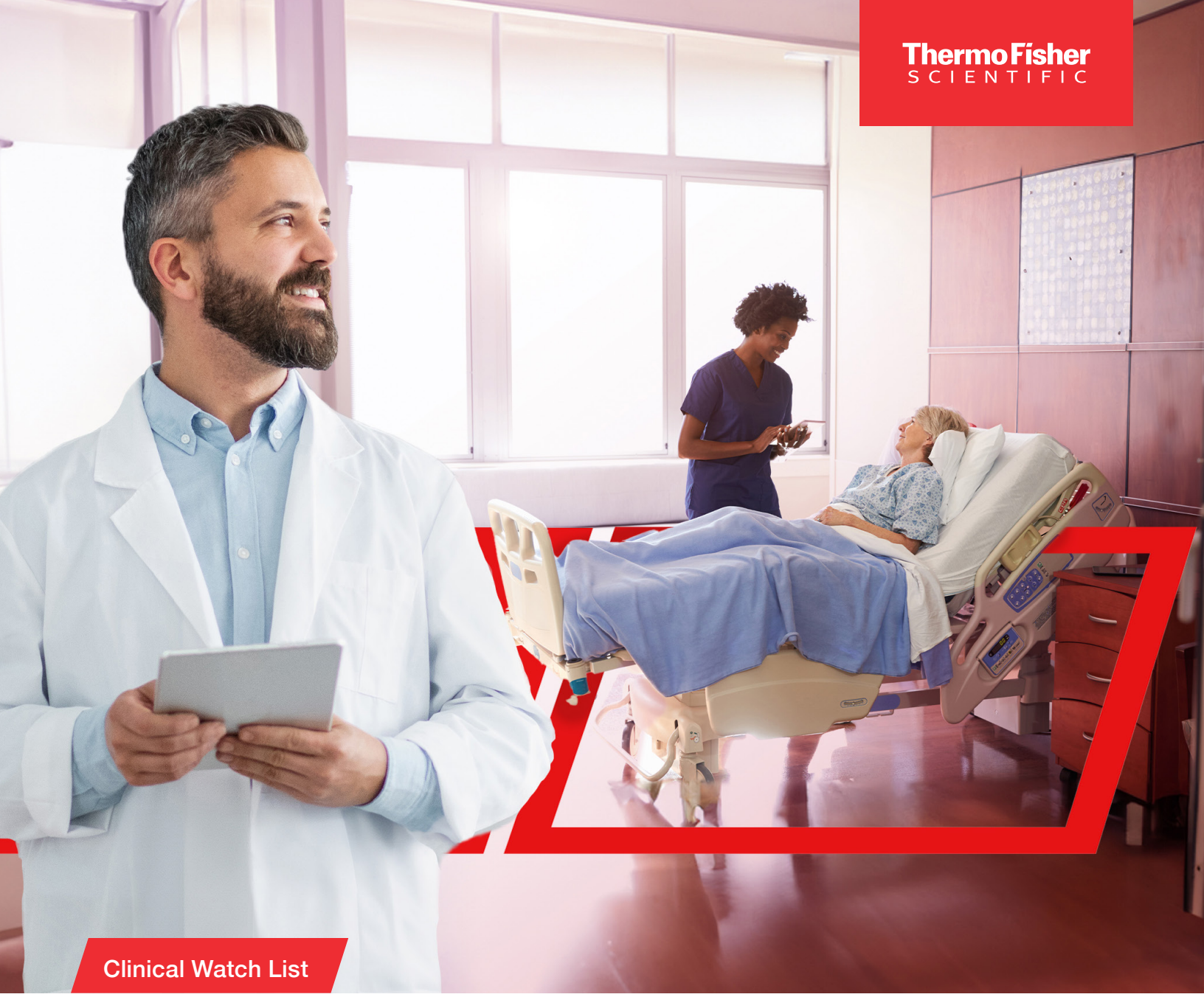
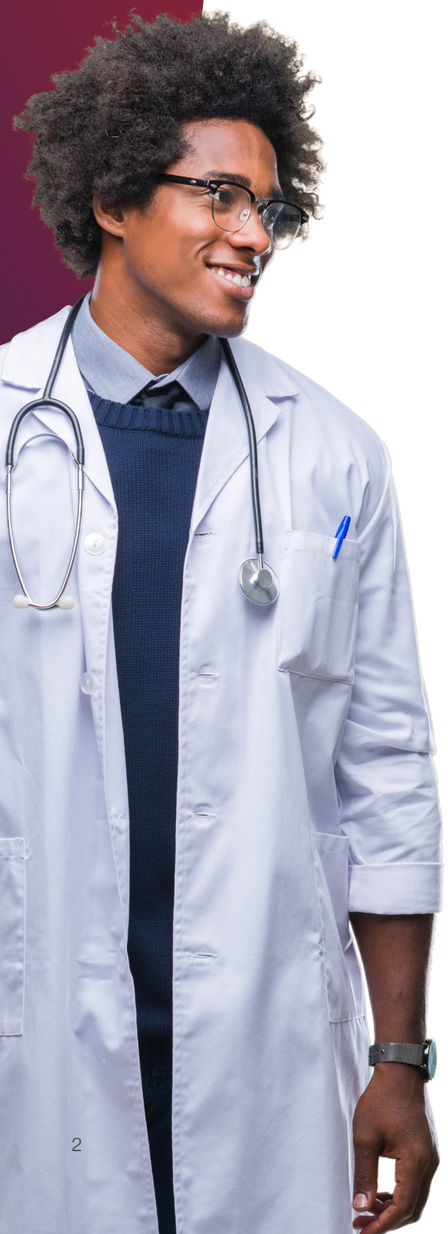


Clinical Watch List

# The high cost and human toll of multidrug-resistant organisms (MDROs)



# Introduction to MDROs

Clinicians and laboratory workers around the world fight a dynamic battle against the rising tide of multidrug-resistant organisms (MDROs). When these organisms make their way into healthcare and hospital settings, the stakes become even higher.

Every minute counts when MDROs cause healthcare-associated infections (HAIs) – infections patients acquire during healthcare treatment. These infections can quickly spiral out of control and become costly and deadly emergencies. While not all HAIs are caused by MDROs, those that are, pose a particularly serious threat. Labs, clinicians and antimicrobial stewardship teams make consequential decisions each and every day as pathogens, such as MRSA, *Acinetobacter baumannii* and *Clostridioides difficile*, become more prevalent and present greater risks to patients and hospital operations.

But while clinicians and labs may feel the odds are stacked against them in preventing MDROs and the dangerous and costly HAIs they can cause, there is hope. Let's explore the new tools, techniques, and clinical perspectives that can help even the score.



# Contents



# Compounded costs of antimicrobial resistance

Labs, doctors, nurses, and operational leaders must all re-examine their processes, technology, and capabilities surrounding MDROs and HAIs. Understanding the depth and breadth of MDROs as a threat to hospitals and healthcare settings is a critical first step in the process.

## The impact of MDROs and HAIs

Serious HAIs, particularly antimicrobial-resistant ones like MRSA or VRE, affect hundreds of thousands of patients each year in the United States alone, leading to significant morbidity and mortality. The financial impact is staggering, with HAIs adding billions to annual healthcare costs.[1] The burden doesn't end there though: these infections overwhelm laboratories with increased testing demands and extended hospital stays, further straining healthcare resources.[2,4]

However, HAIs and MDROs don't just complicate hospital stays – they also lead to long-term health issues and frequent readmissions for patients. The emotional and psychological toll on patients and their families is profound, with stress and anxiety often accompanying the physical health challenges. In addition, the financial strain on healthcare systems is immense. Infections caused by pathogens, for example *Acinetobacter*, can cost healthcare facilities $20K to $128K per infection.[3]

## Implications for treatment

Treating resistant infections is a complex and evolving challenge. The rise of antimicrobial resistance (AMR) often leaves clinicians with limited therapeutic options, necessitating the use of last-resort antibiotics such as colistin, which can be less effective and more toxic. This predicament not only complicates treatment protocols but also heightens the risk of adverse side effects.

## Global and local efforts

Combating AMR requires coordinated global and local strategies. The WHO's Global Action Plan on Antimicrobial Resistance and national antimicrobial stewardship programs are pivotal in reducing resistance rates[4]. These initiatives emphasize the judicious use of antibiotics, optimize treatment protocols, and support the development of new antimicrobial agents to stay ahead of evolving resistance mechanisms. Antimicrobial stewardship programs have been shown to reduce antibiotic usage, thereby decreasing selection pressure for resistant strains.[5]

The compounded costs of antimicrobial resistance underscores the critical need for advanced treatment strategies, improved patient outcomes, and robust global and local efforts to combat this escalating threat. The nuanced understanding is essential in managing and mitigating the impacts of AMR.

*Availability of product in each country depends on local regulatory marketing authorization status.


"The urgency of getting the right drug to the patient is the same as how fast we get someone who's had a heart attack into the cath lab to restore blood flow."

—Dr. James McKinnell, MD, Associate Professor of Medicine, David Geffen School of Medicine, UCLA, Division of Infectious Disease, LA-Biomed at Harbor UCLA Medical Center.

# Problem pathogens: Spotlight on *Acinetobacter baumannii*

*Acinetobacter baumannii* has emerged as a significant pathogen, particularly in healthcare settings, due to its remarkable ability to develop resistance to multiple antimicrobial agents. This bacterium employs various resistance mechanisms, making it a formidable challenge for healthcare providers:

1. Beta-lactamases: *A. baumannii* produces enzymes like OXA-type carbapenemases (e.g., OXA-23, OXA-24/40, OXA-58) that confer resistance to beta-lactam antibiotics, including carbapenems.
2. Efflux pumps: These proteins, such as Tet and AdeABC, expel antibiotics out of the bacterial cell, reducing drug efficacy.
3. Porin alterations: Changes in porin proteins decrease antibiotic uptake.
4. Target site modifications: Alterations in bacterial targets, such as penicillin binding protein mutations, reduce antibiotic binding.[6]

The prevalence of carbapenem-resistant *A. baumannii* (CRAB) is particularly concerning. In 2021, the overall incidence rate of CRAB was 1.9 cases per 100,000 persons, with higher rates among men, older adults, and African Americans. Two-thirds of patients were in acute care hospitals or long-term care facilities, and most cases had multiple underlying conditions.[7]

The impact of CRAB infections is severe, with 13.3% of cases requiring ICU admission and an overall mortality rate of 17.1%. Mortality rates were even higher in patients with CRAB isolated from sterile sites or lower respiratory tract specimens.[8]

## Treatment challenges and new hope

Treatment options for carbapenem-resistant and MDR *A. baumannii* strains are severely limited. Clinicians have been forced to revive older drugs like colistin, often used in combination with other antimicrobials. However, this approach lacks robust supporting data and conflicts with stewardship efforts aimed at decreasing carbapenem use.[9]

Fortunately, there is hope on the horizon with the development of novel drugs. Sulbactam/durlobactam is a new therapeutic option for treating hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP) caused by *A. baumannii*, including carbapenem-resistant and multidrug-resistant strains.

This combination drug works through a dual mechanism:

- Sulbactam: A beta-lactam antibiotic with intrinsic activity against *A. baumannii*.
- Durlobactam: A novel beta-lactamase inhibitor that counters the enzymes responsible for antibiotic resistance.

Sulbactam/durlobactam represents the first novel antimicrobial with activity against *Acinetobacter* since 2005 and appear to be more effective and safer than colistin[10] for treating pneumonia. This advancement offers new hope in the ongoing battle against MDROs and underscores the importance of continued research and development in antimicrobial therapies.

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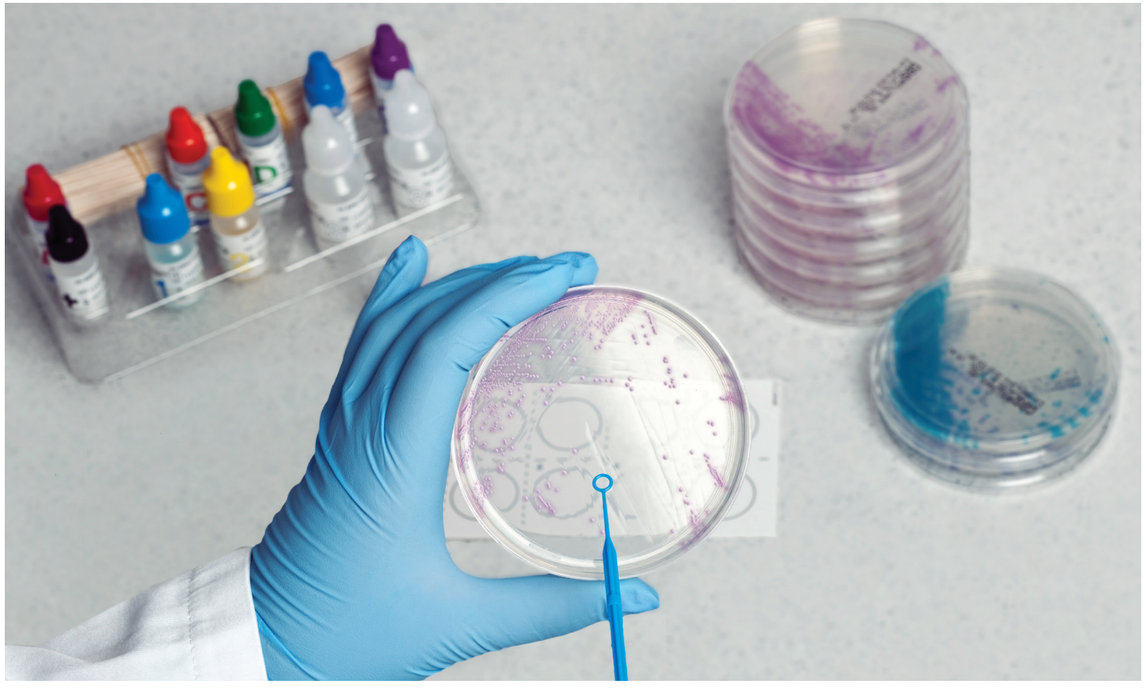
# Advances in screening, detection, and testing for MDROs

Vigilance is key in the fight against AMR. Commitment to AMR surveillance helps inform public health decisions, track the spread of resistant pathogens, and guide the use of antimicrobials with a focus on preserving their efficacy. Regional programs form the backbone of this commitment, and help:

- Monitor resistance trends over time.
- Evaluate effectiveness of interventions aimed at reducing AMR.
- Identify and communicate emerging resistance patterns and hotspots.
- Provide data for risk assessments and predictive modeling.
- Guide clinical treatment guidelines and public health policies.

The stakes are high when it comes to surveillance — accurate and timely diagnostics play a critical role ensuring MDROs and HAIs remain under control.



## Advancements in screening and detection

Several technologies play a pivotal role in preventing the spread of HAIs in healthcare facilities:

1. **Chromogenic media**: These advanced culture media have been a mainstay in microbial diagnosis through enhanced specificity and selectivity when compared to traditional culture media. Chromogenic testing allows for quicker and more accurate identification of specific pathogens, including various bacterial species. Key advantages include:

- Precise, cost-effective targeting and detection of pathogens in a simple process.
- Enhanced ability to identify co-infections.
- Ready-to-use formats produce quicker results and require less reagent use, leading to cost savings and less labor in the lab.
- Easy interpretation requires less extensive expertise compared to molecular methods.
- New versatility allows for detection of MRSA, VRE, ESBL-producing bacteria, and organisms causing UTIs.

2. **Polymerase chain reaction (PCR):** This molecular technique offers rapid detection of specific genetic material from pathogens. While it provides quick results, it may not distinguish between live and dead organisms.

3. **MALDI-TOF MS (Matrix-Assisted Laser Desorption/ Ionization-Time of Flight Mass Spectrometry)**: This method provides rapid microbial identification based on protein fingerprinting. It offers quick results but requires specialized equipment and extensive databases.

## Advancements in AST

Antibiotic resistance complicates treatment protocols and jeopardizes patient health. AST is crucial in guiding appropriate and targeted use of antibiotics, helping prevent further resistance development. Several methods are available to detect antimicrobial resistance:

1. **Phenotypic methods**: a) Broth microdilution: Provides true minimum inhibitory concentration (MIC) results with precise and observable endpoints. b) Disk diffusion: A cost-effective method that measures zones of inhibition around antibiotic-impregnated disks.

2. **Genotypic methods:** a) PCR: Can detect specific resistance genes but may not always correlate with phenotypic resistance. b) Next-generation sequencing (NGS): Offers high-precision identification of a wide range of resistant genes but is currently cost-prohibitive for routine use.

3. **Rapid AST methods:** Emerging technologies aim to reduce AST results to hours instead of days.

Advanced diagnostics and AMR surveillance will be crucial in our ongoing fight against MDROs and HAIs. With more accurate, timely data, these tools empower healthcare professionals to make informed decisions, implement targeted interventions, and contribute to global efforts in combating antimicrobial resistance.

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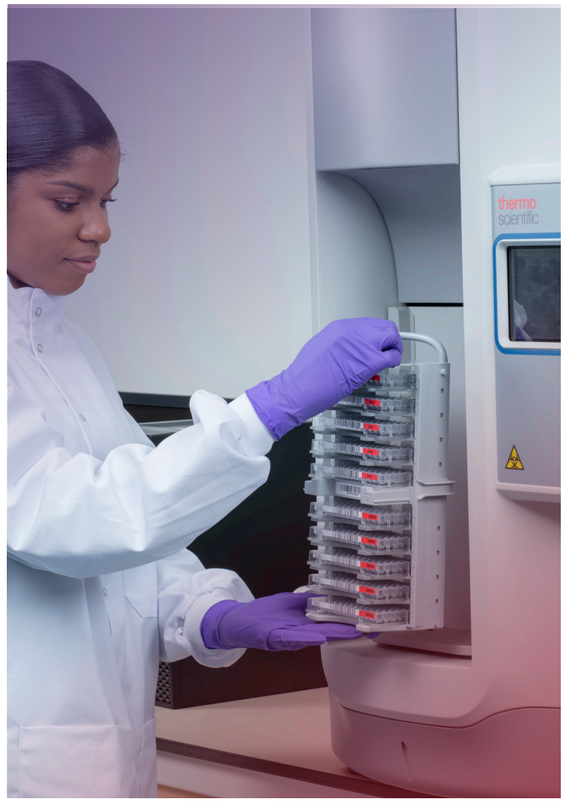
# Precise tools for a targeted fight against MDROs

## Unwavering commitment to public health

AMR is one of the most significant threats to global health, predicted to cause 10 million deaths annually by 205011. At Thermo Fisher Scientific, we are dedicated to supporting antimicrobial stewardship efforts and protecting public health with state-of-the-art solutions to combat MDROs




## Key solutions for combating AMR

**1. Thermo Scientific™ Sensititre™ AST System:**

- **Definitive MIC results:** Provides accurate and reliable MIC values that are essential for guiding tailored antibiotic therapy.
- **The latest antimicrobials:** Owing to our partnerships with pharmaceutical companies, we're able to quickly incorporate new antimicrobials into panel formats, ensuring that the latest compounds are available for laboratory use. Examples include plazomicin for complex urinary tract infections and eravacycline, effective in treatments for complex intra-abdominal infections and many multidrug-resistant strains of bacteria.

  *The system offers the only FDA-cleared automated AST assay for sulbactam/durlobactam susceptibility testing of Acinetobacter baumannii-calcoaceticus complex isolates*.
- **Comprehensive AST panels:** Offers extensive panels that cover a wide range of pathogens, ensuring comprehensive testing capabilities and tailored panels to meet the specific needs of different healthcare settings.

**2. Thermo Scientific™ *Brilliance*™ and Spectra™ chromogenic media:**

- **Advanced detection:** Enhances the speed and accuracy of pathogen identification, including multidrug-resistant organisms, when compared to traditional culture media.
- **User-friendly:** Simple diagnostic process with clear, color-based differentiation of pathogens.
- **Cost-saving**: Chromogenic media offers a more cost-effective alternative to molecular methods of testing.

**3. Thermo Scientific™ Oxoid ™ AST Discs**

- **Simplicity of disc diffusion:** For categorizing resistant, intermediate, and sensitive organisms – as well as providing visual indicators for inoculum levels, presence of contamination, and resistant mutants.
- **Advanced antimicrobials:** Latest lines of defense include eravacycline and omadacycline for treatment of complicated intra-abdominal infections (cIAI) and CABP and ABSSSI respectively. Lefamulin for treating CABP.
- **Ease-of-use:** Make testing simple with spring-loaded cartridges with end-of-cartridge indicators.

**4. Thermo Scientific™ Culti-Loops™ Quality Control Organisms:**

- **Ready-to-use:** Utilize disposable bacteriological loops containing viable microorganisms for stringent quality control, to ensure accurate and reproducible laboratory results.
- **Convenience:** Decrease time and unnecessary costs of laboratory resources with a direct-streak inoculating loop that requires no rehydration.
- **Coming soon: A new addition to our Culti-Loops portfolio for *Clostridioides difficile.***

## A shared responsibility

We believe that combating AMR is a shared responsibility. Thermo Fisher Scientific is committed to providing the tools and support necessary for healthcare professionals to succeed in this fight. By delivering innovative, reliable, and accurate diagnostic solutions, we help empower clinicians to make informed decisions, improve patient outcomes, and ultimately, protect public health.

**For more information, visit thermofisher.com/onehealth.**

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**Footnotes**


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