



**MEDICAL DEVICES ADVISORY COMMITTEE
MEETING OF THE GENERAL HOSPITAL AND PERSONAL
USE DEVICES PANEL**

**Antimicrobial Agents on Personal
Protective Equipment (PPE)**

May 4, 2007

Infection Control Devices Branch
Division of Anesthesiology, General Hospital,
Infection Control and Dental Devices
Center for Devices and Radiological Health

Antimicrobial Agents on Personal Protective Equipment

Introduction

Sheila A. Murphey, MD

Branch Chief
Infection Control Devices Branch

Division of Anesthesiology, General Hospital, Infection
Control and Dental Devices

Center for Devices and Radiological Health

Antimicrobial Agents on Personal Protective Equipment

Presentations by FDA

Sheila A. Murphey, MD

Michelle Rios, MS

Terrell Cunningham, RN, BSN

R. Kapil Panguluri, Ph D

Geetha C. Jayan, Ph D

Katherine Spooner, MD

General Hospital and Personal Use Devices Advisory Panel

- The Advisory Panel is asked to address the scientific and clinical issues raised by the incorporation of antimicrobial agents into personal protective equipment (PPE).
- PPE include medical gloves, surgical masks and surgical respirators and isolation/surgical gowns.
- PPE function as protective “barrier” devices

Antimicrobial Agents on Personal Protective Equipment

- FDA, to date, has not cleared any medical gloves or surgical masks or N95 respirators which incorporate antimicrobial agents.
- FDA is aware of just 2 surgical gowns, cleared many years ago as part of lines of surgical textiles of various types, which included an antimicrobial agent

Antimicrobial Agents on Personal Protective Equipment

- FDA is aware that PPE which incorporate antimicrobial agents on PPE are being marketed in other countries.
- FDA believes that there may be interest in developing and marketing such products in the United States.

Antimicrobial Agents on Personal Protective Equipment

- FDA believes that the addition of antimicrobial agents to PPE raises important scientific and clinical issues related to safety and to the performance of such devices.
- FDA wishes to seek the guidance of this Advisory Panel as it prepares for the review of PPE incorporating antimicrobial agents.

Antimicrobial Agents on Personal Protective Equipment

- Devices cleared for marketing by FDA which incorporate antimicrobial agents have generally been devices associated with “device-related infections” such as intravascular catheters, urinary catheters, ventricular catheters, etc.

Antimicrobial Agents on Personal Protective Equipment

FDA has also cleared for marketing devices incorporating antimicrobial agents which may become “contaminated” during use over periods of days or longer, such as wound care products.

Antimicrobial Agents on Personal Protective Equipment

- FDA believes that there are several important differences between personal protective equipment (PPE) and devices previously cleared with antimicrobial agents.
- FDA believes that these differences are important to the potential review process for PPE which incorporate antimicrobial agents.

Antimicrobial Agents on Personal Protective Equipment

Important characteristics of PPE include

- Used for short periods of time
- Mostly single use, disposable devices
- Not associated with “device-related” nosocomial infections, although gloves, like human hands, can spread pathogens from one location to another when not removed and discarded between tasks which could contaminate them

Antimicrobial Agents on Personal Protective Equipment

- Can antimicrobial agents “enhance” the protective barrier function of PPE for the wearer of the PPE?
- Can antimicrobial agents prevent the “spread of contamination” by PPE, especially medical gloves?

Antimicrobial Agents on Personal Protective Equipment

- FDA is aware that there is great concern about the current incidence of hospital-acquired (nosocomial) infections
- FDA is also aware of the great concern about the increasing incidence of nosocomial infections caused by highly antibiotic-resistant pathogens such as MRSA and VRE

Antimicrobial Agents on Personal Protective Equipment

- FDA is also aware of the concern over the difficulties in achieving complete compliance among health care personnel with such important infection prevention measures as handwashing and appropriate use of personal protective equipment and proper aseptic technique

Antimicrobial Agents on Personal Protective equipment

The increasing incidence of antimicrobial-resistant pathogens in both the hospital setting and the community has also increased interest in appropriate prescribing practices for systemic antibiotics

Antimicrobial Agents on Personal Protective Equipment

Is there a potential role for antimicrobial agents on PPE in ameliorating such problems as:

- The contact transfer of nosocomial pathogens in health care?
- The need for frequent handwashing by health care personnel?
- The appropriate use of PPE by health care personnel?

Antimicrobial Agents on Personal Protective Equipment

Are there risks associated with the use of antimicrobial agents on PPE?

- Will health care personnel wearing PPE with antimicrobial agents assume that the presence of the antimicrobial agent will prevent the adverse effects of failures to remove and discard contaminated PPE and to wash their hands when needed?

Antimicrobial Agents on Personal Protective Equipment

Are there risks associated with the use of antimicrobial agents on PPE?

- Will antimicrobial agents leach off or physically detach from the PPE?
- What safety issues for patients or health care personnel could arise from the antimicrobial agents added to PPE?

Antimicrobial Agents on Personal Protective Equipment

Can antimicrobial agents on PPE work quickly enough to actually inhibit the growth of or kill pathogens on the surface of PPE before a health care worker wearing the PPE moves from one patient care site to another or from one patient care task to another?

Antimicrobial Agents on Personal Protective Equipment

FDA reviewers will describe for the Panel:

- Current review process for PPE
- Current FDA thinking on the data needed on antimicrobial agents added to devices
- Performance testing issues noted in the review of antimicrobial agents on other devices
- Scientific and clinical issues raised by the addition of antimicrobial agents to PPE

Antimicrobial Agents on Personal Protective Equipment

- FDA will ask the Panel to address, after hearing from Industry and Public Speakers, the following questions.

Questions for the Advisory Panel

1. Various “indications for use” might be sought for PPE incorporating antimicrobial agents.
 - Please discuss what types of indications may be appropriate for PPE with antimicrobial agents.
 - Please describe the meaning of various indications and what types of performance data should support such indications.

Questions for the Advisory Panel

- What would a “reduces contamination” or a “protects from microbial contamination” indication mean for PPE with added antimicrobial agents?
- How might performance for such an indication for use be evaluated?

Questions for the Advisory Panel

- What might a “reduces colonization” indication mean for PPE which can become contaminated during use but are promptly discarded after use?
- How should such an indication be supported?

Questions for the Advisory Panel

2. For each of the following types of PPE with added antimicrobial agents, please discuss what time frame would be appropriate for demonstrating antimicrobial efficacy in order to:
 - Kill/inhibit microbes
 - Reduce the risk of transferring microbes from one site to another

Questions for the Advisory Panel

- Medical Gloves
 - Examination Gloves
 - Surgeons' Gloves
- Surgical Masks
- Surgical N95 Respirators
- Medical Gowns
 - Surgical Gowns
 - Isolation Gowns

Questions for the Advisory Panel

3. For surgical masks or surgical N95 respirators with antimicrobial agents, please comment on whether performance testing should be expected to support:
 - Significant reduction of an aerosol of a infectious inoculum compared to a control device
 - Simply demonstrate an ability to kill microbes on the surface of the device

Questions for the Advisory Panel

- As surgical masks and surgical N95 respirators conventionally have at least 3 layers, the middle layer serving as the “filter” for the device, please also discuss whether the location of the antimicrobial agent in the device should determine, in part at least, the type of performance testing needed?

Questions for the Advisory Panel

4. For antimicrobial agents added to surgical masks and N95 respirators, please discuss the safety issues for the device wearer and how these might be evaluated, including but not limited to:
 - Effects on the oral, nasal or ocular mucosa
 - Effects on the lower respiratory tract

Questions for the Advisory Panel

5. For antimicrobial agents added to PPE, especially medical gloves, please discuss the safety issues or risks for patients exposed to these devices.
 - Should the potential for leach off or physical detachment of the antimicrobial agent from PPE into body sites or onto objects be evaluated?

Questions for the Advisory Panel

In your discussion, please comment on whether your concerns about such exposure are increased for pediatric and neonatal patients.

Questions for the Advisory Panel

6. Please discuss whether there is a reasonable possibility that the presence of an “antimicrobial agent” on PPE might lead the PPE wearer to be less likely to follow correct infection control procedures or proper techniques. If such a risk seems to be a possibility, what steps could be taken, including product labeling, to help reduce such a risk?



Medical Gloves with Antimicrobial Agents

Terrell Cunningham
Infection Control Devices Branch
DAGID, CDRH, FDA

OVERVIEW of Medical Gloves

- CDC/OSHA REQUIREMENTS
- CLASSIFICATION
- DESCRIPTION
- IDENTIFICATION
- 510(k) REVIEW PROCESS
- SAFETY CONSIDERATIONS

Universal Precautions and OSHA Blood-borne Pathogens Regulation

- 1987 CDC “Universal Precautions” Report - Recommended that healthcare workers use *Protective Barriers* (such as gloves) when contact with blood or other body fluid is anticipated to prevent HIV, HBV and HCV infection
- 1991 OSHA “Blood-borne Pathogens” Standard - Required the practice of “Universal Precaution” to minimize worker exposure to blood-borne pathogens

Medical Glove Usage

- Approximately 39.2 billion pairs of medical gloves were imported into the United States during 2004 (U.S. International Trade Commission, Import Statistics)

Classification of Medical Gloves

Class I Medical Devices

Different Types of Glove Products

- Patient Examination Gloves
- Surgeon's Gloves
- Glove liners
- Under gloves
- Finger cots

Patient Examination Gloves

21 CFR 880.6250

- “A patient examination glove is a disposable device intended for medical purposes that is worn on the examiner's hand or finger to prevent contamination between patient and examiner.”
- Primarily Non-Sterile
- Single-Use/Disposable
- Barrier Protection

Protects wearer from blood-and fluid-borne pathogens

Medical Gloves

Material Composition

- Natural Rubber Latex
- Synthetic Polymers
 - Nitrile
 - Vinyl
 - Isoprene
 - Neoprene/styrene/styrene-butadiene
- Chemical Additives

510(k) Review Process for Medical Gloves

Current evaluation includes:

- Water Leak (Pinhole) Test
- Tensile Strength/Elongation
- Physical dimensions
- Biocompatibility
 - Non-irritating/non-sensitizing
- Sterility evaluation as appropriate
- Guidance Documents: Glove Manual-
<http://www.fda.gov/cdrh/manual/glovmanl.pdf>

Medical Gloves with Antimicrobial Agents

Device review should consider the following:

- Antimicrobial Agent
- Agent's mode of application
- Safety considerations
- Promotional indications
- Performance testing

Medical Gloves with Antimicrobial Agents

Where is the Antimicrobial Agent located?

- Antimicrobial coated or impregnated
 - Wearer skin contact
- Surface modification of glove material
 - Patient contact; surgical site
- Leaching of antimicrobial agent

Safety Considerations for Medical Gloves with Antimicrobial Agents

- Skin irritation (end-user and patient)
- Skin sensitization (end-user and patient)
- Toxicity dermal exposure
- Leaching of chemical agent into mucosal surfaces, open wounds and patient devices such as enteral feedings

Safety Considerations for Medical Gloves with Antimicrobial Agents

- Delivery of the Antimicrobial Agent to various body sites
- Adverse reactions to the Antimicrobial Agent
- Effects on neonates and pediatric populations and other vulnerable patients

Antimicrobial Agents on Medical Gloves

How do we evaluate these products?

- Indications for Use
- Proposed benefits
- Performance testing
 - should evaluate final finished product
 - performance testing should mimic conditions of use of the device

Medical Gloves with Antimicrobial Agents

Possible Indications for Use

- Reduces hospital-acquired (nosocomial) infections
- Prevents pathogens from sticking
- Promotes germless environment
- Prolongs shelf-life of the device

Antimicrobial Agents on Medical Gloves

Performance Testing Considerations

- Safety and biocompatibility studies should include the evaluation of the final finished glove on mucosal surfaces and on open wounds
- RAPID kill of microbes in the presence of organic soil
- Data should support the effectiveness of the device for the stated intended use
- Shelf life/expiration date testing to demonstrate the length of time for which the antimicrobial agent will remain active before use



ADDITION OF ANTIMICROBIAL AGENTS ON SURGICAL MASKS & SURGICAL N95 RESPIRATORS

**Kapil Panguluri, Ph.D.
CDRH/ODE/DAGID/INCB**

Overview-1

Surgical Masks/N95 Respirators:

- Regulatory Classification
- Device Description
- Surgical Mask and Surgical N95 Respirator comparison
- FDA's 510 (k) Review process for Masks/Respirators

Overview-2

Surgical Masks/N95 Respirators with Antimicrobial Agents

Method of application of antimicrobials

- Safety and Effectiveness
- Indications for Use
- Performance Testing

Regulated under Class II Device Classification

Subject to Premarket Notification [510(k)]

- **Surgical Mask**
 - Laser Mask
 - Isolation Mask
 - Dental Mask
 - Medical Procedure Mask
- **Surgical N95 Respirator**



Regulation & Device Identification

21 CFR 878.4040

Surgical apparel are devices that are intended to be worn by operating room personnel during surgical procedures to protect both the surgical patient and the operating room personnel from transfer of microorganisms, body fluids and particulate material.

Surgical Mask Vs. Surgical N95 Respirator comparison

Surgical Mask	Surgical N95 Respirators
<p>May prevent contamination of the sterile work environment from large fluid droplets generated by the wearer.</p> <p>May reduce the risk of splashes of blood, body fluids, secretions and <u>large particulates</u> from reaching the mouth and nose of the wearer.</p>	<p>May reduce wearer's exposure to <u>small airborne particles</u> that are less than 100 micron in size (including bacteria, fungi and viruses)</p>

Surgical Mask vs. Surgical N95 Respirator comparison

Surgical Mask	Surgical N95 Respirators
Fit loosely to the face	Fit tightly to the face
Not designed for seal check	User seal check is required with each use
FDA reviews the 510(k) submission and makes a decision to clear for marketing	Certified by NIOSH and FDA reviews and clears through 510(k) as surgical N95 respirator
Performance testing: <u>Filtration Test, Differential Pressure</u> , Fluid Resistance, Flammability and Biocompatibility	Performance testing: NIOSH Certification, Fluid Resistance, Flammability and Biocompatibility

510(k) Review Process

Device Description:

- Material Composition
- Size
- Dimensions
- Tensile strength
- Design Features

510(k) Review Process

Performance characteristics:

- **Fluid resistance**
 - ASTM F 1862
- **Filtration efficiency**
 - Particulate filtration efficiency (PFE)
 - Bacterial filtration efficiency (BFE)

510(k) Review Process

Performance characteristics:

- **Air exchange** (Differential Pressure, Delta-P)
Measures breathability and comfort of surgical masks)
- **Flammability**
Class 1 and Class 2 flammability rating material for use in the Operating Room)
- **Biocompatibility**
(Testing for Irritant and Sensitization (ISO 10993))

Overview-2

Surgical Masks/N95 Respirators with Antimicrobial Agents

Method of application of antimicrobials

- Safety and Effectiveness
- Indications for Use
- Performance Testing

How does the addition of antimicrobial agents to the surgical masks/N95 respirators change the Device Review process?

Depends on:

- Method of application of antimicrobials
- Safety and Effectiveness attributes
- Indication for Use statements
- Performance Testing

Method of application: Antimicrobials



Addition of Antimicrobials: Safety

Depends on:

- Concentration of the agent (per square cm of the mask/respirator filter)
- Type of Antimicrobial Agent
- Location of the Antimicrobial Agent (Outer, Inner or Middle layers of the filter)

Addition of Antimicrobials: Safety

What kind of Toxicity Issues?

- Inner Layer (close proximity to the Oral, Nasal and Ocular areas)
- Outer Layer and Middle Layer (Gas off/Leach off of antimicrobial agents into the nasal, ocular and oral regions)



The addition of antimicrobial to the filter changes the Traditional Biocompatibility requirements (Irritation and Sensitization tests). The new Biocompatibility requirements may include evaluating leach off/gas off material from the filters and may cause Nasal, Oral and Ocular toxicity

Promotional Indications for Use statements found in the Internet for Antimicrobial Masks/N95 Respirators

- Protects the filtration material from bacteria and fungi
- Protects against Specific bacterial/viral agents
- Antimicrobial agents in the filter material can isolate and kill microorganisms
- Elemental and metal ions in the filters acts as effective antimicrobial agents against viruses and bacteria

Addition of Antimicrobials: Effectiveness

What kind of Performance Testing:

- Antimicrobial Efficacy Testing
(Quantitative and short time-kill)
- Shelf-life of antimicrobial agents on finished masks



Antimicrobial Agents on PPE: Surgical & Isolation Gowns



Geetha C. Jayan, Ph. D

INCB / DAGID / ODE / CDRH / FDA

Overview

- Surgical & Isolation Gowns:
 - Regulation & Classification
 - FDA Review Process of the device
- Antimicrobial Agents on the Surgical & Isolation Gowns: Issues

Gowns: Regulation

Surgical Apparel: The Code of Federal Regulations (21CFR 878.4040)

Examples: surgical gowns, isolation gowns, surgical caps, surgical masks

Devices intended to be worn by operating room (OR) personnel during surgical procedures to protect both the surgical patient and the OR personnel from transfer of microorganisms, body fluids, and particulate material (21CFR 878.4040)



Gowns: Classification

Surgical apparel

(21CFR 878.4040)

Class I:

Surgical apparel except
Surgical gowns & masks

- Exempt from pre-market FDA review
- Isolation gowns

Class II:

Surgical gowns & Surgical
masks

- Subject to pre-market FDA review
- Surgical gowns

FDA Review of Surgical Gowns

- The 510(k) review process:
 - Performance and Safety testing information of the device is an important part

Performance Testing Information

Barrier Integrity
Testing



Physical &
Mechanical



Barrier Integrity

- Resist blood and liquid penetration
 - Water splash resistance
 - Hydrostatic pressure resistance
 - Resistance to artificial blood under pressure



Physical & Mechanical Properties

- Physical Strength :
 - Resist Tears and Punctures
- Comfortable to Wear:
 - Adequate Heat and Water Vapor transmission
- Safe for use in the OR
 - Free from non-color-fast dyes, linting materials, flammable materials



Safety: Biocompatibility

- Should not cause adverse reactions on skin contact:
 - Non Dermal Irritant
 - Non Dermal Sensitizer



Antimicrobial Agents on Surgical and Isolation Gowns



- Potential Performance Indications*
- How does it affect the Submission Review
- Safety and Effectiveness considerations

*From public internet information sources for devices outside the U.S.

Potential Indications

- Enhanced protection of OR patients and personnel from infectious microbes
 - Antibiotic resistant strains of microbes
- Prevent contact transmission of infectious microbes

Antimicrobials Addition: Submission Review Aspects

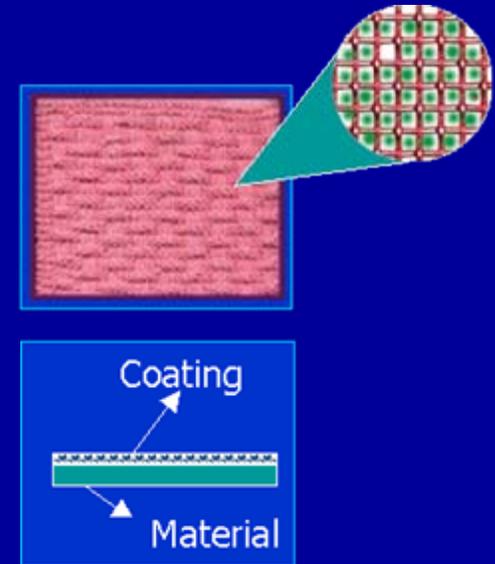
- Addition of Antimicrobials to Isolation Gowns:
 - New increased safety concerns
 - Trip the limitation for exemption from pre-market review

Antimicrobials Addition: Safety Considerations

- Will depend on:
 - Method of application of antimicrobial agent
 - Type of the antimicrobial agent

Safety: Method of Application

- Woven into the fabric or coated on the surface?
- Coating: outside or inside?
 - Outside: Agent leach-off from gown to surgical site/OR patient
 - Inside: Agent leach-off from gown to wearer



Safety: Type of Antimicrobial Agent

- New molecular entity vs. historically known molecules
- Issues specific to Nanoparticulate molecules



Antimicrobials Addition: Effectiveness Considerations

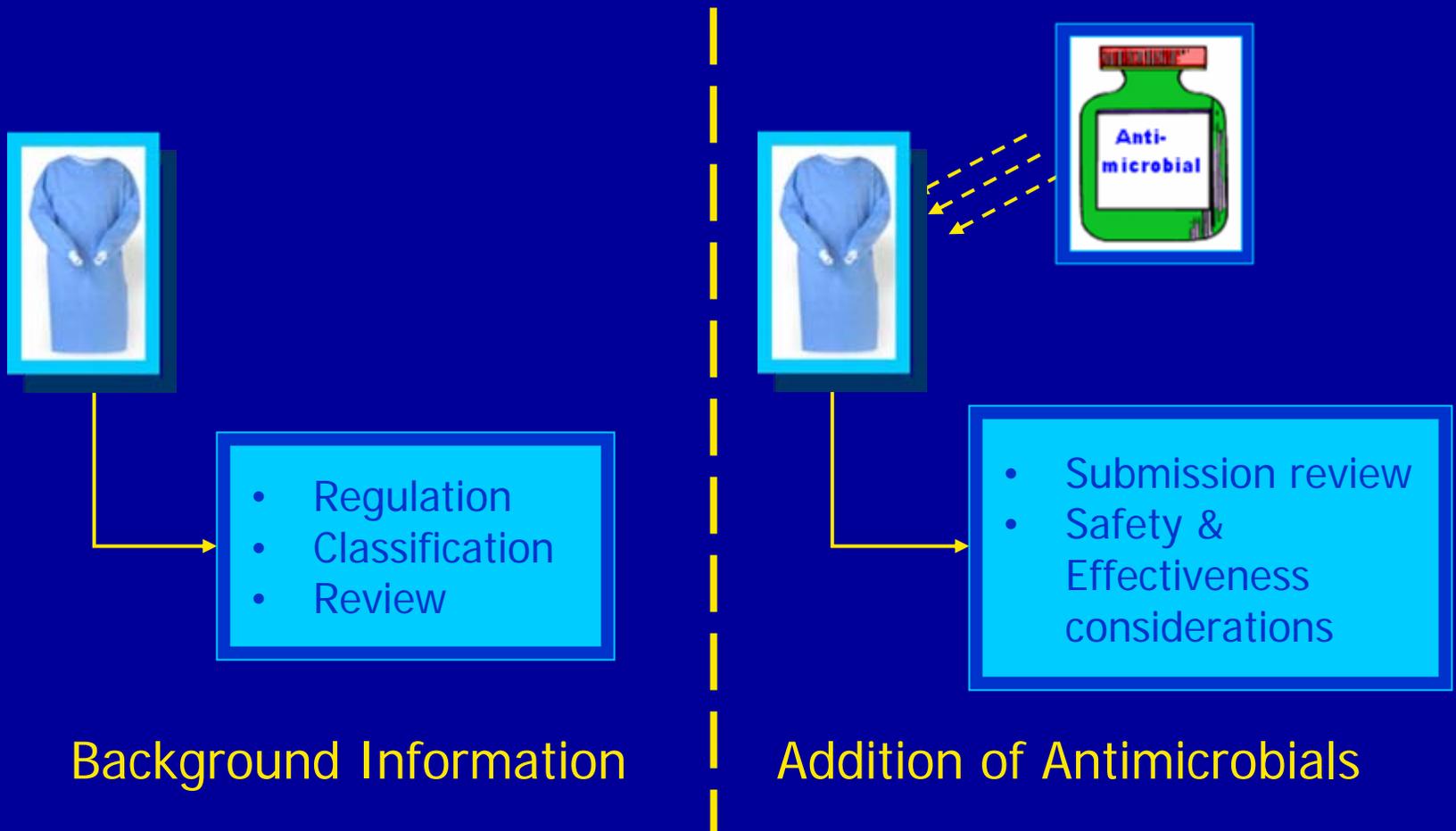
- Antimicrobial Agent: How it affects the Basic Performance Characteristics of the device?
 - Should not compromise the basic barrier integrity



Effectiveness: Performance Testing

- Addition of Antimicrobial Agent: What are the enhanced performance indications?
 - Performance testing should support the new performance indications

Summary: Antimicrobials on Surgical & Isolation Gowns





Antimicrobial Agents On Medical Devices (other than PPE)

FDA Premarket Approaches to Submission Review

DAGID/ ODE/ FDA

Michelle Rios, Microbiologist

Overview

- Current Review Approaches for Medical Devices with Antimicrobial Agents
- Potential Indications for PPE with Antimicrobial Agents
- Issues for Performance Testing for Antimicrobial Agents on PPE
- Summary

Current Review Approach for Medical Devices (other than PPE) with Antimicrobial Agents

- Information on the Antimicrobial Agent
- Information on the Antimicrobial Agent on the Medical Device
- Intended Use/ Indication for Use
- Evaluation of Efficacy of the Antimicrobial Agent

Information on Antimicrobial Agent

- What type of Antimicrobial Agent?
- Has it been previously approved by FDA?
- What is the approved indication?
- What is the effective concentration?

Information on Antimicrobial Agent

- Safety information needed for the antimicrobial agent should address
 - Its use on this device/site
 - How much experience already is available for this agent on devices
 - “leach off/release of agent from the device-should be quantified. If tightly bound, demonstrate this.

Types of Antimicrobial Agents

Cleared/ Approved on Devices

- Systemic Antibiotics (e.g. Minocycline)
- Topical Antimicrobial (e.g. Chlorhexidine)
- Agents (e.g. Silver, Crystal Violet, Amical)

Not Cleared/ Approved on Devices

- Need more information

Information on the Antimicrobial Agent on the Medical Device

- Method of Application to Medical Device
- Location of the Antimicrobial on Device
 - Inside layer
 - Outside layer
 - Imbedded in the device material

Information on Antimicrobial Agent on the Medical Device

- Antimicrobial Agent Characteristics
 - Elution properties – agent release
 - Bound permanently on the device – location of attachment

Intended Use / Indication for Use

- Intended use of the device
- Indication for use of the antimicrobial agent

Intended Use of Medical Device

Intended Use of the Device

Will be dependent on the type of device

Examples:

- Catheters – intravascular, urological, peritoneal, etc
- Implanted devices – surgical mesh, orthopedic fixation, ear tube, heart valve
- Dental – toothbrushes, dental floss, instrument covers
- Wound care products – dressings

Indication for Use of the Antimicrobial Agent on a Device

- Prevents Contamination
- Prevents Colonization
- Prevents or reduces the incidence of infections
- “Preservative” is specific to multiuse products used repeatedly over days and relies on specialized performance testing

Performance Testing Evaluation

There are no recognized standard test methods available to evaluate antimicrobial efficacy on devices since the devices, antimicrobial agents and the indications for the antimicrobial agent vary so widely.

Approaches Used for Evaluation

- Indication for Use is supported with data
- Reflect the environment and site in which the device will be used
- Efficacy testing examines pathogens clinically relevant to the device
- Initial inoculum and inoculum reduction used are clinically relevant
- Efficacy testing uses quantitative assays
- Tests are performed on the “final finished device”

Performance Testing to Support “Prevent Contamination” Indication

- “Contamination” does not refer to a specific “in-use” or clinical state
- Device bioburden often not defined
- Clinical correlation not provided
- Time frame in which “contamination” occurs varies with the device
- Usually supported only by in-vitro testing

Performance Testing to Support “Prevent Colonization” Indication

- “Colonization” - growth of organisms at a site in the absence of signs of infection
- Should be quantified and related to clinical outcomes for devices
 - Example: 25 CFU on an IV catheter tip
- Refers to inserted/implanted devices
- In-vivo testing needed to study colonization in-situ; in-vitro testing also needed

Performance Testing to Support “Prevent Infection” Indication

- “Infection” is a clinical diagnosis
- Its prevention/occurrence needs a clinical trial for evaluation
 - Example: preventing vascular catheter-related infections
- In-vivo and in-vitro studies are also needed to evaluate the safety and likely efficacy of a clinical trial

Potential Indications for Antimicrobial Agents on PPE

From public sources

- “Enhance” protection against infectious microbes
- Prevents microorganisms from penetration or transfer
- Prevents contamination during use

Characteristics of PPE relevant to Evaluation of Added Antimicrobial Agents

- Mostly Single Use and Disposable
- Used for Short Periods of Time
- Do not Directly Cause Device-Related Infections
- Can Passively Transfer Pathogens

Issues for Performance Testing for Antimicrobial Agents on PPE

New challenges for testing to evaluate the efficacy of the antimicrobial agent on the final finished PPE:

- Can device “contamination” be defined for each PPE?
- How will conventional antimicrobial testing be modified to reflect the conditions of use of PPE?
- Should incubation times for antimicrobial efficacy be modified for PPE?
- How should testing address PPE whose antimicrobial agent is not on the surface of the device?

Summary

Currently, the performance testing for Antimicrobial Agents on medical devices (other than PPE) depends on:

- Indication for the Antimicrobial Agent
- Special characteristics of the device with the agent
- How antimicrobial activity testing reflects the conditions in which the device is used

Summary

Antimicrobial Agents on PPE:

The performance testing for Antimicrobial Agents on PPE poses new challenges for testing based on the differences in device characteristics compared to other devices to which antimicrobials have already been added.



Antimicrobials and PPE Devices: Performance Testing and Clinical Implications

Katherine Spooner, MD
CDRH/ODE/DAGID/INCB

May 4, 2007

Overview

- What are the clinically relevant aspects of barrier device PPE performance testing?
- What factors are important in determining testing methods and organisms to be tested?
- How might PPE devices with antimicrobial agents impact health care facilities, providers and patients?

Relevant Aspects of Performance Testing

- FDA believes performance testing should support the indications for use
- How will testing relate to actual clinical use?
 - Consider length of time device used
 - Consider likely pathogens to be encountered
- Consider comparing modified antimicrobial PPE with similar, unmodified control device

Relevant Aspects of Performance Testing

- If terminal sterilization of PPE is performed, FDA would consider the potential effect on the antimicrobial properties of the added agent
- Performance testing on the final, finished pre-shipment product could determine if terminal sterilization has an effect
- FDA believes that antimicrobial testing should support the device as it will be used in practice

Relevant Aspects of Performance Testing

- Shelf-life determination is not usually specified for PPE unless the manufacturer chooses to do so
- If, however, an antimicrobial agent is added, the activity of the antimicrobial over time can be measured
- When antimicrobial activity falls below a critical minimum, this would determine the shelf life of the PPE
- Therefore, FDA believes that the shelf life be determined and that antimicrobial efficacy testing at the end of the shelf life be performed

Antimicrobial Efficacy Testing

- No standardized methods
- FDA suggests quantitative testing methods with quantitative endpoints; i.e., time kill curves
 - Both the inoculum and endpoint should be quantified

Antimicrobial Efficacy Testing

- Inocula of 10^6 is appropriate as it correlates clinically with most infections
- Consider measuring a 4-6 log reduction in inoculum in order to see a significant reduction of organisms beyond the range of error in measurement in antimicrobial activity assays

Antimicrobial Efficacy Testing

- Qualitative Testing
 - Limited value
 - Does not provide a quantitative measurement of the degree of efficacy of an antimicrobial agent
 - Zone of inhibition testing
 - FDA believes that the most appropriate use of zone of inhibition testing is to determine if the antimicrobial agent is “leaching off” the device

Antimicrobial Efficacy Testing

- In clinical practice PPE are used for variable time frames
 - In patient rooms, gloves, isolation gowns and respirators are used for short periods of time; i.e., several minutes to up to an hour
 - In surgical procedures, surgical masks, gowns and gloves may be used for up to several hours
- Therefore, FDA believes that performance testing should evaluate these time frames

Organisms to be Tested

- Historically, antimicrobial indications for devices have been supported by performance testing for bacteria and select fungi
 - Bacteria
 - Activity demonstrated against a reasonable spectrum of bacteria has some predictive value of antimicrobial efficacy against closely related bacterial species
 - Fungi
 - Probably most relevant for respirators; i.e., *Aspergillus sp.*

Organisms to be Tested

- A broad range of clinically relevant pathogens should be considered
- Relevant pathogens may vary by device
- Therefore, FDA believes that testing and indications supported by this performance testing should be device specific

Antiviral Performance Testing

- Not performed on most devices
- Activity against pathogenic viruses is not relevant for many devices, i.e., intravascular catheters
- Historically, FDA has recommended specific viral pathogen testing for indications of antiviral activity
 - The biology of viruses have specific mechanisms considerations that can make broad viral indications problematic

Antiviral Performance Testing

- Considerations for pathogen specific antiviral performance testing are the following:
 - Antiviral agents have limited range of activity
 - Mechanisms of action of antiviral agents tend to be specific and cannot be generalized to a variety of viral pathogens
 - Performance testing results will vary by viral agent tested
- Therefore, very general antiviral indications may not be appropriate

PPE Performance Testing

- Technical aspects of performance testing of N95 respirators/masks:
 - Consider demonstrating a reduction in an aerosol of infectious inoculum in addition to reduction of surface contamination vs. demonstrating reduction of surface contamination alone
 - Consider physical location of antimicrobial agent
 - Respirators typically have several layers of material

Clinical Considerations

- What are the potential clinical benefits of modified PPE?
 - Reduce the passive transfer of microorganisms from one physical location to another
 - Enhance safety for user by improving barrier protection
 - Increased protection of both health care provider and patients

Clinical Considerations

- How can potential benefits be clinically evaluated?
 - Measure rates of colonization
 - Monitor nosocomial infection rates

Clinical Considerations

- What are the potential clinical problems associated with modified PPE?
 - Addition of antimicrobial agents into PPE could change perception of infectious risk for both users and patients
 - Modified devices could provide false sense of security for health care workers
 - This could reduce compliance of other, proven, infection control measures, i.e., hand washing

Clinical Considerations

- How can potential clinical problems be accurately evaluated?
 - Observational studies
 - Handwashing techniques and rates
 - Compliance with use of PPE

Summary

- Performance testing for PPE raises specific issues
- Appropriate performance testing time frames
- Device relevant pathogens should be considered for performance testing
- FDA believes that specific pathogen testing should be performed to support antiviral indications

Summary

- Modified PPE offer potential clinical benefits
- Can clinical benefits be accurately measured and attributed to modified PPE use?
- Is there a possibility that modified PPE will lead to decreased compliance with existing infection control measures?



Antimicrobial Agents on Personal Protective Equipment

Brief Summary of FDA's Presentation

Antimicrobial Agents on Personal Protective Equipment

FDA has reviewed for the Advisory Panel

- The current review process for PPE without antimicrobial agents
- FDA's current thoughts on the evaluation of antimicrobial agents on devices including selected aspects of performance testing
- Potential indications for use for PPE with antimicrobial agents based on public information

Antimicrobial Agents on Personal Protective Equipment

- The Advisory Panel will next hear presentations from Industry and Public Speakers
- The Questions for the Advisory Panel will be repeated for the Panel before your deliberations begin

Questions?

PANEL QUESTIONS

General Hospital and Personal Use Devices Advisory Panel

Antimicrobial Agents on Personal Protective Equipment Summary and Questions for the Advisory Panel

Antimicrobial Agents on Personal Protective Equipment

FDA has reviewed for the Advisory Panel

- The current review process for PPE without antimicrobial agents
- FDA's current thoughts on the evaluation of antimicrobial agents on devices, including selected aspects of antimicrobial performance testing
- Potential indications for use for PPE with antimicrobial agents based on public information

Antimicrobial Agents on Personal Protective Equipment

Now that the Advisory Panel has heard the FDA presentations and the comments from Industry and Public Speakers, FDA asks the Advisory Panel to discuss and comment on the following Questions

Questions for the Advisory Panel

1. Various “Indications for Use” might be sought for PPE incorporating antimicrobial agents.
 - Please discuss what types of indications may be appropriate for PPE with antimicrobial agents.
 - Please describe the meaning of various indications and what types of performance testing should support such indications.

Questions for the Advisory Panel

- What would a “reduces contamination” or a “protects from microbial contamination” indication mean for PPE with added antimicrobial agents?
- How might performance for such an indication for use be evaluated?

Questions for the Advisory Panel

- What might a “reduces colonization” indication mean for PPE which can become contaminated during use but are promptly discarded after use?
- How should such an indication be supported?

Questions for the Advisory Panel

2. For each of the following types of PPE with added antimicrobial agents, please discuss what time frame would be appropriate for demonstrating antimicrobial efficacy in order to:
 - Kill/inhibit microbes
 - Reduce the risk of transferring microbes from one site to another

Questions for the Advisory Panel

- Medical Gloves
 - Examination Gloves
 - Surgeons' Gloves
- Surgical Masks
- Surgical N95 Respirators
- Medical Gowns
 - Surgical Gowns
 - Isolation Gowns

Questions for the Advisory Panel

4. For surgical masks or surgical N95 respirators with antimicrobial agents, please comment on whether performance testing should be expected to support:
 - Significant reduction of an aerosol of an infectious inoculum compared to a control device
 - Simply demonstrate an ability to kill microbes on the surface of the device

Questions for the Advisory Panel

- As surgical masks and surgical N95 respirators conventionally have at least 3 layers, the middle layer serving as the “filter” for the device, please also discuss whether the location of the antimicrobial agent on the device should determine, in part at least, the type of performance testing needed?

Questions for the Advisory Panel

4. For antimicrobial agents added to surgical masks and N95 respirators, please discuss the safety issues for the device wearer and how these might be evaluated, including but not limited to:
- Effects on the oral, nasal or ocular mucosa
 - Effects on the lower respiratory tract

Questions for the Advisory Panel

5. For antimicrobial agents added to PPE, especially medical gloves, please discuss the safety issues or risks for patients exposed to these devices.
 - Should the potential for leach off or physical detachment of the antimicrobial agent from PPE into body sites or onto objects be evaluated?

Questions for the Advisory Panel

In your discussion, please comment on whether your concerns about such exposure are increased for pediatric and neonatal patients.

Questions for the Advisory Panel

6. Please discuss whether there is a reasonable possibility that the presence of an “antimicrobial agent” on PPE might lead the PPE wearer to be less likely to follow correct infection control procedures or proper techniques. If such a risk seems possible, what steps could be taken, including product labeling, to help reduce such a risk?

Thank You

