INTERNATIONAL STANDARD

ISO 20776-2

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Clinical laboratory testing and *in vitro* diagnostic test systems — Susceptibility testing of infectious agents and evaluation of performance of antimicrobial susceptibility test devices —

Part 2:

Evaluation of performance of antimicrobial susceptibility test devices

Systèmes d'essais en laboratoire et de diagnostic in vitro — Sensibilité in vitro des agents infectieux et évaluation des performances des dispositifs pour antibiogrammes —

Partie 2: Évaluation des performances des dispositifs pour antibiogrammes

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Foreword

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International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 20776-2 was prepared by the European Committee for Standardization (CEN) Technical Committee CEN/TC 140, In vitro *diagnostic medical devices,* in collaboration with Technical Committee ISO/TC 212, *Clinical laboratory testing and* in vitro *diagnostic test systems*, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

ISO 20776 consists of the following parts, under the general title *Clinical laboratory testing and* in vitro *diagnostic test systems — Susceptibility testing of infectious agents and evaluation of performance of antimicrobial susceptibility test devices*:

— *Part 1: Reference method for testing the* in vitro *activity of antimicrobial agents against rapidly growing aerobic bacteria involved in infectious diseases*

— *Part 2: Evaluation of performance of antimicrobial susceptibility test devices*

Clinical laboratory testing and *in vitro* diagnostic test systems — Susceptibility testing of infectious agents and evaluation of performance of antimicrobial susceptibility test devices —

Part 2: Evaluation of performance of antimicrobial susceptibility test devices

1 Scope

This part of ISO 20776 establishes acceptable performance criteria for antimicrobial susceptibility test (AST) devices that are used to determine minimum inhibitory concentrations (MIC) and/or interpretive category determinations of susceptible, intermediate and resistant (SIR) strains of bacteria to antimicrobial agents in medical laboratories. This part of ISO 20776 specifies requirements for AST devices (including diffusion test systems) and procedures for assessing performance of such devices. It defines how a performance evaluation of an AST device is to be conducted. This part of ISO 20776 has been developed to guide manufacturers in the conduct of performance evaluation studies.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 20776-1, *Clinical laboratory testing and* in vitro *diagnostic test systems — Susceptibility testing of infectious agents and evaluation of performance of antimicrobial susceptibility test devices — Part 1: Reference method for testing the* in vitro *activity of antimicrobial agents against rapidly growing aerobic bacteria involved in infectious diseases*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1 Agreement of test results

3.1.1
category agreement
CA
agreement of SIR results between a breakpoint test or an MIC test and the reference method (ISO 20776-1)

Another representation of the concept:

$$\frac{N_{CA} \times 100}{N}$$

where

N_{CA} is the number of bacterial isolates with the same SIR category as the reference method category result;

N is the total number of bacterial isolates tested

NOTE The overall CA is expressed as a percentage.

3.1.2
essential agreement
EA
MIC result obtained with the AST device that is within plus or minus one doubling dilution step from the MIC value established with the reference method (ISO 20776-1)

Another representation of the concept:

$$\frac{N_{EA} \times 100}{N}$$

where

N_{EA} is the number of bacterial isolates with an EA;

N is the total number of bacterial isolates tested

NOTE The overall EA is expressed as a percentage.

3.2
antimicrobial susceptibility test device
AST device

device including all specified components used to obtain test results that allow SIR categorization of bacteria with specific antimicrobial agents

NOTE Specific components include inoculators, disposables and reagents, media, disks and readers. Non-specific components, such as swabs, pipettes and tubes, are not part of the device.

3.3
breakpoint
BP
specific values of parameters, such as MICs, on the basis of which bacteria can be assigned to the clinical categories “susceptible”, “intermediate” and “resistant”

NOTE For current interpretive breakpoints, reference can be made to the latest publications of organizations employing this reference method (e.g. CLSI and EUCAST).

3.3.1
susceptible
S
bacterial strain inhibited *in vitro* by a concentration of an antimicrobial agent that is associated with a high likelihood of therapeutic success

NOTE 1 Bacterial strains are categorized as susceptible by applying the appropriate breakpoints in a defined phenotypic test system.

NOTE 2 This breakpoint can be altered due to changes in circumstances (e.g. changes in commonly used drug dosages, emergence of new resistance mechanisms).

3.3.2
intermediate
I
bacterial strain inhibited *in vitro* by a concentration of an antimicrobial agent that is associated with uncertain therapeutic effect

NOTE 1 Bacterial strains are categorized as intermediate by applying the appropriate breakpoints in a defined phenotypic test system.

NOTE 2 This class of susceptibility implies that an infection due to the isolate can be appropriately treated in body sites where the drugs are physiologically concentrated or when a high dosage of drug can be used.

NOTE 3 This class also indicates a “buffer zone”, to prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations.

NOTE 4 These breakpoints can be altered due to changes in circumstances (e.g. changes in commonly used drug dosages, emergence of new resistance mechanisms).

3.3.3
resistant
R
bacterial strain inhibited *in vitro* by a concentration of an antimicrobial agent that is associated with a high likelihood of therapeutic failure

NOTE 1 Bacterial strains are categorized as resistant by applying the appropriate breakpoints in a defined phenotypic test system.

NOTE 2 This breakpoint can be altered due to changes in circumstances (e.g. changes in commonly used drug dosages, emergence of new resistance mechanisms).

3.3.4
non-susceptible
NS
bacterial strain for which the test result exceeds the susceptible breakpoint and for which there are no established intermediate or resistant breakpoints

NOTE This is generally due to lack of strains with resistance to the antimicrobial agent when the breakpoints are defined.

3.4
breakpoint test
BPT
test that has the principal objective to provide categorical results (SIR)

NOTE This can include limited range dilution tests or diffusion tests.

3.5
coordinator
person empowered by the manufacturer or investigator with responsibility for the entire performance evaluation

3.6 Discrepancies

3.6.1
major discrepancy
MD
test result by the reference method interpreted as S and an AST device result of R

Another representation of the concept:

$$\frac{N_{\mathrm{MD}} \times 100}{N_{\mathrm{SREF}}}$$

where

N_{MD} is the number of tests that result in a MD;

N_{SREF} is the number of susceptible bacterial isolates as determined by the reference method (ISO 20776-1)

NOTE The overall MD is expressed as a percentage.

3.6.2
minor discrepancy
mD
test result by the reference method interpreted as R or S and an AST device result of I; or a reference result interpreted as I and an AST device result of R or S

Another representation of the concept:

$$\frac{N_{mD} \times 100}{N}$$

where

N_{mD} is the number of tests that result in a mD;

N is the total number of bacterial isolates tested

NOTE The overall mD is expressed as a percentage.

3.6.3
very major discrepancy
VMD
test result by the reference method interpreted as R and an AST device result of S

Another representation of the concept:

$$\frac{N_{VMD} \times 100}{N_{RREF}}$$

where

N_{VMD} is the number of tests that result in a VMD;

N_{RREF} is the number of resistant bacterial isolates as determined by the reference method (ISO 20776-1)

NOTE The overall VMD is expressed as a percentage.

3.7
evaluation plan
description of a planned performance evaluation

3.8
evaluation report
description of and conclusions from a performance evaluation

3.9 Clinical isolates

3.9.1
fresh isolate
isolate recovered from a clinical sample within the previous seven days that has not been frozen or subcultured more than five times

3.9.2
recent isolate
isolate recovered from a clinical sample within the previous twelve months

3.9.3
stock isolate
isolate recovered from a clinical sample that has been retained, stored or obtained from a culture collection

NOTE Stock isolates are usually included because they have known or rare resistance mechanisms, or are of a genus or species for which the antimicrobial agent is indicated but are not commonly isolated. Such organisms are unlikely to be available in fresh clinical isolates used in the evaluation.

3.10
investigator
person responsible for the execution of the performance evaluation at a certain location

3.11
minimum inhibitory concentration
MIC
lowest concentration that, under defined *in vitro* conditions, prevents visible growth of bacteria within a defined period of time

NOTE The MIC is expressed in mg/l.

3.12
MIC test
test that is capable of determining an MIC covering a range of at least five consecutive doubling dilutions, and for which EA can be determined

3.13
on-scale MIC test result
result from a MIC test when there is growth in at least one but not all concentrations tested

3.14
reference method
reference method described in ISO 20776-1

3.15
zone diameter
diameter (in mm) of the zone of growth inhibition around a disk containing an antimicrobial agent in an agar diffusion test

4 General requirements for a performance evaluation

The manufacturer or investigator takes the responsibility for the initiation and the conduct of a performance evaluation according to the evaluation plan. The manufacturer shall define the responsibility and the interrelation of all personnel who manage and conduct a performance evaluation.

The manufacturer or investigator shall appoint a coordinator with overall responsibility for the performance evaluation and the evaluation report. The coordinator shall assess and document breakpoint criteria used and indicate which performance claims are met.