



केन्द्रीय प्रदूषण नियंत्रण बोर्ड  
CENTRAL POLLUTION CONTROL BOARD

पर्यावरण, वन एवं जलवायु परिवर्तन मंत्रालय भारत सरकार  
MINISTRY OF ENVIRONMENT, FOREST & CLIMATE CHANGE GOVT. OF INDIA

B-29016/04/06/IPC-I

January 31, 2022

To

All SPCBs/PCCs (Listed)

Sub. : Guidelines on Monitoring Mechanism for API residue -reg

Sir,

As directed by Hon'ble NGT on 23.06.2021 in the matter of O.A no 136/2020 Veterans forum for Transparency in Public life Vs. state of Himacahl Pradesh & Ors. the following:

*“CPCB may also suggest monitoring mechanism for API residue through a credible system so as to cover all pharma industries in the country discharging API residue directly or indirectly in river systems. CPCB may propose the timelines to undertake monitoring which may also take a note of water quality monitoring guidelines of CPCB titled “Guidelines on Water Quality Monitoring, 2017” and the performance audit report dated 18.09.2020 filed by CPCB in OA 95/2018, Aryavart Foundation vs M/s Vapi Green Enviro Ltd. & Ors. and the directions of the Tribunal dated 05.02.2021.”*

On further hearing on this matter, the Hon'ble NGT order on 21.01.2022 has passed the order as follows *“CPCB may circulate monitoring mechanism to the State PCBs on API, as directed earlier and file the action taken report before the next date.”*

Central Pollution Control Board has prepared the above stated “Guidelines on Monitoring Mechanism for API residue” and same is attached herewith for your kind perusal and necessary action please.

Encl.: As above

Yours faithfully,

  
(Dinabandhu Gouda)

Additional Director & DH-IPC-I

Copy to:

1. D.H - LAW
2. D.H -Trace Organic Lab
3. DH WQM-I
4. All RDs by email

: for necessary follow up with SPCBs please

  
(Dinabandhu Gouda)

## List of State Pollution Control Boards/Committees

1. The Member Secretary  
Andhra Pradesh State Pollution Control Board  
D.No. 33-26-14 D/2, Near Sunrise Hospital,  
Pushpa Hotel Centre, Chalmvari Street,  
Kasturibaipet, Vijayawada- 520010  
**Andhra Pradesh**
  
2. The Member Secretary  
Arunachal Pradesh State Pollution Control Board  
'Paryavaran Bhavan', Yupla Road,  
PappuNallah,  
Naharlagun – 791110  
**Arunachal Pradesh**
  
3. The Member Secretary  
Assam State Pollution Control Board  
Bamunimaidan,  
Guwahati – 781021  
**Assam**
  
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Bihar State Pollution Control Board  
Parivesh Bhawan, Plot No.N-B/2,  
Patliputra Industrial Area  
**Patna-800023**
  
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Chhattisgarh Environment Conservation Board  
5, 32 Bungalows, Bhilai,  
Chhattisgarh 490009  
**Chhattisgarh**
  
6. The Member Secretary  
Goa State Pollution Control Board  
Dempo Tower, EDC Plaza, 1<sup>st</sup> floor  
Patto Plaza, Panaji,  
**Goa – 403001**
  
7. The Member Secretary  
Gujarat State Pollution Control Board  
Sector 10-A, Gandhi Nagar – 382043  
**Gujarat**
  
8. The Member Secretary  
Haryana State Pollution Control Board  
C-11, Sector 6, Panchkula,  
**Haryana 134109**

9. The Member Secretary  
Himachal Pradesh State Pollution Control Board  
ParyavaranBhavan, Phase III,  
New Shimla – 171009  
**Himachal Pradesh**
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J&K State Pollution Control Board,  
Parivesh Bhawan, Forest Complex  
Gladni, Narwal, Transport Nagar,  
Jammu-180004  
**Jammu and Kashmir**
11. The Member Secretary  
Jharkhand State Pollution Control Board  
T.A Building, HEC Campus, P.O. Dhurwa  
Ranchi – 834004  
**Jharkhand**
12. The Member Secretary  
Karnataka State Pollution Control Board  
ParisaraBhavan, 4<sup>th</sup>& 5<sup>th</sup> floors, Church Street,  
Bangalore – 560 001  
**Karnataka**
13. The Member Secretary  
Kerala State Pollution Control Board  
Head Office, Pattom. P. O  
Thiruvananthapuram-695004  
**Kerala**
14. The Member Secretary  
Maharashtra State Pollution Control Board  
Kalpataru Point, 3<sup>rd</sup>& 4<sup>th</sup> floors  
Sion Matunga Scheme Road No. 6  
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Maharashtra
15. The Member Secretary  
Madhya Pradesh State Pollution Control Board  
ParyavaranParisar, E-5 Arera Colony  
Bhopal – 462016  
**Madhya Pradesh**
16. The Member Secretary  
Manipur State Pollution Control Board  
Lamphelpat, Imphal  
West D.C. Office Complex – 795004  
**Manipur**

17. The Member Secretary  
Meghalaya State Pollution Control Board  
Arden, Lumpyngngad,  
Shillong – 793014  
**Meghalaya**
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Mizoram State Pollution Control Board  
New Secretariat Complex,  
Khatla, Thlanmual Peng, Aizwal  
**Mizoram**- 796001
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Nagaland – 797112  
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Odisha State Pollution Control Board  
Paribesh Bhawan A-118, Nilakanta Nagar,  
Unit –VIII, Bhubaneshwar – 751012.  
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Punjab State Pollution Control Board  
Nabha Road, ITI Rd, Adarsh Nagar,  
Prem Nagar,  
Patiala - 147001.  
**Punjab**
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Rajasthan State Pollution Control Board  
A-4 Institutional Area, Jhalana Doongri  
Jaipur – 302004.  
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State land Use & Environment Cell  
Govt. of Sikkim, Deorali,  
Gangtok, **Sikkim**
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Tamil Nadu State Pollution Control Board  
No. 76, Mount Salai, Guindy,  
Chennai - 600032.  
**Tamil Nadu**

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Telangana State Pollution Control Board  
Paryavaran Bhavan  
A-3, Industrial Estate, Sanath Nagar,  
Hyderabad – 500 018.  
**Telangana**
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Tripura State Pollution Control Board  
Parivesh Bhawan, Pt. Nehru Complex,  
Gorkhabasti P.O., Kunjaban, Agartala,  
West Tripura - 799 006.  
**Tripura**
27. The Member Secretary  
Uttarakhand Pollution Control Board  
94, Haridwar Rd, Saket Colony,  
Dharampure, Dehradun,  
**Uttarakhand- 248001**
28. The Member Secretary  
Uttar Pradesh State Pollution Control Board  
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Lucknow– 226010.  
**Uttar Pradesh**
29. The Member Secretary  
West Bengal State Pollution Control Board  
Paribesh Bhavan  
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Kolkata – 700 091.  
**West Bengal**
30. The Member Secretary  
Andaman & Nicobar Islands Pollution Control Committee  
Department of Science & Technology  
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Port Blair-744102  
**Andaman & Nicobar**
31. The Member Secretary  
Chandigarh Pollution Control Committee  
Paryavaran Bhawan  
Madhya Marg, Sector - 19 B,  
Chandigarh – 160019.  
**Chandigarh**

32. The Member Secretary  
Daman, Diu & Dadra Nagar Haveli Pollution Control Committee  
Office of the Deputy Conservator of Forests  
Moti Daman,  
Daman – 396220.  
**Daman & Diu**
  
33. The Member Secretary  
Delhi Pollution Control Committee  
4<sup>th</sup> floor, ISBT Building,  
Kashmeri Gate,  
**Delhi** - 110006.
  
34. The Member Secretary  
Lakshadweep Pollution Control Committee  
Lakshadweep Administration  
Department of Science, Technology & Environment  
Kavarati – 682555.  
**Lakshadweep**
  
35. The Member Secretary  
Puducherry Pollution Control Committee  
Department of Science, Technology & Environment  
Housing Board Complex,  
3<sup>rd</sup> floor, Anna Nagar, **Pondichery** – 600 005

## **Guidelines on Monitoring Mechanism for API residue**

### **Background**

Hon'ble National Green Tribunal Principal Bench, New Delhi in the matter of Original Application No. 136/2020 sought report from Ministry of Environment, Forests and Climate Change and Central Pollution Control Board with reference to the prayer of the applicant (Dr. Bishwanath Prasad Singh, Wing Commander (Retd.)), to prevent pollution of rivers Sirsa and Satluj by taking remedial action against discharge of waste from CETP at Baddi and from Acme Life Sciences, Nalagarh and Helio Pharmaceuticals at Solan.

The prayer was that pharmaceutical units at Barotiwala and Nalagarh are not connected to the CETP are discharging their effluents directly into the rivers. The effluent that discharged in to the rivers consists pharmaceutical ingredients even after treatment in ETP/STPs as the ETP/STPs are not specialized for the purpose/ for removal of pharmaceutical active ingredients. The CETPs are also not designed to neutralize Active Pharmaceutical Ingredient (API). The applicant stated that the presence of Ciprofloxacin in the concentration of 296.1 ug/l in the effluent discharge of M/s Acme Life Sciences was found on chemical analysis. The increasing occurrence of multi-resistant pathogens is a serious global threat to human health and it is finding its way into the water bodies and drinking water through industrial discharge and also due to heavy use of antibiotics in human and veterinary medicine.

Hon'ble National Green Tribunal passed the order in the aforesaid matter on 23.06.2021. S No. 12. of the said order reads as follows:

*“In view of the above, CPCB may also suggest monitoring mechanism for API residue through a credible system so as to cover all pharma industries in the country discharging API residue directly or indirectly in river systems. CPCB may propose the timelines to undertake monitoring which may also take a note of water quality monitoring guidelines of CPCB titled “Guidelines on Water Quality Monitoring, 2017” and the performance audit report dated 18.09.2020 filed by CPCB in OA 95/2018, Aryavart Foundation vs M/s Vapi Green Enviro Ltd. & Ors. and the directions of the Tribunal dated 05.02.2021.”*

## **Introduction**

Antimicrobial resistance (AMR) is the ability of a microorganism to survive and multiply in the presence of a compound with antimicrobial properties that would normally inhibit or kill this microorganism. Several different mechanisms are involved in the development of resistance to antimicrobials. Antibiotic residues may find their way to the environment via any of the following three modes:

- i) Waste water discharge from pharmaceutical manufacturing:  
Although the treatment of wastewater can partly eliminate or remove pharmaceuticals, some traces are still detectable in effluents and surface/groundwater as well depending on the concentration of antibiotics at the inlet of effluent treatment process and efficiency of effluent treatment process. Process Control to minimize the release of antibiotic residues in the effluent for end of the pipe treatment is seen as a viable option.
- ii) Human and Animal consumption and excretion: 30-90% of orally consumed dose of pharmaceutical consumed, are excreted as per reports available in the literature. Antibiotics used in aquacultures/poultry farms, animal husbandry etc are posing additional threat in this regard.
- iii) Non-scientific disposal of expired and/or unused medicines.

The presence of antibiotic residues in the environment cannot be attributed to a single source, direct release of antibiotic either accidental or due to lack of efficient effluent treatment technologies or process inefficiencies has made pharma industries as a starting point for addressing issue of antibiotic resistance. Besides above, other factors for antibiotic residues in effluents include:

- a) Direct emissions, if any, by pharma industries, although localized, are being considered as a source of discharge in much higher concentration when compared to other indirect sources.
- b) Since the antibiotic residues which are released directly in the pharma effluents, are not consumed and hence not metabolized like other sources and hence reduction in concentration in that ratio may not be achievable. Further, in principle, any compound that is not readily degraded/metabolized, has the potential to reach adverse exposure concentration in environment.
- c) It is unlikely that pharma industries will intentionally discharge their final product in the form of antibiotic residues. But at the same time, if discharged even accidentally or due to inefficient working of effluent treatment process, the concentration can always be several time more in comparison to other sources.



In addition to their indirect discharge, antimicrobials are also used in aquaculture where they are generally used as in-feed preparations. Ultimately, antimicrobials can reach various external environmental compartments such as rivers, lakes and soils where they can continue to exert their effects. Once in the environment, some antibiotics bind strongly to soil and sediments, which contributes to their persistence as they become inaccessible to degradation (these 'trapped' compounds can persist in soil for many years).

Resistance to antibiotics among human and veterinary pathogens increases the risks of treatment failure, increases mortality by increasing the time from an initial diagnosis to an effective therapy, and can also lead to morbidity by increasing the use of more toxic antibiotics as replacements for those rendered ineffective due to resistance. This issue also imposes an additional healthcare cost and productivity loss. Hence it's a necessity to develop guidelines for sampling and monitoring of the Antimicrobials.

Common Antibiotic manufacturing framework should follow the rules as mentioned in the Antimicrobial Industry Alliance (AMR IA). It was found that antibiotics compounds are sold in India in the form of antibiotics either individually or different combinations of 126 antibiotics. The Predicted no-effect concentration (PNEC) data contains two values. PNEC- Environment (PNEC- ENV) values are based on eco-toxicology data generated by Alliance member companies. These values are intended to be protective of ecological species and incorporate assessment factors consistent with standard environmental risk methodologies. The PNEC- Minimum Inhibitory Concentration (PNEC- MIC) values are intended to be protective of resistance promotion. These PNEC values are updated periodically as new reliable and robust data become available. These PNEC values, in absence of national standards for antibiotic residue, may be used as reference limit for self-monitoring purpose to prevent release of high levels of antibiotic residues in the environment.

### **Limit of Quantification**

Trace Organics Laboratory of Central Pollution Control Board, Delhi has validated method for 21 Pharmaceuticals compounds with Limit of quantifications (LOQ) as follows:

<b>S. No.</b>	<b>Name of Antibiotic</b>	<b>Limit of Quantification (LOQ) (µg/L)</b>
(1)	Amoxicillin	0.08
(2)	Cefixime	0.13
(3)	Cefadroxile	0.12

(4)	Fluconazole	0.14
(5)	Levofloxacin	0.16
(6)	Ciprofloxacin	0.15
(7)	Metronidazole	0.12
(8)	Azithromycin	0.03
(9)	Doxycyline	0.03
(10)	Chloramphenicol	0.09
(11)	Norfloxacin	0.045
(12)	Ofloxacin	0.03
(13)	Ampicillin	0.045
(14)	Nalidixic Acid	0.045
(15)	Spiramycin	0.051
(16)	Roxithromycin	0.026
(17)	Lincomycin	0.028
(18)	Enrofloxacin	0.022
(19)	Cloxacillin	0.088
(20)	Diclofenac	0.14
(21)	Mefenamic Acid	0.14

### **Guidelines for Sampling:**

#### **Sample Collection and locations:**

- (1) The procedure for sample collection in respect of surface water shall be as under:
  - a) Samples for Baseline and Trend stations shall be collected from well-mixed section of the river or main stem 30 cm below the water surface using a weighted bottle.
  - b) Samples for Impact stations shall be collected 30 cm below the water surface from the point of interest, such as bathing Ghats, downstream of point discharges, water supply intakes and other sources.
- (2) The procedure for sample collection in respect of reservoir water shall be as under:
  - a) Reservoir water quality has temporal, spatial as well as depth variation. The water is generally not well-mixed and sampling from a single depth may inadequately represent the overall water quality. It is, therefore necessary to ensure that sampling stations are truly representative of the water body.

- b) It is necessary to conduct preliminary survey to determine whether and where differences in water quality occur before deciding on the number of stations to establish. The most important feature of water in reservoir is vertical stratification which results in water quality variation along the depth. The vertical stratification at a sampling station can be detected by taking a temperature reading at 1 m below the surface and another at 1 m above the bottom. If there is a significant difference (more than 3 °C) between the two readings, there is a "thermocline" (a layer where the temperature changes rapidly with depth) and the reservoir is stratified. In stratified reservoirs, more than one sample is necessary to describe water quality.
  - c) For reservoirs of 10 m depth or more, it is essential that the position of the thermocline is first assessed by means of regularly-spaced temperature readings through the water column (e.g. metre intervals). Samples should then be taken according to the position and extent (in depth) of the thermocline. As a general guide, the minimum samples should consist of 1 m below the water surface, just above the determined depth of the thermocline, just below the determined depth of the thermocline, and 1 m above the bottom sediment (or closer if possible without disturbing the sediment). If the thermocline extends through several meters depth, additional samples are necessary from within the thermocline in order to characterise fully the water quality variations with depth.
  - d) In general, if the water depth at the sampling site is less than 10 m, the minimum sampling programme should consist of a sample taken 1 m below the water surface and another sample taken at 1 m above the bottom sediment.
  - e) Access to reservoir sampling stations is usually by boat and returning to precisely to the same locations for subsequent samples can be extremely difficult unless GPS is used or alternatively poles may be installed for the purpose.
- (3) The procedure for sample collection in respect of ground water shall be as under:
- (a) Open dug wells, which are not in use or have been abandoned, shall not be considered as water quality monitoring station. However, such well could be considered for water level monitoring. The ground water quality monitoring agencies should close down the unused open dug wells if they are potential source of microbiological contaminations in the areas without affecting the water level monitoring programme by replacing the abandoned dug wells with piezometers.
  - (b) Weighted sample bottle to collect sample from an open well about 30 cm below the surface of water may be used. The plastic bucket, which is likely to skim the surface layer only, shall not be used.
  - (c) Samples from the production tube wells shall be collected after running the well for about five minutes.

- (d) Non-production piezometers shall be purged using a submersible pump. The purged water volume shall equal 4 to 5 times the standing water volume, before sample is collected.
- (e) For bacteriological samples, when collected from tube wells or hand pump, the spout or outlet of the pump shall be sterilized under flame by spirit lamp before collection of sample in container.

**Sample preservation and transportation:**

- (1) Samples shall be transported (Cool to 0 - 6 °C) concerned laboratory as soon as possible, preferably within forty-eight hours of collection.
- (2) Analysis for coliforms shall be started within twenty-four hours of collection of sample. If time is exceeded, it should be recorded with the result.
- (3) Departments involved in monitoring should provide adequate training to the persons involved in water quality monitoring on collection and preservation techniques of water samples.
- (4) Departments involved should review the sample collection and analysis programme if it is not in conformity with Protocol norms. If it is not possible to adhere to transport time and analysis time due to large number of samples in one laboratory, the departments should outsource the analysis to nearby existing accredited laboratory.
- (5) Sample identification forms for the water sample analysis for surface and ground water samples shall be as per annexed Form-1 and Form-II.

**Quantity of samples to be collected:**

The quantity of samples to be collected for analysis shall be as follows:

- 1. General analysis: 1 litre.
- 2. Bacteriological analysis: 1000 ml. in sterilized bottle.
- 3. Metal analysis: 250 to 500 ml.
- 4. Pesticide analysis: 1000 ml in amber color glass bottle with Teflon lid cap

Collect samples in amber glass containers following conventional sampling practices.

5. Aqueous samples

5.1 Samples that flow freely are collected as grab samples or in refrigerated bottles using automatic sampling equipment. Collect 1 L each for the acid and base fractions (2 L total). If high concentrations of the analytes of interest are expected, collect two smaller volumes (e.g., 100 mL each) in addition to the 1 L samples. Do not rinse the bottle with sample before collection.

5.2 If residual chlorine is present, add 80 mg sodium thiosulfate per liter of water. Any method suitable for field use may be employed to test for residual chlorine.

5.3 Maintain aqueous samples in the dark at  $< 6^{\circ}\text{C}$  from the time of collection until receipt at the laboratory. If the sample will be frozen, allow room for expansion.

**Sample records:**

- (1) Each laboratory shall have a bound register, which shall be used for registering samples as they are received. A format for sample receipt register is annexed as Form- III.
- (2) The Laboratory In-Charge shall maintain a register for assignment of works to specific analyst.

**Analytical Techniques:**

Each agency shall follow the analytical techniques prescribed in the 'Standard Methods for analysis of Water and Wastewater' published by American Public Health Association (latest edition) or 'Methods for Testing Water and Wastewater-methods of sampling and testing (physical and chemical)' by Bureau of Indian Standards - IS:3025.

**Manpower requirements in laboratories:**

The manpower requirements shall be optimized by the concerned monitoring agencies in order to get the maximum utilization of man-days for timely completion of analysis.

**Data Processing, Reporting and Dissemination:**

Each monitoring agency shall process the analytical data and report the data after validation to the Data Centre at the Central Pollution Control Board (CPCB) or Central Water Commission (CWC). The CPCB or CWC shall store the data and disseminate through website or electronic mail to various users on demand. There should be free sharing of data among the various agencies collecting the water quality data.

**Accreditation of laboratories:**

The water quality laboratories shall seek recognition from the Ministry of Environment, Forests and Climate Change, Government of India and accreditation from National Accreditation Board for Testing and Calibration Laboratories (NABL) under Ministry of Science and Technology, Government of India. The water quality monitoring agencies/organizations should provide adequate financial support for

strengthening of their laboratories with adequate manpower and their upgradation with advance instruments for the purpose of recognition / accreditation.

### **Sampling and Analysis:**

1. Sampling of effluent shall be done from the inlet and outlet of the effluent treatment systems viz. Effluent Treatment Plant, Multiple Effect Evaporator, Agitated Thin Film Dryer, Reverse Osmosis etc. (wherever required) along with the point of final discharge of the treated effluent to assess effectiveness of effluent treatment.
2. Composite and 24H flow-proportional sampling may be better than single grab sampling as wastewater composition changes significantly over short time scales and individual samples may be “flooded” by homogenous solid material. Although, Grab sampling, which was the most commonly used method, is convenient and avoids significant auto sampler-associated workload and capital costs. However, sampling of influent and composite sampling optimise the chance of identifying human-wastewater AMR correlations and are most suitable for wastewater-based AMR surveillance studies.
3. Use and cleaning of sample Bottles and Caps: For Liquid Samples (waters, sludge and similar materials containing 5 percent solids or less): the sample bottle, amber glass, 1 L minimum, with screw cap must be used. For Solid samples (soil, sediment, sludge, filter cake, compost, and similar materials that contain more than 5 percent solids): Sample bottle, wide mouth, amber glass, 500-mL minimum must be used. If amber bottles are not available, samples must be protected from light, threaded Caps must be lined with fluoropolymer.  
Before use the bottles are washed with detergent and water, then rinsed with solvent. Similarly, Liners are washed with detergent and water and rinsed with reagent water before use.
4. The determination of pharmaceuticals and personal care products (PPCPs) in multi-media environmental samples must be done by **US EPA Method 1694** [(high performance liquid chromatography combined with tandem mass spectrometry (HPLC/MS/MS)]. This method was developed for use in Clean Water Act (CWA) programs and is based on existing EPA methods. This method is performance-based which means that it may be modified to improve performance (e.g., to overcome interferences or improve the accuracy or precision of the results) provided that all performance requirements of this method are met. The quality of the analysis is assured through reproducible calibration and testing of the extraction, clean-up, and LC/MS/MS systems.
5. For good quality of analysis proper cleaning of glassware is extremely important, because glassware may not only contaminate the samples but may also remove the analytes of interest by adsorption

on the glass surface. Hence, before use Glassware should be rinsed with solvent and washed with a detergent solution. After detergent washing, glassware should be rinsed immediately, first with methanol, then with hot tap water. The tap water rinse is followed by another methanol rinse, then acetone, and then methylene chloride.

6. Safety measures taken during analysis: The toxicity or carcinogenicity of each chemical used in analysis method has not been precisely determined; however, each compound should be treated as a potential health hazard. Pure standards of the compounds should be handled only by highly trained personnel thoroughly familiar with handling and cautionary procedures and the associated risks. The laboratory is responsible for maintaining a current awareness file of OSHA regulations regarding the safe handling of the chemicals.
7. A reference file of material safety data sheets (MSDSs) should also be made available to all personnel involved in these analyses.
8. It is also suggested that the laboratory perform personal hygiene monitoring of each analyst who perform the analysis.
9. The analyst and all personnel involved in these analyses must wear Protective equipment viz. Disposable plastic gloves (Latex or non-Latex (such as nitrile)), apron or lab coat, safety glasses or mask, and a glove box or fume hood should be used. During analytical operations that may give rise to aerosols or dusts, personnel should wear respirators equipped with activated carbon filters. Eye protection (preferably full face shields) should be worn while working with exposed samples or pure analytical standards. Latex or non-Latex (such as nitrile) gloves are commonly used to reduce exposure of the hands.
10. Workers must be trained in the proper method of removing contaminated gloves and clothing without contacting the exterior surfaces.
11. Personal hygiene of all personnel involved in these analyses: Hands and forearms should be washed thoroughly after each operation involving high concentrations of the analytes of interest, and before breaks (coffee, lunch, and shift).
12. Waste handling or techniques for minimizing contaminated waste: Plastic bag liners should be used in waste cans. Janitors (a caretaker or doorkeeper of a building) and other personnel should be trained in the safe handling of waste.
13. Bio solids samples may contain high concentrations of biohazards, and must be handled with gloves and opened in a hood or biological safety cabinet to prevent exposure. Laboratory staff should know and observe the safety procedures required in a microbiology laboratory that handles pathogenic organisms when handling bio solids samples.

14. Sample collection from field: Liquid samples that flow freely are collected as grab samples or in refrigerated bottles using automatic sampling equipment. If residual chlorine is present in the sample, add 80 mg sodium thiosulfate per liter of water.
15. Solid, mixed-phase, and semi-solid samples, including bio solids: Collect samples as grab samples using wide-mouth jars. Collect a sufficient amount of wet material to produce a minimum of 10 g of solids. If the sample will not be extracted within 48 hours of collection, the laboratory should adjust the pH of aqueous samples to 5.0 to 9.0 with a sodium hydroxide or sulfuric acid solution. Record the volume of acid or base used. If extraction of samples within 48 hours is not practical, then samples should be frozen to increase the holding time to seven days. If aqueous samples are stored frozen, extraction should begin within 48 hours of removal from the freezer.

#### Requirements for The Analysis of Antibiotics

S. No.	Requirements	Quantity	Size	Remarks
<b>Requirement of Space</b>				
01	Room with AC and Exhaust	04	<ul style="list-style-type: none"> <li>• ≈ 625.0 Square Feet (Instrument Room)</li> <li>• ≈ 400.0 Square Feet (Process Room)</li> <li>• ≈ 400.0 Square Feet (Sample Storage Room)</li> <li>• ≈ 400.0 Square Feet (Chemical and CRM Storage Room)</li> </ul>	
<b>Requirement of Instruments and Equipment</b>				
02	LC-MS/MS (Tandem Mass)	01		For Qualitative & Quantitative Analysis
03	Solid Phase Extraction System	01	12 or 24 port	For Extraction & Cleanup
04	Ultra Sonicator	01		For sonication of mobile phase and cleaning of HPLC parts
05	MiniVap or Turbovap Concentrator	01	06-10 port	For Concentration
06	Rotatory Evaporator	01		For Concentration
07	Millipore Filtration Assembly	01		For Filtration of sample And Mobile phase



08	MQ Water Assembly	01		For MQ Water
09	Deep Freezer	01		CRM Storage
10	Vici cooler	01		Sample Storage
11	UPS 20KVA	01	20 KVA	Only for LC-MS/MS
12	UPS 10KVA	01	120 KVA	For others equipment
<b>Miscellaneous Requirement</b>				
<b>Chemicals and Glassware/100 Sample (Approx.)</b>				
13	Methanol	1.5L		LC-MS/MS Grade
14	Acetonitrile	1.5L		LC-MS/MS Grade
15	HPLC Water	3.0L		LC-MS/MS Grade
16	Formic Acid	5.0ml		LC-MS/MS Grade
17	Ammonium Acetate	5.0gm		LC-MS/MS Grade
18	Ammonia Liquid	5.0ml		LC-MS/MS Grade
19	Orthophosphoric Acid	100.0ml		AR-Grade
20	Sulphuric Acid	20.0ml		AR-Grade
21	pH paper	150 strip		
22	Filter Paper GF/A	200	0.45µm / 47mm	
23	Filter Paper GF/A	10	0.25 µm / 47mm	
24	Syringe Filter	100	0.25 µm nylon	
25	HLB Cartridge	100	60 mg / 20cc	
26	Micropipette	01	100-1000µl (Variable)	
27	Micropipette	01	10µl (Fixed)	
28	Micropipette	01	25µl (Fixed)	
29	Micropipette	01	50µl (Fixed)	
30	Micropipette tip		As per requirements	
31	Sample Storage Vial	100		
32	Reference Standards for Antibiotics		As per requirements	
<b>(1) Others</b>				

33	Argon Gas Cylinder with Regulator	01	Approx. one cylinder for 500 sample	For LC-MS/MS
34	Nitrogen Gas Cylinder with regulator	01	Approx. one cylinder (47L) for 06 sample	For Sample Preparation
<b>Requirement of Manpower</b>				
35	Manpower	01		1.For Instrument operation, calibration & Analysis.
36	Manpower	02		2.For Sampling, processing including extraction, clean up, & sample preparation.

16.

- I) Pollution Prevention: comprises techniques that reduces or eliminates the quantity or toxicity of waste at the point of generation. Many opportunities for pollution prevention exist in laboratory operation. EPA has established a preferred hierarchy of environmental management techniques that places pollution prevention as the management option of first choice. Whenever feasible, laboratory personnel should use pollution prevention techniques to address waste generation. When wastes cannot be reduced at the source, the Agency recommends recycling as the next best option.
- II) Waste Management: Samples at pH<2, or pH >12 are hazardous and must be neutralized before being poured down a drain, or must be handled as hazardous waste.
- III) Low-level waste such as absorbent paper, tissues, animal remains, and plastic gloves may be burned in an appropriate incinerator. Gross quantities (milligrams) should be packaged securely and disposed of through commercial or governmental channels that are capable of handling toxic wastes.

**Duties of SPCBs/PCCs and frequency of monitoring**

17. The State Pollution Control Boards (SPCBs) and Pollution Control Committees (PCCs) shall conduct regular monitoring of every Technical grade pharmaceutical/ Bulk drug manufacturing /Formulation unit (hereinafter referred as pharma unit) under their jurisdiction. The monitoring of USP grade/ Laboratory grade pharmaceutical manufacturing units shall be conducted at least on half yearly basis and the inspection of Formulation units shall be conducted at least on annual basis.

18. The inspections/monitoring shall be conducted as surprise inspections. Any prior information pertaining to inspection shall not be provided to the industrial units that are to be inspected.
19. On the basis of violations / shortcomings as observed during the inspection/monitoring, the action on the defaulter unit may be taken independently by SPCBs / PCCs as applicable, under the provisions of the extant laws.
20. The inspections shall involve monitoring of treated / discharged effluent w.r.t prescribed parameters including pharmaceutical parameters. The inspections have to be conducted irrespective of mode of treated effluent discharge by the pharmaceutical unit.
21. It shall essentially be verified during inspection whether the pharmaceutical unit (under inspection) is discharging treated /untreated effluent or disposing hazardous wastes in unauthorized manner. In case any unauthorized discharge of effluent/unauthorized disposal of Hazardous Waste is observed, action on the defaulter pharmaceutical unit under extant laws shall immediately be taken.
22. In case, the pharmaceutical unit (under inspection) claims Zero Liquid Discharge (ZLD) compliance, an assessment of feasibility of ZLD compliance shall be made thorough effluent monitoring and mass balance of effluent and it shall be ascertained that the unit does not practise effluent bypassing or discharge of effluent by any other means. ZLD may be defined as ‘The entire quantity of effluent is treated to recover water and recovered water is reused in process and / or utilities, and only solids are discharged (or reused, if possible) in environmentally sound manner. Reuse of treated effluent for horticulture or agriculture purposes will be considered as discharge on land and not as means to achieve ZLD. Similarly, effluent from individual industries being sent to CETP for treatment will not be considered as ZLD.’
23. Excessive concentrations of Pharmaceutical ingredients may be toxic to living being. Hence, it shall essentially be verified during monitoring about any possibility of environmental pollution that may be caused by the pharmaceutical industry (under inspection) owing to mixing of the industrial effluent/any process effluent or leachate from the process / storage area containing minute concentration of Pharmaceutical ingredients with rain water / storm water.
24. In case, the pharmaceutical unit discharges its treated effluent to the inland surface water, river, stream or drain, the monitoring of the water body shall be conducted along with the monitoring of treated effluent. In case of discharge to rivers, streams, drains etc. upstream and downstream monitoring shall be conducted along with the monitoring of treated effluent. The monitoring of water body shall be done for prescribed parameters including pharmaceuticals and heavy metals.
25. Monitoring of the water body (to which the treated effluent is discharged) shall also be conducted w.r.t. pharmaceutical parameters. For the purpose of baseline concentration for reference / comparison, water samples from another location(s) as per discretion of the monitoring officials

shall also be taken so that it may be ascertained whether the pharmaceutical unit (under inspection) is causing any water pollution.

26. Half yearly monitoring of water bodies, if any within the 500 m radius of pharmaceutical units shall be conducted to assess any pharmaceutical contamination/Anti-Microbial Resistance due to continuous discharge of industrial effluent with minor concentration of pharmaceutical ingredients in the water body. If it is observed that the monitored water body (within the 500 m radius of pharmaceutical units) is polluted with pharmaceutical ingredient (s), then further monitoring of water bodies situated beyond 500 m shall be done to assess the extent of pollution. For the purpose of baseline concentration for reference / comparison, fresh water samples from other locations as per discretion of the monitoring officials may be taken.
27. In case, the pharmaceutical unit uses its treated effluent in irrigation / gardening; groundwater monitoring w.r.t. pharmaceutical parameters shall be conducted by SPCBs / PCCs along with the monitoring of treated effluent. For the purpose of baseline concentration for reference / comparison, groundwater samples from another location(s) as per discretion of the monitoring officials shall also be taken so that it may be ascertained whether the pharmaceutical unit (under inspection) is causing any groundwater pollution.
28. In every case, irrespective of mode of discharge of the treated effluent, the inspections shall also involve ground water monitoring w.r.t. pharmaceutical parameters around 500 m of the pharmaceutical unit. If it is observed that the groundwater (within the 500 m radius of pharmaceutical units) is polluted with pharmaceuticals, then further monitoring of groundwater beyond 500 m shall be done to assess the extent of pollution. For the purpose of baseline concentration for reference / comparison, ground water samples from another location(s) as per discretion of the monitoring officials shall also be collected so that it may be ascertained whether the pharmaceutical unit (under inspection) is responsible for ground water pollution (if any).
29. In every case, irrespective of mode of discharge of the treated effluent, the inspections shall also involve water monitoring w.r.t. pharmaceutical parameters around 500m of the pharmaceutical unit. If it is observed that the water (within the 500 m radius of pharmaceutical units) is polluted with pharmaceutical, then further monitoring of soil beyond 500 m shall be done to assess the extent of pollution. For the purpose of baseline concentration for reference/ comparison, water samples from another location(s) as per discretion of the monitoring officials shall also be taken so that it may be ascertained whether the pharmaceutical unit (under inspection) is causing any water pollution.
30. In case the pharmaceutical industry is situated within a notified industrial cluster, the monitoring officials may at their discretion decide the distance from where water, and ground water have to be taken for the purpose of baseline concentration for reference / comparison.

31. SPCBs and PCCs shall conduct effluent monitoring of Common Effluent Treatment Plants and Sewage Treatment Plants under their jurisdiction w.r.t. pharmaceutical parameters. The treated effluent from Common Effluent Treatment Plants and Sewage Treatment Plants shall not contain any pharmaceutical ingredients so that to resist from Anti-microbial resistance in environment. The monitoring has to be done regularly at least on half yearly basis.
32. SPCBs and PCCs shall conduct regular inspections of Hazardous Waste Disposal / Treatment facilities as well as Municipal Waste dumping sites within their jurisdiction. The inspections have to be done at least on half yearly basis. The monitoring shall involve ground water as well as soil sampling around 500m of Hazardous waste disposal facility and Municipal Waste dumping sites w.r.t. pharmaceutical parameters. If it is observed that the groundwater and / or soil (within the 500 m radius of pharmaceutical/Bulk drug manufacturing units) is polluted with pharmaceutical ingredients (s), then further monitoring of groundwater and / or soil beyond 500 m shall be done to assess the extent of pollution. For the purpose of baseline concentration for reference and comparison, ground water samples and soil samples from another location(s) as per discretion of the monitoring officials shall be taken.
33. In case, SPCBs / PCCs observe that any Pharmaceutical/Bulk drug Manufacturing Industry, Common Effluent Treatment Plant, Sewage Treatment Plant, Municipal Waste dumping site or Hazardous Waste Disposal/Treatment facility has caused grave injury to the environment because of discharge of effluent / leachate contaminated with pharmaceutical ingredients or improper disposal of hazardous / other wastes containing pharmaceutical ingredients, action on the defaulter under extant laws shall immediately be taken.
34. The decision whether the pollution of environment and development of anti-microbial resistant in the water bodies has been caused by the pharmaceutical industries or bulk drug manufacturing units run off or by Common Effluent Treatment Plant, Sewage Treatment Plant, Municipal Waste dumping site or Hazardous Waste Disposal/Treatment shall be taken based upon the observed facts, evidences and scientific rationale.
35. SPCBs / PCCs may direct the pharmaceutical industries in their jurisdiction to recycle and reuse the treated effluent to the maximum possible extent.
36. SPCBs / PCCs shall ensure that no pharmaceutical unit shall manufacture or formulate the pharmaceutical products other than the consented products.
37. SPCBs / PCCs jointly with CPCB shall carry out monitoring of water bodies during pre and post monsoon seasons so as to assess the impact of the Anti-microbial resistance/pharmaceutical run off into the water bodies because of industrial discharge.

38. For conducting the above stated inspections / monitoring; SPCBs, PCCs at their discretion may engage any Government organization or Government approved organization having adequate expertise in monitoring of Anti-microbial resistance in water bodies.
39. The analysis of effluent / ground water /soil samples for the pharmaceutical parameters and other than pharmaceuticals parameters shall be carried out in the laboratories of SPCBs / PCCs or in the laboratories recognised by Ministry of Environment, Forests and Climate Change and accredited by National Accreditation Board for Testing and Calibration Laboratories (NABL).

### **Recommendations/Mitigation of AMR in the environment**

40. When a new class of antimicrobials comes on the market, it should be considered “critically important” from the outset unless strong evidence suggests otherwise. The risk assessment of new antimicrobial substances for use in food-producing species should be reinforced. One of the possible options would be to introduce an early hazard characterisation, addressing the risk to public health from antimicrobial resistance (AMR), to be assessed prior to the submission of a Marketing Authorization Application (MAA).
41. At the time of first approval for new antimicrobial substances/a new class of antimicrobials in veterinary medicine, marketing authorisation holders (MAHs) should have plans in place to monitor susceptibility in zoonotic and indicator bacteria through approved programmes; these data should be provided by the MAH to the regulatory authorities and be comparable with human AMR surveillance data.
42. Based on the outcome of antimicrobial resistance surveillance and monitoring of usage, a new risk assessment could be required for all products of a specific antimicrobial class, encompassing both generic and reference products.
43. Put in place a declaration system in order to assess the extent and evolution of off label use of human only authorised antimicrobials. Monitoring of off label use needs to be facilitated. When collecting data on consumption of off label use of antimicrobials in animals the animal species (body weight), product, indication, regimen (dose, duration, treatment interval, route of administration/formulation) are important to assess.
44. Include in future legislation flexible tools to allow banning or limitation of off label use in animals of certain antimicrobials/classes authorised only in human medicine following an unfavourable hazard characterization or benefit-risk assessment.

45. Existing drugs that are already classified as “critically important” antimicrobials but which are not currently used in food production such as carbapenems, oxazolidinones (linezolid) and lipopeptides (daptomycin) should not be used in the future in food animal production”.
46. Recognising the need to preserve the effectiveness of the antimicrobial agents in human medicine, careful consideration should be given regarding their potential use (including extra-label/off label use).”

#### **Reduce the input of antibiotics into environmental**

47. Antimicrobials manufacturing industry should possess a valid authorization for discharge of treated effluent. Compliance with each condition in the authorization should be achieved.
48. Levels of antibiotic in process wastewater are quantified e.g. mass balance.
49. Wastewater sources from operations are characterized and evaluated for treatability and control.
50. Effective waste water treatment plant is equipped with primary, secondary and tertiary treatment (e.g., neutralization, clarification, settling, inactivation, biological or chemical treatment) which is efficacious to eliminate the residual Antibiotics. Industries may deploy the Antibiotic deactivation techniques like acidification, neutralization and others to degrade the active Antibiotics moiety.
51. The technology plays crucial part for conversion and recovery of product i.e. minimizing the product loss into mother liquor. The adoption of best practices during manufacturing process to arrest (minimize) the emission of antibiotics into water stream to reduce the influx into waste water treatment plant or environment.
52. The CETP, waste water treatment plant (WWTP) infrastructure, design and its effectiveness i.e. onsite, offsite and infrastructure & performance of treatment system before discharging to common effluent treatment plant, are to release the emission of residual antibiotics into environment.
53. Sludge from process wastewater treatment is managed in compliance with all local regulations. Assessments are conducted to determine potential risk from sludge application to land.
54. Setting up systems and best practice guidelines to correctly dispose of unused medicines.
55. Limiting the use of antimicrobials (especially critically important compounds).
56. Frequent sampling is important to understand the levels of API residue in the discharge.
57. Samples are collected, stored, and analysed with results reported in accordance with regulatory requirements.
58. Process areas (e.g., tanks, container storage areas, and process sewer systems) are designed, constructed and operated to prevent spills or releases antibiotic residue to the environment.
59. Treatment systems should be in placed to prevent soil, surface water, or groundwater contamination.

60. Waste classification, labelling, storage and disposal methods should be in accordance with the hazard characteristics of the waste, and in accordance with regulatory requirements. i) Waste containers are labelled with contents, hazard characteristics (e.g., flammable, biological), and closed once waste is placed in the container. ii) Disposal methods are based on waste characteristics. Records (e.g., waste classification determinations including analytical results, letters from waste contractors/facility, and certificates of destruction) are maintained.
61. Waste disposal contractors/facility should possess authorizations/certifications from SPCBs/PCCs to manage specific waste streams in accordance with regulations.



## FORM - I

## SAMPLE IDENTIFICATION FOR SURFACE WATER SAMPLES

Sample Code :									
Observer :			Agency :			Project :			
Date :		Station Name and Code :				Longitude :			
Time :		Latitude :		Division :					
Depth of Sample :		River :							
Parameter Code	Container				Preservation				
	Glass	PVC	PE	Teflon	None	Cool	Acid	Other	
(1) General									
(2) Bacteriology									
(3) BOD									
(4) COD, NH <sub>3</sub> , NO <sub>3</sub>									
(5) Toxic Metals									
(6) Trace Organics									
Source of Water									
<input type="checkbox"/> River	<input type="checkbox"/> Main Current		<input type="checkbox"/> Bridge		<input type="checkbox"/> Water		<input type="checkbox"/> Fresh		
<input type="checkbox"/> Drain	<input type="checkbox"/> Right Bank		<input type="checkbox"/> Boat		<input type="checkbox"/> Sediment		<input type="checkbox"/> Brackish		
<input type="checkbox"/> Canal	<input type="checkbox"/> Left Bank		<input type="checkbox"/> Wading		<input type="checkbox"/> Susp. Matter		<input type="checkbox"/> Salt		
<input type="checkbox"/> Reservoir	<input type="checkbox"/> other		<input type="checkbox"/> other		<input type="checkbox"/> Biota		<input type="checkbox"/> Effluent		
Sample Types		<input type="checkbox"/> Grab		<input type="checkbox"/> Time Comp.		<input type="checkbox"/> Flow Comp.		<input type="checkbox"/> Depth-integ	
Sample Device		<input type="checkbox"/> Weighted Bottle			<input type="checkbox"/> Pump		<input type="checkbox"/> Depth Sampler		
Field Determination									
Temperature:		pH		EC		µmhos/cm		DO mg/L	
Odour code	[1] Odour free	[6] Septic		Colour code	[1] Light brown		[6] Dark green		
	[2] Rotten eggs	[7] Aromatic			[2] Brown		[7] Light black		
	[3] Burnt sugar	[8] Chlorinous			[3] Dark brown		[8] Black		
	[4] Soapy	[9] Alcoholic			[4] Light green		[9] Clear		
	[5] Fishy	[10] Unpleasant			[5] Green		[10] Other (Specify)		
Remarks									
Weather		<input type="checkbox"/> Sunny		<input type="checkbox"/> Cloudy		<input type="checkbox"/> Rainy		<input type="checkbox"/> Windy	
Water vel.(m/sec)		<input type="checkbox"/> High (>0.5)		<input type="checkbox"/> Medium (0.1-0.5)		<input type="checkbox"/> Low (<0.1)		<input type="checkbox"/> Standing	
Water Use		<input type="checkbox"/> None				<input type="checkbox"/> Cultivation / Irrigation			
		<input type="checkbox"/> Bathing & Washing				<input type="checkbox"/> Cattle washing			
		<input type="checkbox"/> Melon / vegetable farming				<input type="checkbox"/> Industrial / Organised water supply			

FORM-II

SAMPLE IDENTIFICATION FOR GROUND WATER SAMPLES

Sample Code														
Observer			Agency				Project							
Date Time		Station Address and Code						Latitude:						
		Location:						Longitude:						
		Village:												
		Tehsil:												
		District:												
		State												
Source of Sample		Open dug well / Dug cum bore well			Hand pump		Tube Well/ bore well			Piezometer				
Parameter Code		Container				Preservation								
		Glass	PVC	PE	Teflon	None	Cool	Acid	Other					
(1) General														
(2) Bacteriology														
(3) BOD														
(4) COD														
(5) Toxic Metals														
(6) Trace Organics														
<b>Field Determination</b>														
Temp		°C		pH		EC						micromhos/cm		
Odor code		(1) Odor free		(2) Rotten eggs		Color code			(1) Light brown		(2) Brown			
		(3) Burnt sugar		(4) Soapy					(3) Dark brown		(4) Light green			
		(5) Fishy		(6) Septic					(5) Green		(6) Dark green			
		(7) Aromatic		(8) Chlorinous					(7) Clear		(8) Other(specify)			
		(9) Alcoholic		(10) Unpleasant										
<b>Hydro geological Information</b>														
<b>Well Data</b>														
Diameter				Q									cm	
Total Depth				D									m bgl	
Static Water Level (Avg.)				SWL									M bgl	
Aquifer Characteristics														
Use of the well/tubewell/bore well														
Depth of Slot pipes													M bgl	
Land use in surrounding area														
<b>If the tubewell/bore well/piezometer is purged, complete below</b>														
<b>Field Flow Measurement</b>														
Static Water Level				SWL									mbgl	
Actual pump setting depth													M	
Purging duration													min	
Pump discharge				Q									L/min	
Volume purged				V									L	

FORM-III

Sample Record for Analysis

Date / time received at lab	Date / time collected	Lab. ID No	Station Name and Code	Tehsil/ District	Project	Collecting agency / collector	Preservation	Parameter Code
1	2	3	4	5	6	7	8	9

Sample receipt register

Note:

- Column (3) gives the laboratory sample assigned to the sample as it is received in the laboratory. Note that the numbering has two parts separated by hyphen. The first part is assigned in a sequential manner as samples are received from various stations. If two samples are collected at the same time from a station for different sets of analysis, the first part of the number is the same. The second part corresponds to the parameter code as given in the sample.
- Column (4) gives the station code conventionally followed by the monitoring agency.
- Column (6) gives the project under which the sample is collected.
- Column (9) corresponds to the parameter(s) code given in the sample identification form.
- The result of the analysis of all the samples having the same first part of the code would be entered in the data entry system as one sample having the same station code and time of sample collection.