

INTRODUCTION .....	XV
STUDY GOAL AND OBJECTIVES .....	XV
REASONS FOR DOING THE STUDY .....	XV
CONTRIBUTIONS OF THE STUDY AND FOR WHOM.....	XVI
SCOPE AND FORMAT .....	XVI
METHODOLOGY .....	XVII
INFORMATION SOURCES.....	XVII
AUTHOR'S CREDENTIALS .....	XVII
RELATED BCC WORK CREDENTIALS INCLUDING WORK DONE	
BY OTHER AUTHORS .....	XVII
BCC ON-LINE SERVICES.....	XVIII
INTERNET .....	XVIII
SUMMARY.....	XX
SUMMARY TABLE U.S. SALES OF ANTIFUNGAL DRUGS, BY CATEGORY,	
THROUGH 2007 (\$ MILLIONS).....	XX
SUMMARY FIGURE U.S. MARKET FOR ANTIFUNGAL DRUGS, BY CATEGORY,	
2001, 2002, AND 2007 (\$ MILLIONS).....	XXI
OVERVIEW .....	1
THE CLINICAL THREAT OF FUNGAL INFECTIONS.....	1
TABLE 1 INCIDENCE OF DISEASES CAUSED ANNUALLY BY SELECTED FUNGAL	
PATHOGENS, U.S. ....	2
TABLE 2 INCIDENCE OF CANDIDAL BLOODSTREAM ISOLATED IN THE SICU	
AND NICU (%).....	2
TABLE 3 CANDIDA SPECIES INFECTION INCIDENCE OVER TIME (%).....	3
INFECTION SITES .....	3
TABLE 4 INCIDENCE OF FUNGAL INFECTIONS BY SITE, 1987-1988 TO 1993-1994	
(%).....	3
DOMINANT CLINICALLY SIGNIFICANT SPECIES .....	4
Endemic Mycoses.....	4
Opportunistic Mycoses .....	4
Increase in Incidence of Invasive Mycoses .....	4
Causes of Nosocomial Fungal Infections .....	5
Patients Most at Risk for Nosocomial Infections.....	6
Emerging Nosocomial Opportunistic Fungal Infections.....	6
DIFFICULTY IN DIAGNOSING AND TREATING FUNGAL	
INFECTIONS.....	6
Need for Reliable, Standardized Susceptibility Testing .....	7
Advances in Diagnostics for Fungal Diseases .....	8
Serodiagnostics .....	9
THE THREAT OF RESISTANCE.....	10
A PHARMACOECONOMIC ANALYSIS OF ANTIFUNGAL THERAPY.....	10
THE EMPIRIC NATURE OF ANTIFUNGAL THERAPY.....	11
STRATEGIES TO IMPROVE RESPONSE AND DECREASE	
MORTALITY .....	11

PRE-EMPTIVE THERAPY.....	12
TYPES OF FUNGAL INFECTIONS .....	13
SYSTEMIC FUNGAL INFECTIONS .....	13
PROGRESSION OF INFECTION.....	13
DIAGNOSIS OF SYSTEMIC FUNGAL INFECTIONS .....	13
THE MOST COMMON SYSTEMIC FUNGAL INFECTIONS IN IMMUNOCOMPROMISED PATIENTS.....	14
GEOGRAPHIC DISTRIBUTION OF SYSTEMIC FUNGAL INFECTIONS.....	14
THE MOST CLINICALLY SIGNIFICANT SYSTEMIC FUNGAL INFECTIONS.....	15
Aspergillosis.....	15
Categories of Infection .....	16
Noninvasive Disease.....	16
Primary Superficial Invasive Aspergillosis .....	17
Invasive Pulmonary Aspergillosis .....	17
Disseminated Aspergillosis .....	17
Diagnosis .....	17
Treatment.....	17
Treatment (Continued).....	18
Treatment (Continued).....	19
The War on Aspergillosis.....	20
Blastomycosis.....	20
Categories of Disease .....	21
Treatment.....	21
Candidiasis (Systemic) .....	21
<i>TABLE 5 DISTRIBUTION OF CANDIDA BLOODSTREAM ISOLATES IN SELECTED GEOGRAPHIC AREAS.....</i>	<i>22</i>
Categories of Disease .....	23
Candidemia and Disseminated Candidiasis.....	24
Endocarditis, Myocarditis and Pericarditis .....	24
Esophageal Candidiasis.....	24
Gastrointestinal Candidiasis .....	24
Hepatic and Hepatosplenic Candidiasis .....	24
Intertrigo Candidiasis.....	25
Meningitis (Candidal).....	25
Mucocutaneous Candidiasis.....	25
Neonatal and Congenital Candidiasis .....	25
Ocular Candidiasis.....	25
Oropharyngeal Candidiasis.....	25
Osteoarticular Candidiasis.....	26
Paronychia Candidiasis.....	26
Peritonitis (Candidal) .....	26
Pulmonary Candidiasis .....	26
Renal Candidiasis .....	26

Urinary Tract Candidiasis .....	27
Vulvovaginal Candidiasis.....	27
Diagnosis .....	27
TABLE 6 AVAILABLE LABORATORY TESTS FOR PRESUMPTIVE IDENTIFICATION OF CANDIDA.....	28
Treatment.....	28
TABLE 7 ACTIVITY OF FLUCONAZOLE AND ITRACONAZOLE AGAINST BLOODSTREAM ISOLATES OF CANDIDA SPECIES .....	29
Resistance Among <i>Candidas</i> Species.....	29
TABLE 8 SUSCEPTIBILITY OF NOSOCOMIAL AND COMMUNITY-ACQUIRED CANDIDA BLOODSTREAM ISOLATES (%).....	30
Chromomycosis and Phaeohyphomycosis.....	30
Treatment.....	31
Coccidioidomycosis .....	31
Categories of Disease .....	31
Treatment.....	32
Cryptococcosis.....	32
Treatment.....	33
Histoplasmosis.....	34
Categories of Disease .....	35
Acute Primary Histoplasmosis .....	35
Progressive Disseminated Histoplasmosis .....	35
Chronic Cavitory Histoplasmosis .....	35
Diagnosis .....	36
Treatment.....	36
Mucormycosis.....	36
Treatment.....	37
Mycetoma .....	37
Treatment.....	37
Paracoccidioidomycosis.....	37
Treatment.....	38
<i>Pneumocystis Carinii</i> Pneumonia .....	38
Treatment.....	39
Sporotrichosis .....	39
Treatment.....	39
Other Opportunistic Systemic Fungal Infections .....	40
DERMATOLOGIC FUNGAL INFECTIONS.....	40
DERMATOPHYTE INFECTIONS .....	40
Tinea Barbae.....	41
Treatment.....	41
Tinea Capitis.....	41
Treatment.....	41
Tinea Corporis .....	42
Treatment.....	42
Tinea Cruris.....	42

Treatment.....	42
Tinea Pedis .....	43
Treatment.....	43
Tinea Unguium.....	43
Treatment.....	44
YEAST INFECTIONS.....	44
Candidiasis .....	44
Treatment.....	45
Tinea Versicolor.....	45
Treatment.....	45
GYNECOLOGIC FUNGAL INFECTIONS.....	45
CANDIDIASIS.....	46
Treatment .....	46
TABLE 9 DRUGS USED TO TREAT VAGINAL CANDIDIASIS.....	46
NASO-ORAL FUNGAL INFECTIONS.....	47
TREATMENT .....	47
PATIENT POPULATIONS MOST SUSCEPTIBLE TO SYSTEMIC FUNGAL INFECTIONS .....	47
TABLE 10 FACTORS PREDISPOSING PATIENTS TO FUNGAL INFECTION.....	48
TABLE 11 SURVEILLANCE STRATEGIES FOR IDENTIFICATION OF FUNGAL INFECTIONS IN AT-RISK PATIENTS.....	48
PATIENTS WITH ACQUIRED IMMUNE DEFICIENCY SYNDROME.....	49
TABLE 12 SIGNIFICANT MYCOSES IN PATIENTS WITH AIDS.....	49
CANCER PATIENTS.....	50
TABLE 13 RISK CATEGORIES FOR INVASIVE FUNGAL INFECTIONS IN CANCER PATIENTS.....	50
Bone Marrow and Stem Cell Transplant Patients.....	51
Bone Marrow and Stem Cell Transplant Patients (Continued) .....	52
CATEGORIES OF SYSTEMIC ANTIFUNGAL DRUGS.....	53
ALLYLAMINES AND OTHER NONAZOLE ERGOSTEROL BIOSYNTHESIS INHIBITORS .....	53
ANTIMETABOLITES .....	53
AZOLES.....	53
ECHINOCANDINS (GLUCAN SYNTHESIS INHIBITORS).....	54
POLYENES .....	54
CATEGORIES OF TOPICAL ANTIFUNGAL AGENTS .....	54
THE USE OF LONG-TERM THERAPY.....	54
TAKING ANTIFUNGAL DRUGS OVER THE COUNTER—GREATER CONVENIENCE BUT ALSO HIGHER COSTS TO CONSUMERS.....	55
PRODUCTS .....	56
ANTIFUNGAL AGENTS ON THE MARKET IN 2002 .....	56
TABLE 14 PRESCRIPTION BRANDED ANTIFUNGAL DRUGS ON THE MARKET, 2002.....	56

<i>TABLE 15 SELECTED PRESCRIPTION ANTIFUNGAL DRUGS: WORLDWIDE SALES, 2001 AND 2002 (\$ MILLIONS)</i> .....	57
<i>TABLE 16 PATENT EXPIRATION OF LEADING ANTIFUNGAL AGENTS</i> .....	58
<i>TABLE 17 WORLDWIDE SALES OF PRESCRIPTION SYSTEMIC ANTIFUNGAL DRUGS, BY CATEGORY: THROUGH 2007 (\$ MILLIONS)</i> .....	58
<i>FIGURE 1 PERCENTAGE OF THE WORLDWIDE PRESCRIPTION ANTIFUNGAL DRUGS, BY CATEGORY, 2002 AND 2007 (%)</i> .....	59
SYSTEMIC ANTIFUNGAL AGENTS .....	59
<i>TABLE 18 PREFERRED DRUGS FOR THE TREATMENT OF SYSTEMIC FUNGAL INFECTIONS</i> .....	60
<i>TABLE 19 USE OF DRUGS TO TREAT SYSTEMIC FUNGAL INFECTIONS, BY COUNTRY, 2000 (%)</i> .....	60
ALLYLAMINES AND OTHER NONAZOLE ERGOSTEROL BIOSYNTHESIS INHIBITORS .....	61
Amorolfine.....	61
Butenafine.....	61
Terbinafine.....	61
ANTIMETABOLITES .....	62
Flucytosine.....	62
AZOLES .....	62
Fluconazole .....	63
Itraconazole.....	64
Ketoconazole .....	64
Voriconazole.....	65
ECHINOCANDINS .....	66
Caspofungin .....	66
Synergistic Effects .....	67
Shortages.....	67
Market Potential.....	67
POLYENES .....	68
Amphotericin B.....	68
Lipid Formulations .....	68
Pharmacoeconomics of Lipid Formulations Versus Conventional Amphotericin B.....	69
The Market for AmBisome and Amphotec.....	70
The Market for Amphotericin B Products .....	70
<i>TABLE 20 THE MARKET FOR AMPHOTERICIN B PRODUCTS: WORLDWIDE SALES, THROUGH 2007 (\$ MILLIONS)</i> .....	70
OTHERS .....	70
Griseofulvin.....	70
TOPICAL ANTIFUNGAL AGENTS .....	71
ALLYLAMINES AND OTHER NONAZOLE ERGOSTEROL BIOSYNTHESIS INHIBITORS .....	71
Butenafine.....	71
Terbinafine.....	72
AZOLES.....	72
OTHER PRODUCTS.....	73

Ciclopirox .....	73
Lithium Succinate .....	73
Haloprogin .....	73
Tolnaftate.....	73
<b>THE U.S. MARKET FOR PRESCRIPTION TOPICAL</b>	
<b>ANTIFUNGAL AGENTS.....</b>	<b>73</b>
<b>TABLE 21 THE MARKET FOR PRESCRIPTION TOPICAL ANTIFUNGAL</b>	
<b>PRODUCTS: U.S. SALES, THROUGH 2007 (\$ MILLIONS).....</b>	<b>74</b>
<b>GENERIC ANTIFUNGAL DRUGS .....</b>	<b>74</b>
<b>TABLE 22 ANTIFUNGAL AGENTS AMONG THE TOP-SELLING PRESCRIPTION</b>	
<b>GENERIC DRUGS IN THE U.S., 2001 .....</b>	<b>74</b>
<b>TABLE 23 ESTIMATES OF MARKET SHARE OF PRESCRIPTION GENERIC ANTI-</b>	
<b>FUNGAL DRUGS, U.S., THROUGH 2007.....</b>	<b>75</b>
<b>OVER-THE-COUNTER ANTIFUNGAL AGENTS .....</b>	<b>75</b>
<b>TABLE 24 THE MARKET FOR OTC TOPICAL ANTIFUNGAL DRUGS: U.S. SALES,</b>	
<b>THROUGH 2007 (\$ MILLIONS).....</b>	<b>76</b>
<b>RX-TO-OTC SWITCHES .....</b>	<b>76</b>
<b>TABLE 25 RX-TO-OTC SWITCHES OF ANTIFUNGAL DRUGS, BY MANUFACTURER</b>	
<b>AND YEAR, 1975-2002.....</b>	<b>77</b>
Rx-to-OTC Switches (Continued).....	78
Potential Rx-to-OTC Switches .....	79
<b>TABLE 26 ANTIFUNGAL RX-TO-OTC SWITCH CANDIDATES .....</b>	<b>79</b>
Potential Rx-to-OTC Switches (Continued).....	80
The Market for Rx-to-OTC Switches.....	81
<b>TABLE 27 MARKET FOR BRAND NAME OTC ANTIFUNGALS CONTAINING RX-TO-</b>	
<b>OTC SWITCHED INGREDIENTS: U.S., THROUGH 2007 (\$ MILLIONS).....</b>	<b>81</b>
The Market for Generic OTC Switched Ingredients .....	82
<b>TABLE 28 MARKET FOR OTC GENERIC ANTIFUNGALS CONTAINING RX-TO-OTC</b>	
<b>SWITCHED INGREDIENTS: U.S., THROUGH 2007 (\$ MILLIONS).....</b>	<b>82</b>
<b>TABLE 29 THE MARKET FOR RX-TO-OTC ANTIFUNGAL DRUGS: U.S., THROUGH</b>	
<b>2007 (\$ MILLIONS) .....</b>	<b>83</b>
<b>FIGURE 2 THE MARKET FOR RX-TO-OTC ANTIFUNGAL DRUGS: U.S., 2002 AND</b>	
<b>2007 (%) .....</b>	<b>83</b>
Competitor Analysis .....	83
<b>TABLE 30 OTC ANTIFUNGALS MANUFACTURER MARKET SHARE BY</b>	
<b>REVENUES, 2001 (%).....</b>	<b>84</b>
<b>FIGURE 3 OTC ANTIFUNGALS MANUFACTURER MARKET SHARE BY</b>	
<b>REVENUES, 2001 (%).....</b>	<b>84</b>
<b>TABLE 31 LEADING SUPPLIERS OF RX-TO-OTC SWITCHED ANTIFUNGALS, 2001 .....</b>	<b>85</b>
<b>ANTIFUNGAL AGENTS IN DEVELOPMENT .....</b>	<b>85</b>
<b>TABLE 32 ANTIFUNGAL DRUGS IN CLINICAL DEVELOPMENT .....</b>	<b>85</b>
<b>TABLE 32 (CONTINUED) .....</b>	<b>86</b>
<b>SYSTEMIC AGENTS.....</b>	<b>86</b>
Allylamines .....	87
Butenafine.....	87
Azoles .....	87
Second-Generation Azoles .....	87
Posaconazole.....	87
Ravuconazole.....	87

Azoles Used in Combination with Immunosuppressants .....	88
Echinocandins.....	88
Anidulafungin .....	88
Anidulafungin (Continued) .....	89
Caspofungin .....	90
Micafungin .....	90
Other Systemic Agents.....	90
MBI 226.....	91
Oramed.....	91
P-113.....	91
PLD-118.....	92
UK-292-663 .....	93
The Possibility of an Antifungal Vaccine.....	93
TOPICAL AGENTS.....	94
EcoNail.....	94
Extina.....	94
Mentax .....	95
THE ROLE OF GENOMICS AND PROTEOMICS IN THE DEVELOPMENT OF NEW ANTIFUNGAL DRUGS .....	95
OBSTACLES TO THE DEVELOPMENT OF ANTIFUNGAL DRUGS .....	95
Obstacles to the Development of Antifungal Drugs (Continued).....	96
APPLICATIONS.....	97
DERMATOLOGIC FUNGAL INFECTIONS.....	97
ONYCHOMYCOSIS.....	97
<i>TABLE 33 AVERAGE WHOLESALE PRICE OF ITRACONAZOLE AND TERBINAFINE         FOR THE TREATMENT OF ONYCHOMYCOSIS (\$)</i> .....	97
PARONYCHIA .....	98
TINEA DISEASES .....	98
Tinea Pedis .....	98
<i>TABLE 34 THE MARKET FOR OTC TOPICAL ANTIFUNGAL DRUGS TO TREAT         TINEA PEDIS: U.S., THROUGH 2007 (\$ MILLIONS)</i> .....	99
VAGINAL FUNGAL INFECTIONS.....	99
<i>TABLE 35 DOSING REGIMENS OF ANTIFUNGAL AGENTS USED TO TREAT         VAGINAL CANDIDIASIS</i> .....	100
<i>TABLE 36 LEADERS IN THE U.S. OTC VAGINAL ANTIFUNGALS MARKET: SALES         AND UNIT VOLUME, 2001 (\$ MILLIONS, RETAIL)</i> .....	101
THE U.S. MARKET FOR OTC VAGINAL ANTIFUNGAL TREATMENTS .....	101
<i>TABLE 37 THE U.S. MARKET FOR OTC VAGINAL ANTIFUNGAL DRUGS,         THROUGH 2007 (\$ MILLIONS)</i> .....	102
INDUSTRY .....	103

REGIONAL SALES OF ANTIFUNGAL DRUGS.....	103
<i>TABLE 38 PERCENTAGE OF SALES OF ANTIFUNGAL DRUGS BY GEOGRAPHIC REGION, 2001 (%).....</i>	<i>103</i>
<i>FIGURE 4 PERCENTAGE OF SALES BY GEOGRAPHIC REGION, 2001.....</i>	<i>103</i>
LEADERS IN THE PRESCRIPTION ANTIFUNGAL DRUG MARKET ...	104
<i>FIGURE 5 MARKET SHARES OF LEADING COMPANIES IN THE ANTIFUNGAL DRUG MARKET, 2001 AND 2007.....</i>	<i>104</i>
COMPANY PROFILES .....	105
BRISTOL-MYERS SQUIBB COMPANY .....	105
BUSINESS OVERVIEW.....	105
FINANCIAL INFORMATION.....	105
PRODUCTS .....	105
COMPANY STRATEGY.....	106
CONNETICS CORPORATION .....	106
BUSINESS OVERVIEW.....	106
FINANCIAL INFORMATION.....	106
PRODUCTS .....	107
COMPANY STRATEGY.....	107
Company Strategy (Continued) .....	108
DEMEGEN, INC.....	109
BUSINESS OVERVIEW.....	109
FINANCIAL INFORMATION.....	109
PRODUCTS .....	109
<i>TABLE 39 DEMEGEN'S PRODUCT PIPELINE .....</i>	<i>110</i>
CORPORATE STRATEGY .....	110
FUJISAWA PHARMACEUTICAL COMPANY, LTD. ....	110
BUSINESS OVERVIEW.....	110
FINANCIAL INFORMATION.....	111
PRODUCTS .....	111
<i>TABLE 40 FUJISAWA'S PRODUCT PIPELINE .....</i>	<i>112</i>
<i>TABLE 40 (CONTINUED) .....</i>	<i>113</i>
GILEAD SCIENCES INC.....	113
BUSINESS OVERVIEW.....	113
FINANCIAL INFORMATION.....	114
PRODUCTS .....	114
<i>TABLE 41 GILEAD'S PRODUCT PIPELINE .....</i>	<i>115</i>
CORPORATE STRATEGY .....	115
INTERMUNE, INC.....	116
BUSINESS OVERVIEW.....	116
FINANCIAL INFORMATION.....	116
PRODUCTS .....	117
<i>TABLE 42 INTERMUNE'S PRODUCT PIPELINE.....</i>	<i>117</i>
JOHNSON & JOHNSON .....	118
BUSINESS OVERVIEW.....	118
FINANCIAL INFORMATION.....	118



PRODUCTS .....	119
CORPORATE STRATEGY .....	119
MACROCHEM CORPORATION .....	119
BUSINESS OVERVIEW .....	119
FINANCIAL INFORMATION .....	119
PRODUCTS .....	120
<i>TABLE 43 MACROCHEM'S PRODUCT PIPELINE .....</i>	<i>121</i>
CORPORATE STRATEGY .....	121
MICROLOGIX BIOTECH INC. ....	121
BUSINESS OVERVIEW .....	121
FINANCIAL INFORMATION .....	121
PRODUCTS .....	122
<i>TABLE 44 MICROLOGIX'S PRODUCT PIPELINE .....</i>	<i>123</i>
COMPANY STRATEGY .....	123
Company Strategy (Continued) .....	124
MYLAN LABORATORIES, INC. ....	125
BUSINESS OVERVIEW .....	125
FINANCIAL INFORMATION .....	125
PRODUCTS .....	126
CORPORATE STRATEGY .....	126
NOVARTIS .....	127
BUSINESS OVERVIEW .....	127
FINANCIAL INFORMATION .....	127
PRODUCTS .....	128
CORPORATE STRATEGY .....	128
PFIZER CORPORATION .....	128
BUSINESS OVERVIEW .....	128
FINANCIAL INFORMATION .....	128
LEADING PRODUCTS .....	129
CORPORATE STRATEGY .....	130
SCHERING-PLOUGH CORPORATION .....	131
BUSINESS OVERVIEW .....	131
FINANCIAL INFORMATION .....	131
LEADING PRODUCTS .....	131
<i>TABLE 45 SCHERING-PLOUGH'S PRODUCT PIPELINE .....</i>	<i>132</i>
CORPORATE STRATEGY .....	133
VERSOR, INC. ....	133
BUSINESS OVERVIEW .....	133
FINANCIAL INFORMATION .....	133
LEADING PRODUCT CANDIDATES .....	133
<i>TABLE 46 VERSICOR'S PRODUCT PIPELINE .....</i>	<i>134</i>
CORPORATE STRATEGY .....	134
Corporate Strategy (Continued) .....	135