication with firm on dated: 28-01-2019 **|**

Date of Retesting Request of Firm: 16-04-2019

Fate of Retesting Request: -Allowed in 10th Committee Meeting dated 22-07-2019

| Investigation Report Dated: 08-04-2023 **|**

**CURRENT
PROCEEDINGS
AND DECISION
OF THE
BOARD**

Case No. 27

PQCB/R-751/2019

Ahmedpur East, Bahawalpur

ATTENDANCE

Secretary DQCB	<u>Accused Persons involved in subject case</u>
Drug Inspector	1. M/S City Pharmaceutical Laboratories, 1-5, Sector 5, Korangi Industrial Area Karachi through its Chief Executive Officer/Warrantor Muhammad Taufiq. 2. Muhammad Taufiq Chief Executive Officer/Warrantor 3. Ahmed Idrees Plant Manager 4. Gulshan Tahira Quality Control Manger 5. Abida Parveen Production manager 6. Afsheen Waqar Quality Assurance Manager of M/S City Pharmaceutical Laboratories, 1-5, Sector 5, Korangi Industrial Area Karachi.

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Tehsil Ahmed Pur East & District Bahawalpur reported that: -

- His Predessor, on 31-01-2019, inspected the business premises of M/S Sherooz Medical Store, Noshehra Jadeed, Tehsil Ahmed Pur East, District Bahawalpur and took one drug samples on Form No.04 for the purpose of test/analysis and sent to Drug Testing Laboratory Bahawalpur.
- Following Drug sample after test/analysis was declared as **Substandard** by Government Analyst Drug Testing Laboratory Bahawalpur, as detailed below:

Name of Drug	Batch No.	Name of Manufacturer	DTL Report TRA No. & Date
Film Coated Tablet Adik SR [Diclofenac Sodium 100mg]	T.004	M/S City Pharmaceutical Laboratories, 1-5, Sector 5, Korangi Industrial Area Karachi	01-65000525/DTL Dated. 03-04-2019
<u>DTL Test Report Result</u> <u>Analysis with specifications applied:</u> MS/USP 2018. <u>Composition:</u> Each film coated tablet contains: Diclofenac Sodium U.S.P.....100mg <u>Description (MS):</u> A tea pink colored, biconvex, round shaped film coated tablets, plain from both sides and packed in a blister of 10 tablets.			

Identification (USP):

Diclofenac Sodium is identified.

Assay (USP):

Diclofenac Sodium:

Stated	100mg/tab
Determined	102.95mg/tab
Percentage	102.95%
Limit	90-110%

Dissolution Test (MS/USP):

Does not comply with the specifications of MS/USP Test 2 as detailed below:

Tolerance Limit: Dissolution test should be

<u>After 01 Hour</u>	<u>After 02 Hour</u>	<u>After 04 Hour</u>	<u>After 06 Hour</u>	<u>After 10 Hour</u>
NMT 28%	20-40%	35-60%	50-80%	NLT 65%

Level	Number Tested	Acceptance Criteria	Average	Remarks					
L1	6	No individual value lies outside each of stated ranges, no individual value is less than stated amount (L1) and none of the units is more than 20% of labeled content outside each of the stated ranges (L3).	L1	Two units are more than stated ranges after 01, 02 and 04 hours,					
Time	Limit of Range	<table><tr><td></td><td></td><td></td><td></td><td></td><td></td></tr></table>							

After 1 hour	NMT 28%	Unit 1	Unit 2	Unit 3	Unit 4	Unit 5	Unit 6	29.32%	One unit after 01 hour and two units after 02 and 04 hours are outside of the stated ranges by more than 20%.
		20.37%	17.89%	17.34%	47.07%	48.72%	24.50%		
After 02 Hour	20-40%	30.17%	28.74%	25.70%	72.60%	64.38%	36.60%	43.03%	
		48.28%	45.50%	43.51%	97.67%	82.07%	53.93%		
After 04 Hour	35-60%	64.37%	61.83%	59.04%	97.72%	99.53%	84.04%	61.83%	
After 06 Hour	50-80%	102.5%	105.2%	98.84%	99.68%	104.4%	103.0%	77.76%	
After 10 Hour	NLT 65%							102.27%	

Result:

The sample is declared **Substandard** on the basis of Dissolution test (MS/USP).

- iii. M/S Sheroz Medical Store, Noshehra Jadeed, Tehsil Ahmed Pur East, District Bahawalpur provided Invoice/warranty No 15585, dated 20-01-2019 issued by M/S Al-Ghani Medicine Company, House No. 83/13 Street No. 11, Muhammadia Colony, Bahawalpur who inturn provided invoice/warranty no. 7500, Dated. 15-01-2019 issued by M/S Mehran Traders, Medicine Market Town Hall, Multan who inturn provided invoice/warranty no. 1001192, Dated. 10-01-2019 issued by M/S Qasim Traders (Wholesale Chemist Druggist), Shop No. 1, Medicine Center Kutchi Gali No. 1, Marriott Road, Karachi who inturn provided invoice/warranty no. 0301192, Dated. 03-01-2019 issued by M/S City Pharmaceutical Laboratories, 1-5, Sector 5, Korangi Industrial Area Karachi as a proof of its purchase.
- iv. Warrantor portion of drug sample was sent to M/S Al-Ghani Medicine Company, House No. 83/13 Street No. 11, Muhammadia Colony, Bahawalpur and they were asked to explain their position in this regard.
- v. A copy of test/analysis report was sent to M/S City Pharmaceutical Laboratories, 1-5, Sector 5, Korangi Industrial Area Karachi and they were asked to provide the requisite information in this regard. In Response, the firm challenged the test/analysis report and requested to re-test the above-mentioned drug sample from Appellate laboratory NIH, the said retesting request was placed in 14th retesting committee meeting held on 17-12-2020 and the Board decided to allow to send the sample to NIH, Islamabad.
- vi. Pursuant to the request of manufacturer the sample was sent to NIH, Islamabad, from where the same was declared as **Substandard**,as detailed below:

Name of Drug	Batch No.	Name of Manufacturer	NIH Test Report No. & Date	NIH Test Report Result

ADIK SR [Diclofenac Sodium 100mg]	T.004	M/S City Pharmaceutical Laboratories, 1-5, Sector 5, Korangi Industrial Area Karachi	0219-P/2020 Dated 28-12-2020	<u>Analysis with specifications applied:</u> USP 39. <u>Description:</u> Light pink colored, Circular, biconvex, coated tablets packed in blister packing further contained in an outer carton. <u>Identification:</u> Diclofenac Sodium identified. <u>Weight Variation:</u> Complies with USP-39. <u>Dissolution Test:</u> <table><tr><td></td><td>Determined</td><td>Determined</td><td>Limit</td></tr><tr><td>After 1 Hour</td><td>Average 34.68%</td><td>Two tablets out of six tablets deviated from the limit</td><td>15- 35%</td></tr><tr><td>After 5 Hours</td><td>80.13%</td><td>Five Tablets out of six tablets deviated from limit</td><td>45- 65%</td></tr></table> Does not comply with USP -39. <u>Assay:</u> Diclofenac Sodium: <table><tr><td>Stated</td><td>100mg/tablet</td></tr><tr><td>Found</td><td>101.91mg/tablet</td></tr><tr><td>Percentage</td><td>101.91%</td></tr><tr><td>Limit</td><td>90-110%</td></tr></table> <u>complies with USP -39.</u>		Determined	Determined	Limit	After 1 Hour	Average 34.68%	Two tablets out of six tablets deviated from the limit	15- 35%	After 5 Hours	80.13%	Five Tablets out of six tablets deviated from limit	45- 65%	Stated	100mg/tablet	Found	101.91mg/tablet	Percentage	101.91%	Limit	90-110%
	Determined	Determined	Limit																					
After 1 Hour	Average 34.68%	Two tablets out of six tablets deviated from the limit	15- 35%																					
After 5 Hours	80.13%	Five Tablets out of six tablets deviated from limit	45- 65%																					
Stated	100mg/tablet																							
Found	101.91mg/tablet																							
Percentage	101.91%																							
Limit	90-110%																							

				<u>Remarks:</u> Dissolution for 10, 16, and 24 hours did not proceeded due to technical constraints. <u>Result:</u> The sample is of <u>Substandard</u> Quality on the basis of tests performed.
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vii. A copy of NIH Test Report was sent to M/S City Pharmaceutical Laboratories, 1-5, Sector 5, Korangi Industrial Area Karachi by Drug Inspector with directions to provide the requisite information and to explain their position in this regard but they failed to do so

2. In this way You have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended) / DRAP Act 2012 and Rules framed there under by the way of: -

a. **Manufacture for sale/Sale of Substandard drug**

b. **Issuance of false warranty**

3. Showcause was issued to accused person(s) vide dated 30.05.2022

1. It is respectfully stated that the product Diclofenac SR tablet is sensitive to temperature and physical handling. Our all integrated records pertaining to the quality of the batch confirm its compliance with its pre-defined specifications. We investigated the matter both through our internal and independent external system, no clue was found on even alert limit as dozens of other batches and sufficient number of other samples found compliant. For the sake of your trust and concern, allow us to present a valid view on the matter. It is the NIH test report of the product that itself confirms its testing on last days of its life and as a matter of practice, we call back short expiry product in its last 3 months. This practice does not allow to keep product in market having one month shelf life in any case.
2. NIH had asked us to submit fee for retesting in April 2021 after the expiry of the product. It was subsequently submitted to NIH that the product is expired. It is logical to connect that the sensitivity of this product may not give conclusive results upon testing after its expiry and because of reasons that include but not limited to its storage/handling throughout the year experienced harsh weathers.
3. We will be honored to explain the scientific position on the matter, we gathered during the study of this case for sharing of knowledge and your kind consideration.

4. Personnel Hearing notice(s) issued to accused person 19.06.2023

Case was placed before the Board for Decision

Summary:

Manufacturing Date: 12.2018

Expiry Date: 12.2020

Sampling Date (Form 4): 31.01.2019

Sent to DTL (Form 6): 07.02.2019

Date of receipt in DTL: 09.02.2019

DTL Report Date (Form 7): 03.04.2018

Time Extension: N/A

1ST DI Communication with firm on dated: 11.12.2019

Date of Retesting Request of Firm: 12.12.2019

Fate of Retesting Request: Allowed (Substandard by NIH)

Investigation Report Dated:09.04.2022

PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 28

PQCB/R-569/2018

DHQ Teaching Hospital Sahiwal

ATTENDENCE

Secretary DQCB	<u>Accused Persons involved in subject case</u>
Drug Inspector	1. M/S Rehman Rainbow (Pvt) Ltd, 82-Industrial Estate Kot Lakhpat, Lahore-Pakistan through its Managing Director Waleed Rizwan. 2. Waleed Rizwan Managing Director 3. Khair-un-Nisa Production Incharge 4. Tajamul Hussain Quality Control Manager/Warrantor of M/S Rehman Rainbow (Pvt) Ltd, 82-Industrial Estate Kot Lakhpat, Lahore-Pakistan.

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, DHQ Teaching Hospital, Sahiwal reported that: -

- He, on 07-06-2018, inspected the premises of Main Medicine Store DHQ Teaching Hospital Sahiwal and took different types of drug samples on Form No.04 for the purpose of test/analysis and sent to Drug Testing Laboratory Bahawalpur vide Memo. No.779/DI DHQ Teaching Hospital, Sahiwal, dated. 07-06-2018.
- Following Drug sample after test/analysis was declared as **Substandard** by Government Analyst Drug Testing Laboratory **Bahawalpur**, as detailed below:

Name of Drug	Batch No.	Name of Manufacturer	DTL Report TRA No. & Date	DTL Test Report Result				
Guaze Surge Gauzes [10cm x 10cm x 8ply] Mfg Date: Feb-2018 Exp Date: Jan-2021 Registration No. 030742	GS1218	M/S Rehman Rainbow (Pvt) Ltd, 82-Industrial Estate Kot Lakhpat, Lahore- Pakistan	01- 54001285/DTL Dated. 17-07- 2018	<u>Analysis with specifications applied:</u> BP 1993. <u>Description:</u> White color cut piece of cotton cloth of plain weave. The cloth is resonably free from cotton leaf and shell <u>Weight/Unit Area:</u> <table><tr><td>Limit</td><td>Not less than 14gm/m²</td></tr><tr><td>Determined</td><td>17.67gm/m²</td></tr></table> <u>Threads/Stated Length:</u> <u>Warp:</u>	Limit	Not less than 14gm/m ²	Determined	17.67gm/m ²
Limit	Not less than 14gm/m ²							
Determined	17.67gm/m ²							

				<table><tr><td>Limit</td><td>69-77/10cm</td></tr><tr><td>Determined</td><td>71/10cm</td></tr></table>	Limit	69-77/10cm	Determined	71/10cm
Limit	69-77/10cm							
Determined	71/10cm							
				<u>Weft:</u> <table><tr><td>Limit</td><td>53-61/10cm</td></tr><tr><td>Determined</td><td>54/10cm</td></tr></table>	Limit	53-61/10cm	Determined	54/10cm
Limit	53-61/10cm							
Determined	54/10cm							
				<u>Sinking Time</u> <table><tr><td>Limit</td><td>Not more than 10 sec</td></tr><tr><td>Determined</td><td>5.6sec</td></tr></table>	Limit	Not more than 10 sec	Determined	5.6sec
Limit	Not more than 10 sec							
Determined	5.6sec							
				<u>Acidity/Alkalinity:</u> <table><tr><td>Limit</td><td>No pink color appeared</td></tr><tr><td>Determined</td><td>Not pink color appeared</td></tr></table>	Limit	No pink color appeared	Determined	Not pink color appeared
Limit	No pink color appeared							
Determined	Not pink color appeared							
				<u>Sterility:</u> The product is non-sterile. Does not comply with the specifications. <u>Result:</u> The sample is declared Substandard on the basis of Sterility Test.				

- iii. Main Medicine Store DHQ Teaching Hospital Sahiwal provided Invoice/warranty No 213, dated 06-06-2018 issued by M/S Sameed Enterprises 16-Karim Block Allama Iqbal Town Lahore who inturn provided invoice/warranty no. 2407, dated. 19-07-2018 issued by M/S Rehman Rainbow (Pvt) Ltd, 82-Industrial Estate Kot Lakhpat, Lahore-Pakistan as a proof of its purchase.
- iv. Warrantor portion of drug sample was sent to M/S Sameed Enterprises 16-Karim Block Allama Iqbal Town Lahore and they were asked to explain their position in this regard.
- v. A copy of test/analysis report was sent to M/S Rehman Rainbow (Pvt) Ltd, 82-Industrial Estate Kot Lakhpat, Lahore-Pakistan and they were asked to provide the requisite information.

2. In this way You have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended) / DRAP Act 2012 and Rules framed there under by the way of:-

a. Manufacture for sale/Sale of Substandard drug

b. Issuance of false warranty

3. Showcause was issued to accused person(s) vide dated 29.08.2022

4. Personnel Hearing notice(s) issued to accused person 19.06.2023

Case was placed before the Board for Decision

Summary:

Manufacturing Date: 02.2018

Expiry Date: 01.2021

Sampling Date (Form 4): 07.06.2018

Sent to DTL (Form 6): 07.06.2018

Date of receipt in DTL: 12.06.2018

DTL Report Date (Form 7): 17.07.2018

Time Extension: N/A

1ST DI Communication with firm on dated: 20.07.2018

Date of Retesting Request of Firm: N/A

Fate of Retesting Request: N/A

Investigation Report Dated:16.02.2021

PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 29

PQCB/R-711/2020

Chishtian, Bahawalnagar

ATTENDENCE

Secretary DQCB	<u>Accused Persons involved in subject case</u>
Drug Inspector	1. M/S Batala Pharmaceuticals, 23/B Small Industrial Estate # 2, Gujranwala Pakistan through its Chief Executive Officer Rana Muhammad Yousaf. 2. Rana Muhammad Yousaf Chief Executive Officer 3. Muhammad Umer Shakir Production Manager 4. Hafiz Shabbir Ahmad Incharge Quality Control/Warrantor of M/S Batala Pharmaceuticals, 23/B Small Industrial Estate # 2, Gujranwala Pakistan.

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Tehsil Chishtian, District Bahawalnager reported that: -

- His Predecessor, on 27-10-2020, inspected the business premises of M/S Madina Medical Store Highway Road Tehsil Chishtian, District Bahawalnager and took below mentioned drug sample on Form No.04 for the purpose of test/analysis and sent to Drug Testing Laboratory Bahawalpur vide Memo. No.0000076985, dated. 28-10-2020.
- Following Drug sample after test/analysis was declared as **Substandard** by Government Analyst Drug Testing Laboratory **Bahawalpur**, as detailed below:

Name of Drug	Batch No.	Name of Manufacturer	DTL Report TRA No. & Date	DTL Test Report Result	
Film Coated Tablet. Bytec [Cetirizine 2HCl 10mg] 					

Registration No. 036183				Determined		94.55-103.82%					
				<u>Dissolution Test (BP):</u>							
				Tolerance Limit: Not less than 80% (Q) in 45 minutes.							
				Stage	Number Tested	Acceptance Criteria					
				S1	06	Each unit is equal to or greater than Q+5%=85% (Q=80%) and no unit is less than Q-25%=55% AFTER 45 minutes.					
				Determined	Cetirizine 2HCl	Unit 1	Unit 2	Unit 3	Unit 4	Unit 5	Unit 6
						90.73%	94.90%	91.56%	91.01%	96.02%	97.96%
								<u>Identification (MS):</u>			
								Cetirizine 2HCl is identified.			
				<u>Assay (BP):</u>							
				<u>Cetirizine 2HCl:</u>							
Stated		10mg/tab									
Determined		9.795mg/tablet									
Percentage		97.95%									
Limit		95.0-105.0%									
				<u>Result:</u>							
				The sample is Substandard on the basis of Physical Description Test.							

- iii. M/S Madina Medical Store Highway Road Tehsil Chishtian, District Bahawalnager provided Invoice/warranty No 519, dated 15-10-2020 issued by M/S Al-Hussain Medical Store Khan Baba Road Tehsil and District Bahawalnager who in turn provided invoice/warranty no. 4872, dated. 19-07-2020 issued by M/S Batala Pharmaceuticals, 23/B Small Industrial Estate # 2, Gujranwala Pakistan as a proof of its purchase.
- iv. Warrantor portion of drug sample was sent to M/S Al-Hussain Medical Store Khan Baba Road Tehsil and

District Bahawalnager.

- v. A copy of test/analysis report was sent to M/S Batala Pharmaceuticals, 23/B Small Industrial Estate # 2, Gujranwala Pakistan and they were asked to provide the requisite information in this regard. In response the firm challenged the Drug Testing Laboratory report and the office of Provincial Quality Control Board placed the said retesting request in the 246th Meeting of Retesting dated 05-07-2022 and Board unanimously decided to allow the firm to **withdraw** its said retesting request.

2. In this way You have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended) / DRAP Act 2012 and Rules framed there under by the way of:-

a. Manufacture for sale/Sale of Substandard drug

b. Issuance of false warranty

3. Showcause was issued to accused person(s) vide dated 01.12.2022

1. With reference to your letter No: PQCB/R-711/2020 dated 01/12/2022. It is hereby stated that our registered product Bytec 10mg Tablet registration No. 036183 is Film Coated Tablet. On receiving the DTL Bahawalpur Report, we made an inquiry for investigation for that matter. According to our Analytical Investigation Report the physical appearance of our retaining sample of Bytec 10mg Tablet Batch # 8154 complies with standard Specifications. (Analytical Investigation Report attached).

2. It is our opinion that pigmented surface of above said batch might be due to the storage condition of market. We assure that we would be more vigilant in future and complaint will never be repeated. Therefore, we requested to take lenient view from the Board. So therefore we request you to withdraw the case.

4. Personnel Hearing notice(s) issued to accused person 19.06.2023

Case was placed before the Board for Decision

Summary:

Manufacturing Date: 06.2020

Expiry Date: 05.2023

Sampling Date (Form 4): 27.10.2020

Sent to DTL (Form 6): 28.10.2020

Date of receipt in DTL: 03.11.2020

DTL Report Date (Form 7): 31.12.2020

Time Extension: N/A

1ST DI Communication with firm on dated: 24.04.2021

Date of Retesting Request of Firm: 06.05.2021

Fate of Retesting Request: Withdrawn by firm

Investigation Report Dated: 07.11.2022

PROCEEDINGS & DECISION BY THE BOARD:

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Case No. 30**PQCB/R-350, R-351/2022****Tehsil Pattoki, District Kasur****ATTENDENCE**

Secretary DQCB	<u>Accused Persons involved in subject case</u>
Drug Inspector	1. M/s Selmore Pharmaceuticals (Pvt.) Ltd. 36-Km, Multan Road, Lahore-Pakistan through its Chief Executive Officer (CEO), Akbar Ali 2. Akbar Ali Chief Executive Officer (CEO) 3. Riaz Hussain Production Incharge / Warrantor 4. M. Ijaz Ashraf Quality Control Incharge of M/s Selmore Pharmaceuticals (Pvt.) Ltd. 36-Km, Multan Road, Lahore-Pakistan.

BRIEF FACTS OF THE CASE

Provincial Inspector of Drugs, Tehsil Pattoki, District Kasur reported that: -

- The then drug inspector, on 23-04-2022, inspected the premises of M/s Main Medicine Store of Director Livestock Lahore Division, situated at Buffalo Research Institute Tehsil Pattoki, District Kasur, took below-mentioned drug samples on Form No.04 for the purpose of test/analysis and sent the drug samples to Drug Testing Laboratory Lahore vide memorandum no. 124620 & 124619 both dated 23-04-2022.
- The subject drug samples after test/analysis were declared as **Substandard** by Government Analyst Drug Testing Laboratory **Lahore**, as detailed below:

Sr. No.	Name of Drug	Batch No.	Name of Manufacturer	DTL Report No. & Date	DTL Test Report Result
1	Injection. MULTIMINO-V 250ML [EACH 100ML CONTAINS: L- Carnitine ... 500MG, Thioctic Acid ... 20MG, Pyridoxine Hydrochloride ... 15MG, Cyanocobalamin ... 3MG, DL- Acetylmethionine 2000MG, L-Arginine 240MG, L- Ornithine ... 120MG, L-Citrulline ... 120MG,	MV-128	M/S Selmore Pharmaceuticals (Pvt.) Ltd. 36- Km, Multan Road, Lahore- Pakistan.	01- 177000946/DTL dated 15-06-2022	Analysis with Specifications Applied: MS <u>PHYSICAL DESCRIPTION:</u> <u>Stated as per MS:</u> White to light brown suspension filled in a labeled vial packed in a unit carton. <u>Observed:</u> Red color clear liquid preparation filled in transparent glass vial having label pasted on it, sealed with aluminium seal, rubber stopper and red flip off cover, packed in unit carton. Claimed Volume= 250ml (DOES NOT COMPLY) <u>IDENTIFICATION OF PYRIDOXINE HCL:</u> The retention time of the major peak in the

	L-Lysine ... 50MG, Glycine ... 150M, Taurine ... 150MG, Aspartic Acid ... 150MG, Glutamic Acid ... 150MG, Fructose ...5000MG, SorbitoL ... 8000MG] Mfg Date: March 2022 Expiry Date: March 2024 Regn No. 058712				sample chromatogram corresponds to the retention time of the major peak in standard chromatogram. (Pyridoxine HCL identified) <u>ASSAY OF PYRIDOXINE HCL:</u> Stated Potency: 15 mg/ 100 ml Determined Potency: 15.75 mg/ 100 ml Percentage: 105.02% Limit: 90-120% of Label Claim <u>IDENTIFICATION</u> OF <u>CYANOCOBALAMIN:</u> The absorbance pattern of sample solution corresponds to absorbance pattern of standard solution. (Cyanocobalamin identified) <u>ASSAY OF CYANOCOBALAMIN:</u> Stated Potency: 3 mg/ 100 ml Determined Potency: 3.68 mg/ 100 ml Percentage: 122.71% Limit: 90-130% of Label Claim <u>STERILITY:</u> The sample is sterile. <u>RESULT:</u> The sample is <u>SUB-STANDARD</u>, on the basis of Physical Description as per manufacturer provided method of analysis.
2	Injection. MULTIMINO-V 250ML [EACH 100ML CONTAINS: L- Camitine ... 500MG, Thioctic Acid ... 20MG, Pyridoxine Hydrochloride ...	MV-129	M/S Selmore Pharmaceuticals (Pvt.) Ltd. 36- Km, Multan Road, Lahore- Pakistan.	01- 177000947/DTL dated 15-06-2022	Analysis with Specifications Applied: MS <u>PHYSICAL DESCRIPTION:</u> <u>Stated as per MS:</u> White to light brown suspension filled in a labeled vial packed in a unit carton. <u>Observed:</u> Red color clear liquid preparation filled in transparent glass vial

15MG, Cyanocobalamin ... 3MG, DL- Acetylmethionine 2000MG, L-Arginine 240MG, L- Ornithine ... 120MG, L-Citruline ... 120MG, L-Lysine ... 50MG, Glycine ... 150M, Taurine ... 150MG, Aspartic Acid ... 150MG, Glutamic Acid ... 150MG, Fructose ...5000MG, SorbitoL ... 8000MG]				having label pasted on it, sealed with aluminium seal, rubber stopper and red flip off cover, packed in unit carton. Claimed Volume= 250mL (DOES NOT COMPLY) <u>IDENTIFICATION OF PYRIDOXINE HCL:</u> The retention time of the major peak in the sample chromatogram corresponds to the retention time of the major peak in standard chromatogram. (Pyridoxine HCL identified) <u>ASSAY OF PYRIDOXINE HCL:</u> Stated Potency: 15 mg/ 100 ml Determined Potency: 15.93 mg/ 100 ml Percentage: 106.17% Limit: 90-120% of Label Claim <u>IDENTIFICATION OF CYANOCOBALAMIN:</u> The absorbance pattern of sample solution corresponds to absorbance pattern of standard solution. (Cyanocobalamin identified) <u>ASSAY OF CYANOCOBALAMIN:</u> Stated Potency: 3 mg/ 100 ml Determined Potency: 3.57 mg/ 100 ml Percentage: 119.00% Limit: 90-130% of Label Claim <u>STERILITY:</u> The sample is sterile. RESULT: The sample is SUB-STANDARD, on the basis of Physical Description as per manufacturer provided method of analysis.
Mfg Date: March 2022 Expiry Date: March 2024 Regn No. 058712				

iii. Store In-charge of Main Medicine Store of Director Livestock Lahore Division, situated at

Buffalo Research Institute Tehsil Pattoki, District Kasur provided warranty bearing No. SEL/INV22/APR/5879 dated 19-04-2022 issued by M/s Selmore Pharmaceuticals (Pvt.) Ltd. 36-Km, Multan Road, Lahore-Pakistan as a proof of its purchase of the subject drug samples.

- iv. Warrantor portion of drug samples were sent to M/s Selmore Pharmaceuticals (Pvt.) Ltd. 36-Km, Multan Road, Lahore-Pakistan.
- v. Copies of test/analyses reports were sent to M/s Selmore Pharmaceuticals (Pvt.) Ltd. 36-Km, Multan Road, Lahore-Pakistan with directions to explain their position and provide requisite information in this regard.

2. The Drug Inspector requested for grant of permission for prosecution against the above-mentioned accused person(s), who have contravened the provisions of Section 23/27 of the Drugs Act 1976 (as amended), DRAP Act 2012 and Rules framed there under by the way of:

a. **Manufacture for sale /Sale of Substandard drugs**

b. **Issuance of false warranty**

3. Show-cause notice(s) issued to accused person(s) dated 09-05-2023

Firm submitted written reply vide letter no. SPL/G-16-1/22

1. The Government Analyst Drug Testing Laboratory Lahore vide test report No. TRA 01-177000946/DTL and TRA 01-177000946/DTL dated (15.09.2022 declared that sample of Multimino-V Injection 250mg Batch No. MV-128 and MV-129 are Sub-Standard on the basis of Physical Description.
2. That M/s Selmore Pharmaceuticals(Pvt) Ltd is one of the leading and fast growing national Pharmaceutical company, best known for its high quality products including the Injection Multimino-V Injection which are in full conformity with the Drugs Act 1976 and Rules framed thereunder.
3. We had supplied our product **Multimino-V Injection to livestock sector in all over the Punjab**. The Government Analyst Drug Testing Laboratory Multan, Bahawalpur, Faisalabad and Rawalpindi declared our product of standard quality.
4. We had supplied our product Mutimino-V Injection Batch No. MV-129 (same product and batch) to Director Live Stock Rawalpindi. The Government Analyst Drug Testing Laboratory Rawalpindi declared our product of standard quality.
5. Lastly the same drug with same batch No. Mutimino-V Injection Batch No. MV-129 when supplied to Director Live Stock, Lahore and the sample of the drug was taken by the Drug Inspector Tehsil Pattoki and sent to the Govt. Analyst DTL Lahore. The Drug Testing Laboratory Lahore, when subjected the drug Mutimino-V Injection Batch No. MV-128 & MV-129 to strict test, Analysis and Assay of the ingredients **Pyridoxine HCl and Cyanocobalamin was found to be of standard quality** within the permitted range of potency and sterility. The only discrepancy found by the analyst was with regard to the physical description/color of the drug. **It was correctly observed by the Govt. Analyst that the drug contained in the vial was of red color clear liquid preparation filled in transparent glass vial. This physical finding of the sample of the drug analyzed by the analyst is in clear compliance and conformity with the original manufacturing specifications supplied by the company at the time of registration of the drug with the Ministry of Health Islamabad.**
6. Ironically, the method of test and analysis supplied to the DTL Lahore, later on, **was mistakenly contained a sentence bearing typographic mistake** where by it was inadvertently written as "white to light brown suspension". **This error committed by the company officials is purely a bonafide human error, which undoubtedly is to be rectified and taken care of in future.**
7. In view of the above submissions and clarification, we therefore, **request that a lenient**

view may kindly be taken under the Rules 5 (5) of the Punjab Drug Rules 2007 by ignoring this human error as no offence has been found to be committed in the sample of the drug Mutimino-V Injection Batch No. MV-128 and MV 129.

8. *It is further, requested that keeping in view of the whole scenario of the case the concerned **drug inspector may graciously be directed to allow the use of the stock of the drug** Mutimino-V Injection Batch No. MV-128 and MV129 as the drug is of Standard Quality in terms of test Analysis and Assay.*

7. Personal hearing notice(s) issued to accused person(s) dated 19-06-2023

8. Case is placed before the Board for decision.

Summary:

Manufacturing Date: 03-2022

Expiry Date: 03-2024

Sampling Date (Form 4): 23-04-2022

Sent to DTL (Form 6): 23-04-2022

Date of receipt in DTL: 26-04-2022

DTL Report Date (Form 7): 15-06-2022

Time Extension: Not Time Barred

DI Communication with firm on dated: 07-09-2022

Retesting Request of Firm: NA

Investigation Report Dated: 24-03-2023

PROCEEDINGS & DECISION BY THE BOARD:

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