20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
of the Quality Control laboratory

Part 1	**General information**
Laboratory Details	
Laboratory information	
Name of the laboratory	Ezequiel Dias Foundation (FUNED), Central Laboratory of Public Health of Minas Gerais (Lacen-MG)
Address of Laboratory	Conde Pereira Carneiro Street 80, Gameleira Neighbourhood, Belo Horizonte, Minas Gerais , 30510-030, Brazil
Inspected Laboratory	
Address of inspected Laboratory if different from that given above	As above
Summary of activities performed at the laboratory	**Type of Analysis** / **Finished Products** Physicochemical analysis: pH, Friability, Disintegration, Density, Dissolution, Uniformity of dosage units (content), Uniformity of dosage units (mass), Loss on drying, Water content (K. Fischer) Identification: FTIR, TLC, HPLC, UV-VIS Spectrophotometry, Basic tests Assay, impurities and related substances: HPLC (UV-VIS, DAD, Fluorescence detection), TLC, FTIR, UV-VIS Spectrophotometry, Volumetric Titrations, Potentiometric Titrations, Determination of related substances/impurities, Degradation products Microbiological Tests: Microbial limit tests , Bacterial Endotoxins test (LAL), Sterility test
Inspection details	
Dates of inspection	9 – 11 April 2018
Type of inspection	Routine

Introduction	
General information	The Octávio Magalhães Institute (IOM) is the Central Laboratory of Public Health of Minas Gerais State (Lacen-MG) and belongs to the Ezequiel Dias Foundation (Funed). The Lacen-MG works on epidemiological and health surveillance. In addition to the Octávio Magalhães Institute (IOM), the Ezequiel Dias Foundation (Funed) contains 3 other boards : • Planning, Management and Finances Board (DPGF) • Research and Development Board (DPD) • Industrial Board (DI) The laboratory (IOM) is a component of the Health Surveillance National System (SNVS) working in cooperation with the Brazilian Health Surveillance Agency (ANVISA) the national medicines regulatory authority and local health surveillance authorities. Main activities are focused on the sanitary control of products by fiscal analysis in: medicines, cosmetics, sanitizers, hemodialysis solutions, water and drinking water, food and blood components. The laboratory quality management system is based on ABNT NBR ISO / IEC 17025:2005 - General requirements for testing and calibration laboratories. Lacen-MG has been accredited for performing physico-chemical and microbiological tests since 2008. The laboratory is holds the following certification: ABNT NBR ISO 9001:2015 - Quality management systems – Requirements.
History of regulatory authorities inspections	This was the second inspection performed by the WHO. Laboratory was inspected by: Minas Gerais Health Surveillance Secretariat.
Scope and limitations	
Areas inspected	See Part 2 below
Restrictions	N/A
Out of scope	Production Culture Media Department DHPMC
Abbreviations	

AHU	air handling unit
ALCOA	attributable, legible, contemporaneous, original and accurate
API	active pharmaceutical ingredient
BDL	below detection limit
CAPA	corrective actions and preventive actions
CC	change control

	CFU	colony-forming unit		
	CoA	certificate of analysis		
	DQ	design qualification		
	EM	environmental monitoring		
	FAT	factory acceptance test		
	FMEA	failure modes and effects analysis		
	FPP	finished pharmaceutical product		
	FTA	fault tree analysis		
	FTIR	Fourier transform infrared spectrometer		
	GC	gas chromatograph		
	GMP	good manufacturing practice		
	HACCP	hazard analysis and critical control points		
	HPLC	high-performance liquid chromatograph		
	HVAC	heating, ventilation and air conditioning		
	IR	infrared spectrophotometer		
	IQ	installation qualification		
	KF	Karl Fisher		
	LAF	laminar air flow		
	LIMS	laboratory information management system		
	LoD	limit of detection		
	LOD	loss on drying		
	MB	Microbiology		
	MBL	microbiology laboratory		
	MR	management review		
	NMR	nuclear magnetic resonance spectroscopy		
	NRA	national regulatory agency		
	OQ	operational qualification		
	PHA	process hazard analysis		
	PM	preventive maintenance		
	PQ	performance qualification		
	QA	quality assurance		
	QC	quality control		
	QCL	quality control laboratory		
	QRM	quality risk management		
	RA	risk assessment		
	RCA	root cause analysis		
	SOP	standard operating procedure		
	TAMC	total aerobic microbial count		
	TFC	total fungi count		

	TLC	thin layer chromatography		
	URS	user requirements specifications		
	UV	ultraviolet-visible spectrophotometer		

Part 2	**Brief summary of the findings and recommendations**

Brief summary of the findings and comments

1. Organization and management

The laboratory was legally authorized and had managerial and technical personnel to identify the occurrence of departures from the quality management system or the procedures for performing tests and/or calibrations, validation and verification, and to initiate actions to prevent or minimize such departures. Management and personnel were not subject to commercial, political, financial and other pressures or conflicts of interest.

Roles and responsibilities were specified in signed job descriptions.

The laboratory maintained a registry for receiving, distributing and supervising the consignment of the samples to the specific testing units; and keeping records on all incoming samples and accompanying documents.

None of the products were analyzed following a request from the WHO.

2. Quality management system

A quality management system was in place which included policies, systems, programmes, procedures and instructions. A Quality Manual established by the FUNED was available. In addition, for each of the four boards (Finance, Development, Industrial and IOM) a specific Quality Manuals was published and enforced.

The IOM Quality Manual which was based on ISO17025 and WHO guidelines was approved and signed by the Quality manager.

The IOM Quality Manual contained a commitment to establishing, implementing and maintaining an effective quality management system and compliance with standards of good practice and WHO guidelines.

The FUNED Quality Manual and the IOM Quality Manual were briefly discussed. Generally, the Quality Manuals described the Quality policy and covered aspects according to good practices for pharmaceutical quality control laboratories. The contents included e.g. qualification of personnel, control of documents, contracts, purchasing services, validation of analytical methods, non-conforming testing, corrective actions (CA), complaints, internal audits, protection of confidential information.

The SOP "Internal audits" was briefly discussed. According to the SOP internal audits were performed once in a year. Internal audit of laboratory was performed by laboratory staff, avoiding conflict of interests. Last Internal audit of the laboratory was performed November 2017. Audit report was discussed; it was very detailed document and covered all section of WHO guidelines (WHO TRS No. 961, 957), Annex 1 and WHO TRS No. 961, Annex 2). CAPAs were proposed by the persons audited, implementation of CAPAs was check by Quality of the IOM board.

The SOP “Customer support and complaints” was briefly discussed. Laboratory customers were state and city level health surveillance agencies and ANVISA. No complaints were received regarding inspected laboratory in 2017. Customer satisfaction surveys for internal and external customers were performed annually.

The SOP “Management review” was briefly discussed. MR was performed annually. MR meeting minutes of February 2018 was discussed. MR was carried out following WHO guideline section 2.5.

The SOP “Handling of anomalies” was briefly discussed. The SOP explained dealing with corrective and preventive actions and root cause analysis (RCA).

The SOP “Risk management” was briefly discussed. FMEA and Risk matrix were used for risk assessment. Scoring from 1 -5 was used for RPN calculations.

The following, but not limited registers were maintained electronically:
- Anomalies
- Non-compliances
- CAPAs
- RCA

The SOP "Procedure for sample registration and receipt” was briefly discussed.

The document “Physical-chemical and Microbiological tests of products” as briefly discussed. It showed a table summarizing parameters to be tested and a list of tests to be performed according to the relevant pharmacopoeia and the customer’s requirements for all products. It was found to be an uncontrolled document neither dated nor signed, although it was a reference document for the analysts regarding the information about the tests to be performed.

3. Control of documentation

Documented procedures were in place for documents control. Authorized SOP Master List identifying the current version status and distribution of documents was available. Documents last version in electronic format was available for authorized persons in SE Suite system. One hard controlled copy was available at the Quality Department. Documents were stored in the laboratory according to the form.

The SOP "Elaboration of Standard Operating Procedure – Methodology" nd "Elaboration of Procedures and working instructions" were briefly discussed.

The SOP "Document control" was briefly discussed.

4. Change control

The SOP "Change control" was briefly discussed. The SOP was applicable, but not limited for the following changes:

- Procedures,
- Equipment
- Infrastructure
- Premises
- Systems and utilities

Change control register was presented to the inspectors. Changes were classified as:

- Emergency
- Non-emergency
- Temporary
- Permanent

Risk analyses were performed for critical CCs using FMEA, by person or persons who initiated change. Assessment of CC was performed by Quality team of IOM.

5. Records

Analytical data were recorded in analyst work sheets and were fully traceable to samples, instruments, test procedures and reference standards. Records related to laboratory activities such as instrument qualification, calibration, raw data, test results and reports were appropriately stored in a chronological order. Software - Sample management system (SMP) was used in the laboratory. Analytical raw data to the system was entered by the responsible analyst or technician and verified by the Head of the laboratory.

6. Data processing equipment

HPLCs, UV and IR instruments were linked to computers operated by their respective software. All raw data generated by these instruments were stored as hard copies and electronically on a server. Hard copies of raw data were kept; the system was in place to back-up the raw data from the server, what was located at another location.

The SOP "Back up procedure" was briefly discussed. Daily and weekly back-ups were done automatically. Monthly back up was done by IT on external media and stored on external server in separate facility.

7. Personnel

Generally the laboratory had sufficient personnel with the necessary education, training, technical knowledge and experience for their assigned functions. Staff members undergoing training were trained by qualified trainers, internally or externally and training effectiveness was assessed on completion of the training. Personnel performing specific tasks were appropriately qualified in terms of their education, training and experience, as required. During training analysts were supervised and they performance was evaluated before they were allowed to perform analysis alone. Current, detailed job descriptions were maintained.

The laboratory employed 17 persons.

The SOP "Identification of the needs for training" was briefly discussed.

The SOP "Training development action" was briefly discussed. The assessment of the training efficacy was done either by an oral discussion, a written or oral evaluation or by an on job evaluation.

8. Premises

The laboratory premises were, clean, and tidy and provided adequate room for laboratory activities. The laboratory environment was appropriate for performing different tests. Access to the laboratories was biometrically controlled. Physico-chemical laboratory consisted of several separate rooms; one room was dedicated to chemical tests (dissolution, disintegration, friability, pH and potentiometrical titration) and other room to HPLC, GC and UV instruments.

Limited amounts of reagents were stored in separate room. Reagents were purchased centrally.

Samples for analysis and retention samples were stored in one room, in dedicated and locked cabinets. The environmental conditions (T and RH) were monitored, controlled and documented. Environmental conditions were controlled by the wireless system, provided with visual alarms. T and RH was recorded every 5 minutes and verified daily.

The Microbiology Laboratory consisted of a sterility testing room, a testing room containing two biological safety cabinets and a general work area with refrigerators and incubators and other general equipment. The area was clean and tidy.

Sterility Testing was carried out in an isolator, located in class "D" room. Two Biological Safety Cabinets were used for non-sterile testing and work with master strains. During inspection one cabinet was out of order. It was explained to inspectors that work with master stains and products were done in different days to avoid contamination and cross-contamination. Environmental monitoring of biological Safety Cabinets was carried out weekly and during testing.

9. Equipment, instrument and other devices

Generally the laboratory had test equipment, instruments and other devices for the performance of the tests and/or calibrations, validations and verifications. Calibration status labels were attached to instruments. All laboratory instruments had “instrument log books”.
Calibration of laboratory instruments was contracted out to external agencies. Verification of instruments was done by laboratory staff.

Laboratory used only class “A” glassware, which was verified every two years in-house and calibrated every 4 years by external agency.

In the Microbiology Laboratory incubators and refrigerators were monitored daily for temperature. Manual recording was conducted using a thermometer placed in a tube of water in the incubator or refrigerator. The temperature of incubators and refrigerators was also monitored continuously with a probe inserted in the chamber. The probe was also connected to an alarm system.

Sterility test incubator was installed in December 2017. DQ, IQ, OQ and PQ were performed by external agency. Fumigation and decontamination was done automatically. Pressure differentials in isolator were monitored automatically.

Schematic drawing of AHU supplying air to the room where isolator was located was briefly discussed. It was said that re-qualification of the room was carried out every 6 months.

Qualification report XX “Environment qualification report” was briefly discussed.

Laboratory explained that digital pressure differential manometer will be installed in the nearest future to monitor pressure differential between laboratory and class “D” room.

10. Contracts

Contracts with service providers were available. Laboratory tests were not subcontracted or outsourced to another laboratory.

11. Reagents

Laboratory reagents were purchased centrally via tenders. Reagents arrived to the central storage, where invoice was checked against purchase order. Afterwards reagents were distributed to the laboratories where those were visually examined and checked. All reagents had expiry dates and MSDS. Laboratory maintained reagents inventory, the stocks were regularly monitored.

Solutions prepared in the laboratory were labeled and stored appropriately, preparation records were available and traceable to the reagent batch/lot numbers and expiry dates.

Water supplied by a Millipore system was used for tests. Conductivity, TOC and flow rate were monitored on-line. Off-line (external) conductivity test and microbiological tests were carried out once per months. TOC test was carried out daily.

The majority of the Media used in the Microbiology Laboratory was prepared within the IOM by the Production Culture Media Department DHPMC. Dried media was tested for suitability before it was released for used. It was stored in the controlled location.

Inspectors were informed that media was sterilized according to the media manufacturer's specifications e.g. 121 °C for 15 minutes.

Solid media was tested for growth promotion; selective media was tested using positive and negative controls. Prepared media was sent to the laboratory along with media certificate. A copy of the quality check list was used to verify media certificate. Received media was checked visually and also according to the media evaluation check list. As an example Agar Sabouraud media certificate was checked. Three months expiry date was assigned to this media. Inspectors were told that stability studies were carried out to prove expiry date.

Some ready-made Medias were purchase from an outside supplier. In this case growth promotion tests were performed at DHPMC laboratory and manufacturer's certificate was verified.

12. Reference substances and reference materials

Reference standard register and usage log books were available and traceable to the analysis these were used for. Reference standards were stored in the chemical laboratory in locked desiccators (humidity controlled box), fridge and freezer. Before used reference standards what were stored in the fridge or freezer were relocated to the desiccator to reach the room temperature. Laboratory used only Pharmacopeia reference standards.

Reagents and solvents, acids and bases were stored in the reagent storage room. Only limited quantities of these materials were kept in the laboratory.

In the Microbiology Laboratory reference cultures were obtained from the Institute Micro Biologics. The strains were originally derived from ATCC strains. Strains were subject to purity checks, gram stain and presumptive identification. Working cultures were less than 5 subcultures from the original source strain. VITEK microbial identification system was used for identification of the organisms.

13. Calibration, verification of performance and qualification of equipment, instruments and other devices

Equipment items were uniquely identified and log books were available for all instruments. Calibration of instruments was carried out annually by the external accredited contract organizations. Calibration certificates with the details of actual tests performed, results and acceptance criteria, were available from the agencies.

Laboratory instruments were properly labeled with unique identification numbers and calibrations labels indicating date of calibration and due to calibration date.

pH meters were verified with standard buffer solutions before use. A number of analytical balances were available. Individually calibrated standard weights were presented to the inspectors.

Biological Safety Cabinets were calibrated twice annually by an external agency.

14. Traceability

Test results were traceable to analyst, analytical instruments, equipment, reagents, reference substances and test procedures.

15. Incoming samples

The laboratory had a central registry dealing with registration and distribution of the samples. Records of incoming samples were properly kept for all incoming samples according to the SOP by logging in a register and HARPYA software provided by INCQS (National Institute of Quality Control in Health). Samples were received in sealed bags. Three sets of samples were collected by supervisory bodies. One set of samples was stored at the place of collection of the sample and two sets were received in the laboratory. One set was sent for analysis and one was kept as retention sample.

Each individual sample had label indicating HARPYA number. Incoming samples were checked against "Test Request Form" and verified visually. Afterwards samples were distributed together with sample distribution form to the respective laboratories. Sample identification number was recorded on all documents; forms, test reports, CoA, etc.

The SOP "Incoming samples register" was briefly discussed. SOP was applicable for all incoming samples, for example; medicines, cosmetics, food. Samples were received by incoming samples service.

16. Analytical worksheet

Analysts recorded tests performed, raw data, calculations and results in analytical work sheets. Calculations were checked by second analyst. Sufficient details were recorded in analytical work sheets to establish traceability. This was confirmed by verifying Amoxicillin suspension sample.

HARPYA software was used to record analytical test results. Validated excel sheets were used for calculations. Excel sheets validation status was checked every two years.

17. Validation of analytical procedures

The laboratories did not develop or validate Pharmacopoeia methods.

Physico-chemical laboratory carried out verification of Pharmacopeia methods according to written procedure.

The SOP "Procedure of selection of the method of analysis of medicines, cosmetics and sanitizers" was briefly discussed. It described the process how to select the method of analyses which could be the manufacturers' method or one of the pharmacopeia method.

The methods available in the Brazilian Pharmacopoeia were used in first place, followed by the European Pharmacopoeia or the International Pharmacopoeia or the USP.

For pharmaceutical products, the method verifications were done for each active ingredient and for each manufacturer and detailed information on all verifications done were listed in table. In case the method was not verified it was considered as an OOS and verification should be done as corrective action. An assistance of the technical assessment group was needed when a method failed to be verified second time.

Validation of the Sterility Test was carried for all medicines to be analysed. The procedure followed the requirements of the European Pharmacopoeia. Enumeration test for non-sterile products was verified for all products to be analysed.

18. Testing

The samples were tested in accordance with the state surveillance program. Test results were recorded in analysts' analytical work sheets. Tests were performed following pharmacopeia methods or manufacturer's methods.

Sterility testing was carried out according to the SOP "Sterility test perofemd in isolator" In case of growth microorganisms were isolated and identified.

Proficiency testing scheme

The laboratory participates in Proficiency testing: Scheme PHASE 7 "WHO - World Health Organization - External Quality Assurance Assessment". The laboratory also participates in Control lab – Brazil proficiency scheme.

19. Evaluation of test results and OOS investigation

Analytical test results were checked by another analyst and reviewed by Laboratory Coordinator.

Out of specification results (OOS) of chemical testing were investigated according to The SOP "Out of specification of a chemical and microbiology tests". The OOS procedures included a flow chart which was briefly discussed.

A number of OOS were briefly discussed.

20. Certificate of analysis

CoA`s were signed by the responsible analyst and head of the laboratory and approved by the coordinator of the division.

21. Retained samples

Retained samples were appropriately stored. The samples were kept until the end of analysis. If the product did not comply with the specifications the retained samples were kept till the expiry date of the product.

22. Safety

Laboratory personnel were appropriately attired with protective clothing while working in the laboratory and safety instructions were followed. Emergency water shower was available in the laboratory. MSDS were available to staff for general reagents and chemicals used in the laboratory.

PART 3
CONCLUSION

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, as well as the corrective actions taken **Ezequiel Dias Foundation (FUNED), Central Laboratory of Public Health of Minas Gerais (Lacen-MG), located at Conde Pereira Carneiro Street 80, Gameleira Neighbourhood, Belo Horizonte, Minas Gerais , 30510-030, Brazil**,was considered to be operating at an acceptable level of compliance with WHO Good Practices for Pharmaceutical Quality Control Laboratories for the following expertise:

Type of Analysis	Finished Products
Physicochemical analysis	pH, Friability, Disintegration, Density, Dissolution, Uniformity of dosage units (content), Uniformity of dosage units (mass), Loss on drying, Water content (K. Fischer)
Identification	FTIR, TLC, HPLC, UV-VIS Spectrophotometry, Basic tests
Assay, impurities and related substances	HPLC (UV-VIS, DAD, Fluorescence detection), TLC, FTIR, UV-VIS Spectrophotometry, Volumetric Titrations, Potentiometric Titrations, Determination of related substances/impurities, Degradation products
Microbiological Tests	Microbial limit tests , Bacterial Endotoxins test (LAL), Sterility test

PART 4
List of GMP guidelines referenced in the inspection

1. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1
   Short name: WHO TRS No. 961, 957)

   http://www.who.int/medicines/publications/44threport/en/

2. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2
   Short name: WHO TRS No. 961, Annex 2
   http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

3. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2.
   Short name: WHO TRS No. 986, Annex 2
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

4. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2
   Short name: WHO TRS No. 970, Annex 2
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/

5. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4
   Short name: WHO TRS No. 929, Annex 4
   http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

6. WHO guidelines on good manufacturing practices for heating, ventilation and air-conditioning systems for non-sterile pharmaceutical dosage forms. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 5
Short name: WHO TRS No. 961, Annex 5
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

7. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4
Short name: WHO TRS No. 937, Annex 4
http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1

9. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 6
Short name: WHO TRS No. 961, Annex 6
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7
Short name: WHO TRS No. 961, Annex 7
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

12. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-first Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3
Short name: WHO TRS No. 943, Annex 3
http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1

13. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2
Short name: WHO TRS No. 981, Annex 2
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

15. Guidance on good data and record management practices. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5
Short name: WHO TRS No. 996, Annex 5
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf