



M39

Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data

This guideline describes methods for recording and analyzing antimicrobial susceptibility test data, consisting of cumulative and ongoing summaries of susceptibility patterns of clinically significant microorganisms.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.

Clinical and Laboratory Standards Institute

Setting the standard for quality in medical laboratory testing around the world.

The Clinical and Laboratory Standards Institute (CLSI) is a not-for-profit membership organization that brings together the varied perspectives and expertise of the worldwide laboratory community for the advancement of a common cause: to foster excellence in laboratory medicine by developing and implementing medical laboratory standards and guidelines that help laboratories fulfill their responsibilities with efficiency, effectiveness, and global applicability.

Consensus Process

Consensus—the substantial agreement by materially affected, competent, and interested parties—is core to the development of all CLSI documents. It does not always connote unanimous agreement but does mean that the participants in the development of a consensus document have considered and resolved all relevant objections and accept the resulting agreement.

Commenting on Documents

CLSI documents undergo periodic evaluation and modification to keep pace with advances in technologies, procedures, methods, and protocols affecting the laboratory or health care.

CLSI's consensus process depends on experts who volunteer to serve as contributing authors and/or as participants in the reviewing and commenting process. At the end of each comment period, the committee that developed the document is obligated to review all comments, respond in writing to all substantive comments, and revise the draft document as appropriate.

Comments on published CLSI documents are equally essential and may be submitted by anyone, at any time, on any document. All comments are managed according to the consensus process by a committee of experts.

Appeal Process

When it is believed that an objection has not been adequately considered and responded to, the process for appeal, documented in the *CLSI Standards Development Policies and Processes*, is followed.

All comments and responses submitted on draft and published documents are retained on file at CLSI and are available upon request.

Get Involved—Volunteer!

Do you use CLSI documents in your workplace? Do you see room for improvement? Would you like to get involved in the revision process? Or maybe you see a need to develop a new document for an emerging technology? CLSI wants to hear from you. We are always looking for volunteers. By donating your time and talents to improve the standards that affect your own work, you will play an active role in improving public health across the globe.

For additional information on committee participation or to submit comments, contact CLSI.

Clinical and Laboratory Standards Institute

P: +1.610.688.0100

F: +1.610.688.0700

www.clsi.org

standard@clsi.org

Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data

Janet A. Hindler, MCLS, MT(ASCP), F(AAM)
Patricia J. Simner, PhD, D(ABMM)
April Abbott, PhD, (ABMM)
Faiza H. Benahmed, MS
Tanaya Bhowmick, MD
Sanchita Das, MD, D(ABMM)
Sharon M. Erdman, PharmD, FIDP
Andrea L. Ferrell, MLS^{CM}(ASCP)
Kristie Johnson, PhD, D(ABMM)

Brian V. Lubbers, DVM, PhD, DACVCP
Ron Master, SM(AAM)
Jimish M. Mehta, PharmD, MSCE
Ian Morrissey, BSc, MBA, PhD, FRSM
Mark A. Redell, PharmD
Helio S. Sader, MD
Dawn M. Sievert, PhD, MS
Paula M. Snippes Vagnone, MT(ASCP)
John Stelling, MD, MPH

Abstract

Susceptibility statistical data, consisting of the cumulative and ongoing summary of the antimicrobial susceptibility patterns of clinically important microorganisms, are important to the practice of medicine on several levels. If the methods used to create, record, and analyze the data are not reliable and consistent, many of the most important applications and benefits of the data will not be realized. Clinical and Laboratory Standards Institute document M39—*Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data* provides guidelines for medical laboratories and data analysis software providers for the routine generation and storage of susceptibility data and for the compilation of susceptibility statistics. This guideline also provides suggestions for medical laboratories, clinicians, and others involved in antimicrobial stewardship on effective use of their cumulative susceptibility statistics when empirical antimicrobial therapy is selected.

Clinical and Laboratory Standards Institute (CLSI). *Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data*. 5th ed. CLSI guideline M39 (ISBN 978-1-68440-132-1 [Print]; ISBN 978-1-68440-133-8 [Electronic]). Clinical and Laboratory Standards Institute, USA, 2012.

The Clinical and Laboratory Standards Institute consensus process, which is the mechanism for moving a document through two or more levels of review by the health care community, is an ongoing process. Users should expect revised editions of any given document. Because rapid changes in technology may affect the procedures, methods, and protocols in a standard or guideline, users should replace outdated editions with the current editions of CLSI documents. Current editions are listed in the CLSI catalog and posted on our website at www.clsi.org.

If you or your organization is not a member and would like to become one, or to request a copy of the catalog, contact us at:

P: +1.610.688.0100 **F:** +1.610.688.0700 **E:** customerservice@clsi.org **W:** www.clsi.org

Copyright ©2022 Clinical and Laboratory Standards Institute. Except as stated below, any reproduction of content from a CLSI copyrighted standard, guideline, derivative product, or other material requires express written consent from CLSI. All rights reserved. Interested parties may send permission requests to permissions@clsi.org.

CLSI hereby grants permission to each individual member or purchaser to make a single reproduction of this publication for use in its laboratory procedures manual at a single site. To request permission to use this publication in any other manner, e-mail permissions@clsi.org.

Suggested Citation

CLSI. *Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data*. 5th ed. CLSI guideline M39. Clinical and Laboratory Standards Institute; 2022.

Previous Editions:

December 2000, May 2002, November 2005, February 2009, January 2014

M39-Ed5

ISBN 978-1-558-68440-132-1 (Print)

ISBN 978-1-558-68440-133-8 (Electronic)

ISSN 1558-6502 (Print)

ISSN 2162-2914 (Electronic)

Volume 42, Number 1

Committee Membership

Consensus Council

James R. Petisce, PhD
Chairholder
BD Diagnostic Systems
 USA

Avis Danishefsky, PhD
 FDA Center for Devices and
 Radiological Health
 USA

M. Laura Parnas, PhD, DABCC
 Roche Diagnostics
 USA

Tania Motschman, MS, MT(ASCP)SBB
Vice-Chairholder
 USA

Collette Fitzgerald, PhD
 Centers for Disease Control and
 Prevention
 USA

Victoria Petrides, MS
 Abbott
 USA

Deirdre Astin, MS, MT(ASCP)
 USA

Michelle McLean, MS, MT(ASCP), BS
 Greiner Bio-One, Inc.
 USA

Matthew A. Wikler, MD, FIDSA, MBA
 IDTD Consulting
 USA

Anne T. Daley, MS, MT(ASCP)DLM,
 CMQ/OE(ASQ)CSBB
 USA

James H. Nichols, PhD, DABCC, FAAC
 Vanderbilt University School of
 Medicine
 USA

Subcommittee on Antimicrobial Susceptibility Testing

James S. Lewis II, PharmD, FIDSA
Chairholder
Oregon Health and Science University
 USA

Romney M. Humphries, PhD, D(ABMM)
 Vanderbilt University Medical Center
 USA

Sandra S. Richter, MD, D(ABMM), FIDSA
 bioMérieux, Inc.
 USA

Melvin P. Weinstein, MD
Vice-Chairholder
Rutgers Robert Wood Johnson
University Hospital
 USA

Thomas J. Kirn Jr., MD, PhD
 Rutgers Robert Wood Johnson Medical
 School
 USA

Michael Satlin, MD, MS
 New York Presbyterian Hospital
 USA

Sharon K. Cullen, BS, RAC
 Beckman Coulter, Inc., Microbiology
 Business
 USA

Pradi Umbago, PhD
 Centers for Disease Control and
 Prevention
 USA

Audrey N. Schuetz, MD, MPH,
 D(ABMM)
 Mayo Clinic
 USA

Marcelo F. Galas, BSc
 Pan American Health Organization
 USA

Amy J. Mathers, MD, D(ABMM)
 University of Virginia Medical Center
 USA

Patricia J. Simner, PhD, D(ABMM)
 Johns Hopkins School of Medicine –
 Department of Pathology
 USA

Howard Gold, MD, FIDSA
 Beth Israel Deaconess Medical Center
 USA

Tony Mazzulli, MD, FACP, FRCP(C)
 Sinai Health System
 Canada

Expert Panel on Microbiology

Jean B. Patel, PhD, D(ABMM)
Chairholder
Beckman Coulter
USA

Karissa Culbreath, PhD, D(ABMM)
 University of New Mexico
 Department of Pathology
 USA

Margie Morgan, PhD, D(ABMM)
 Cedars-Sinai Medical Center
 USA

Audrey N. Schuetz, MD, MPH, D(ABMM)
Vice-Chairholder
Mayo Clinic
USA

Marcelo F. Galas, BSc
 Pan American Health Organization
 USA

Sandra S. Richter, MD, D(ABMM),
 FIDSA
 bioMérieux, Inc.
 USA

Kevin Alby, PhD, D(ABMM)
 University of North Carolina
 USA

Shawn R. Lockhart, PhD, D(ABMM),
 F(AAM)
 Centers for Disease Control and
 Prevention
 USA

Susan Sharp, PhD, D(ABMM), F(AAM)
 Copan Diagnostics, Inc.
 USA

Esther Babady, PhD, D(ABMM)
 Memorial Sloan Kettering Cancer
 Center
 USA

Brian V. Lubbers, DVM, PhD, DACVCP
 Kansas State Veterinary Diagnostic
 Laboratory
 USA

Ribhi M. Shawar, PhD, D(ABMM),
 F(AAM)
 FDA Center for Devices and
 Radiological Health
 USA

Working Group on Cumulative AST Data Analysis

Janet A. Hindler, MCLS, MT(ASCP), F(AAM)
Co-Chairholder
Los Angeles County Department of Health
USA

Sanchita Das, MD, D(ABMM)
 National Institutes of Health,
 Department of Laboratory Medicine
 USA

John Morrissey, BsC, MBA, PhD, FRSM
 HMA Europe Sàrl
 Switzerland

Patricia J. Simner, PhD, D(ABMM)
Co-Chairholder
Johns Hopkins University School of Medicine – Department of Pathology
USA

Sharon M. Erdman, PharmD, CPEP
 Purdue University College of
 Pharmacy/Eskenazi Health
 USA

Mark A. Redell, PharmD
 Melinta Therapeutics
 USA

April Abbott, PhD, D(ABMM)
Committee Secretary
Deaconess Hospital Laboratory
USA

Andrea C. Farrell, MLS^{CM}(ASCP)
 Becton Dickinson
 USA

Helio S. Sader, MD
 JMI Laboratories
 USA

Faiza H. Benahmed, MS
 FDA Center for Devices and
 Radiological Health
 USA

Christine Johnson, PhD, D(ABMM)
 University of Maryland, Baltimore
 USA

Dawn M. Sievert, PhD, MS
 Centers for Disease Control and
 Prevention
 USA

Tanaya Bhowmik, MSc
 Rutgers Robert Wood Johnson
 Medical School
 USA

Brian V. Lubbers, DVM, PhD, DACVCP
 Kansas State Veterinary Diagnostic
 Laboratory
 USA

Paula M. Snippes Vagnone, MT(ASCP)
 Minnesota Department of Health
 USA

Ron Master, SM(AAM)
 Quest Diagnostics Nichols Institute
 USA

John Stelling, MD, MPH
 Brigham and Women's Hospital –
 Microbiology
 USA

Jimish M. Mehta, PharmD, MSCE
 CSL Behring
 USA

Staff

Clinical and Laboratory Standards
Institute
USA

Laura Martin
Editorial Manager

Kristy L. Leirer, MS
Editor

Marcy L. Hackenbrack, MCM, M(ASCP)
Project Manager

Catherine E.M. Jenkins, ELS
Editor

Currently in preview, click buy full version



This page is intentionally left blank.

Contents

Abstract	i
Committee Membership	iii
Foreword	xi
Part I. Introduction and Data Acquisition	1
Chapter 1: Introduction	1
1.1 Scope	2
1.2 Background	2
1.3 Standard Precautions	4
1.4 Terminology	4
Chapter 2: Information System Design	13
2.1 Data Export or Transmission	14
2.2 Desirable Attributes of the Data Analysis System	15
2.3 Patient Demographic Information	16
2.4 Specimen Information	16
2.5 Organism Information	16
2.6 Antimicrobial Susceptibility Testing Information	17
2.7 Comparing Data Sources for Antibigram Preparation	17
Part II. Routine Antibigrams	21
Chapter 3: Data Analysis for Preparation of the Routine Antibigram	21
3.1 Verifying Data From Individual Organism Identification and Antimicrobial Susceptibility Testing	22
3.2 Facility	22
3.3 Frequency of Data Analysis	22
3.4 Isolates to Include in the Analysis	23
3.5 Antimicrobial Agents to Include in the Analysis	24
3.6 Antimicrobial Results Suppression, Selective Reporting, and Cascade Reporting	25
3.7 Performing Calculations	27
3.8 Issues Related to Determining the Interpretation of Minimal Inhibitory Concentration Values	28
3.9 Validating the Calculations	29
3.10 Additional Analyses and Selection Criteria Options for the Routine Antibigram With Select Organisms	29
Chapter 4: Data Presentation	33
4.1 Information to Include in the Antibigram	34
4.2 Information to Consider for Inclusion Within Specific Tables	34
4.3 Final Checks of the Antibigram Report	38
4.4 Data, Data Analysis, and Data Presentation Limitations	38

Contents (Continued)

Chapter 5: Special Situations Related to Data Analysis and Presentation for Routine Antibigrams	39
5.1 Susceptible-Dose Dependent Interpretive Category	40
5.2 Intermediate Interpretive Category	40
5.3 Cefazolin	41
5.4 Managing Small Numbers of Isolates	41
5.5 Combining Data From Two or More Datasets	42
5.6 Changes in Breakpoints	42
5.7 Variations in Drugs Available for Analysis	43
5.8 Epidemiological Cutoff Values	45
Part III. Other Types of Antibigrams	47
Chapter 6: Enhanced Antibigrams	47
6.1 Stratifying Antibigram Data by Various Parameters	48
6.2 Highlighting the Prevalence of Multidrug-Resistant Organisms on the Antibigram	49
6.3 Examining Percent Susceptible for Antimicrobial Agent Combinations	50
6.4 Calculating Percent Susceptible for Select Organism Groups	51
6.5 Incorporating Antimicrobial Resistance Marker Test Results With the Antibigram	52
6.6 Using Data From All Isolates to Identify Emerging Resistance	56
6.7 Analyzing Antimicrobial Resistance Profiles of Select Organisms	57
Chapter 7: The Long-Term Care Facility Antibigram	59
7.1 Antibigram Preparation in Long-Term Care Facilities	60
7.2 Responsibility for Antibigram Preparation in Long-Term Care Facilities	60
7.3 Optimizing Culturing Practices in Long-Term Care Facilities	60
7.4 Data Source and Data Analysis for Long-Term Care Facility Antibigrams	61
7.5 Data Analysis Based on Long-Term Care Facility Patient Referral Base	62
7.6 Distribution and Use of Antibigrams in Long-Term Care Facilities	62
Chapter 8: The Veterinary Antibigram	63
8.1 Preparing Antibigrams for Veterinary Medicine	64
8.2 Inclusion of Isolates in Veterinary Antibigrams	65
8.3 Antibigram Presentation	68
8.4 Using Veterinary Antibigrams	70

Contents (Continued)

Part IV. Multifacility Antibiograms	71
Chapter 9: Preparation and Use of Multifacility Antibiograms	71
9.1 Single-Facility Antibiograms vs Multifacility Antibiograms	72
9.2 Sources of Data and Parameters to Consider for Preparing Multifacility Antibiograms	72
9.3 Presentation of Multifacility Antibiograms	76
9.4 Utility of Multifacility Antibiograms	77
9.5 Considerations When Multifacility Antibiograms Are Used to Guide Local Empirical Therapy Recommendations	77
9.6 Use of Multifacility Antibiograms by Various Stakeholders	78
Part V. Using the Routine and Enhanced Antibiogram	79
Chapter 10: Using the Antibiogram to Guide Empirical Therapy of Initial Infections	79
10.1 Percent Susceptibility Threshold to Guide Empirical Antimicrobial Therapy	80
10.2 Using Antibiograms to Guide Empirical Antimicrobial Therapy When the Causative Organism and Susceptibility Are Unknown	81
10.3 Using Antibiograms to Guide Empirical Antimicrobial Therapy When the Organism Is Known but the Susceptibility Is Unknown	81
Chapter 11: Distributing and Communicating Antibiogram Data	83
11.1 “Pocket” Guides or Other Hard Copy	84
11.2 Website Application, Portable Document Format, Smartphone, or Tablet Application	84
11.3 Connecting Users With the Antibiogram Report	84
Chapter 12: Antimicrobial Stewardship Programs and the Antibiogram	85
12.1 Role of Antimicrobial Stewardship Programs	86
12.2 Using Antibiograms for Antimicrobial Selection Education by Antimicrobial Stewardship Programs	87
12.3 Combining Rapid Diagnostic Test Results With the Antibiogram for Empirical Antimicrobial Therapy Selection	87
12.4 Using Antibiograms to Guide Addition of Antimicrobial Agents to the Institutional Formulary	87
12.5 Using Antibiograms for Developing Facility-Specific Empirical Antimicrobial Treatment Guidelines	88
Part VI. Using Statistics With Cumulative Antimicrobial Susceptibility Test Data	89
Chapter 13: Statistical Considerations	89
13.1 Use and Limitations of Statistical Methods	90
13.2 Confidence Intervals	91
13.3 Statistical Significance of Changes in Susceptibility Rates	91
13.4 Using Percentiles for Additional Assessment of Multifacility Antibiogram Data	92
13.5 Calculating Minimal Inhibitory Concentration Required to Inhibit the Growth of 50% of the Organisms and Minimal Inhibitory Concentration Required to Inhibit the Growth of 90% of the Organisms	93

Contents (Continued)

Part VII. Publishing Cumulative Antimicrobial Susceptibility Test Data	95
Chapter 14: Considerations for Peer-Reviewed Publication of Cumulative Antimicrobial Susceptibility Test Data	95
14.1 Study Goal	96
14.2 Materials and Methods	96
14.3 Results	98
14.4 Discussion or Summary	98
Part VIII. Conclusion and Supplemental Information	99
Chapter 15: Conclusion	99
Chapter 16: Supplemental Information	101
References	102
Additional Resources	105
Appendix A. Rationale for the “First Isolate per Patient” Analysis Recommendation	111
Appendix B. Routine Antibigram Examples	115
Appendix C. Using a Line Listing to Verify Susceptibility Rates Determined by the Analysis Software	123
Appendix D. Review of Antibigram Content Before Release of the Report	127
Appendix E. Examples of Enhanced Antibigrams	132
Appendix F. Examples of Antimicrobial Agent Combination Antibigrams	135
Appendix G. Examples of Graphs to Illustrate Trends in Susceptibility	137
Appendix H. Stepwise Instructions for Preparing a Multifacility Antibigram	141
Appendix I. Examples of Tables and Graphs to Consider for Use in Peer-Reviewed Publications Containing Cumulative Antimicrobial Susceptibility Test Data	147
Appendix J. Steps for Presenting Local Antibigram Data to Health Care Professionals	153
Appendix K. Statistical Methods for Examining Percent Susceptible	158
Appendix L. Frequently Asked Questions	168
The Quality Management System Approach	174
Related CLSI Reference Materials	175

Foreword

Cumulative results from antimicrobial susceptibility tests performed on individual patients' microbial isolates can be useful when compiled and reported at regular intervals. For a cumulative report (eg, antibiogram) to be compared with reports from previous years or from other facilities, data need to be analyzed and presented in a clear and consistent manner.

The primary aim of M39 is to guide the preparation and use of antibiograms by clinicians for selecting the most appropriate antimicrobial agents for empirical therapy for initial infections when definitive antimicrobial susceptibility test results are not available. Various types of cumulative antimicrobial susceptibility test data reports are used to support antimicrobial stewardship and infection prevention efforts. In addition, cumulative antimicrobial susceptibility test data may be of value to researchers when antimicrobial resistance is assessed.

Since the last edition of this guideline, there have been many changes in public health and medical microbiology laboratories with the introduction of rapid diagnostic tools (eg, multiplex molecular panels) and advanced informatics. Furthermore, there has been an increased emphasis on antimicrobial stewardship and public health initiatives to help contend with the global health threat of antimicrobial resistant microorganisms. Therefore, many of the changes in this guideline reflect how the antibiogram and other types of cumulative antimicrobial susceptibility test data reports can support these needs.

Overview of Changes

This guideline replaces the previous edition of the approved guideline, M39-A4, published in 2014. Several changes were made in this edition, including:

- Adding definitions for “cumulative antimicrobial susceptibility test data report” and “antibiogram”
- Adding considerations for extracting data from different sources (eg, automated antimicrobial susceptibility testing instrument, LIS, electronic health record) for antibiogram preparation
- Combining results from rapid diagnostics and antimicrobial resistance marker testing with the antibiogram for empirical therapy selection
- Developing antibiograms for yeast and antifungal agents
- Developing antibiograms for multiple facilities, long-term care facilities, and veterinary practices
- Describing ways in which antimicrobial stewardship programs may use antibiogram data
- Adding considerations for preparing cumulative antimicrobial susceptibility test data for peer-reviewed publication
- Using statistical analysis techniques including the calculation of percentiles, interquartile ranges, minimal inhibitory concentration (MIC) required to inhibit the growth of 50% of the organisms (MIC_{50}), and MIC required to inhibit the growth of 90% of the organisms (MIC_{90})
- Adding general comment explaining the use of the “^” with intermediate breakpoints for applicable antimicrobial agents known to have the ability to concentrate in the urine
- Deleting recommendation to list percent intermediate in addition to percent susceptible for penicillin with viridans group streptococci

NOTE: The content of this guideline is supported by the CLSI consensus process and does not necessarily reflect the views of any single individual or organization.

KEY WORDS

Antibiogram

Antimicrobial resistance

Cumulative antibiogram

Antimicrobial agent

Antimicrobial stewardship

Epidemiology

Uses of LOINC® and SNOMED CT® in this guideline are not endorsements on the part of CLSI.

Part I. Introduction and Data Acquisition

Chapter ①

Introduction

Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data

Part I. Introduction and Data Acquisition

1 Introduction

1.1 Scope

This guideline provides individuals involved with assessment of cumulative antimicrobial susceptibility test data with recommendations for the storage, analysis, and presentation of the data. The antimicrobial susceptibility test data from individual patient's isolates available for analysis are assumed to be final, accurate and in a usable format for health care providers. Recommendations cover the preparation of reports (eg, routine and enhanced antibiograms) to guide selection of empirical antimicrobial therapy. Reference to preparation of reports for other purposes is briefly discussed. This guideline is intended for use by individuals involved with:

- Analyzing and presenting cumulative antimicrobial susceptibility test data generated from testing microbial isolates from both humans and animals from single or multiple facilities (eg, clinical microbiologists, pharmacists, physicians, veterinarians, epidemiologists, infection prevention practitioners)
- Using antibiograms and other types of cumulative antimicrobial susceptibility test data to make clinical decisions, participate in antimicrobial stewardship programs, and/or participate in public health initiatives (eg, clinical microbiologists, infectious diseases specialists and other clinicians, infection prevention practitioners, pharmacists, epidemiologists, other health care personnel, and public health officials)
- Designing information systems for the storage and analysis of antimicrobial susceptibility test data (eg, LIS vendors, electronic health record [EHR] vendors, manufacturers of diagnostic products that include epidemiology analysis software, and manufacturers of epidemiology analysis or surveillance software)

This guideline does not include procedures for selecting isolates for antimicrobial susceptibility testing (AST), performing AST, interpreting AST results, nor confirming the accuracy of AST results.

1.2 Background

This guideline presents specific recommendations for collection, analysis, and presentation of cumulative antimicrobial susceptibility test data.

It is important to recognize that many of the specific recommendations presented for routine antibiogram development (eg, including only the first isolate of a given species from an individual patient during the analysis period) are made with the primary aim of guiding clinicians in the selection of empirical antimicrobial therapy for initial infections when definitive susceptibility results are not available. This report may not reveal some trends in emerging resistance, and thus cannot be used as a substitute for the careful analysis of all antimicrobial susceptibility test data derived from examining and/or analyzing all antimicrobial susceptibility test results obtained for individual patient management. For reports intended for purposes other than guiding empirical therapy (eg, identifying emergence of resistance, trending antimicrobial resistance for public health initiatives), alternative analyses may be more appropriate, and these are discussed briefly in this guideline, primarily in Subchapter 6.6.