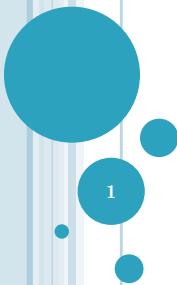


UPDATE ON ANTIBACTERIAL WASHES AND RUBS



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Rhonda Jones, RM(NRM)

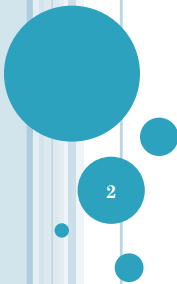
President

Scientific & Regulatory Consultants, Inc.

October 17, 2017



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OTC antiseptics

are at

risk

in all markets!

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AGENDA

- ❖ **Background**
- ❖ **OTC Monographs:**
 - **Consumer Antibacterial Washes**
 - **Consumer Antibacterial Rubs**
 - **Healthcare Antibacterial Washes/Rubs**
 - **Foodhandler Antibacterial Washes/Rubs**
- ❖ **Current Reality**

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BACKGROUND



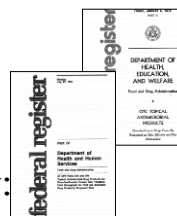
Description	OTC (Over-the-Counter)	NDA (New Drug Application)
FDA Premarket Approval	None	Required (2->3yrs)
FDA Fee for Service	None	\$2,038,100 (2017)
FDA Listing	Required (\$0)	Required (\$0)
Active Ingredient/Level	Monograph List	Open
Safety Testing	Historically None/Minimal	Extensive
Efficacy Testing	Historically Minimal	Extensive
Labeling	FDA Requirements	FDA Requirements
Manufacturing	FDA Requirements	FDA Requirements

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BACKGROUND

❖ Tentative Final Monograph History:

- 1978: Topical Antiseptic Products
- 1991: First Aid Antiseptics
- 1994: Healthcare Antiseptics



❖ 2013 NRDC-FDA Consent Decree

➤ *Paradigm Change:*

- Court ordered timeline to complete monographs
- FDA elects to requalify Active Ingredients (AI)
 - GRAS = Generally Recognized as Safe
 - GRAE = Generally Recognized as Effective
 - Prior GRAS/E (Category I) AI status have been rescinded

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BACKGROUND



❖ FDA Process:

- FR Proposed Rule ➡ Public Comment ➡ Final Rule on Actives
- Approx. 33 month process
- Select AI deferrals have been granted - renewed annually
- Draft monographs for end products, if any AI remain in a given category

▪ FDA Data Request:

- Efficacy
- Safety
 - MuST (Maximal Use Systemic Absorption Study)
 - Hormonal Effects
 - Antibacterial Resistance

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BACKGROUND

- ❖ **Consumer** – used by General population in homes, institutions, or public settings (e.g. homes, offices, hotels, planes)
- ❖ **Healthcare** – used by Healthcare professionals in a hospital or other healthcare situation/setting
- ❖ **Foodhandler** – used by Foodhandler professionals or food manufacturer's on the job
- ❖ **Wash** – Intended for use with water and rinsed off after use (hand and body wash);
 - ❖ May be liquid, foam, gel, leaflets, bar, etc.
- ❖ **Rub** – Intended for use without water or rinsing
 - ❖ “leave-on”, hand sanitizer, hand rub
 - ❖ May be liquid, foam, gel, wipe, towelette, etc.

Germ Farm



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BACKGROUND

- ❖ **Monograph Categories:**
 - ❖ Consumer Antibacterial Washes
 - ❖ Consumer Antibacterial Rubs
 - ❖ Healthcare Antibacterial Washes/Rubs
 - ❖ Foodhandler Antibacterial Washes/Rubs



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CONSUMER ANTIBACTERIAL WASHES



- Intended for use with water by general population in home or public settings on a frequent or daily basis
 - Hand and Body washes

- Monograph Status:

- Dec 2013 Proposed Rule
- Sept 2016 Final (AI) Rule
- Sept 2017 **Now in Effect!**



- FDA:

"Retailers should not sell these products because any OTC consumer antiseptic wash drug product containing an ingredient covered in the final rule cannot lawfully be introduced or delivered for introduction into interstate commerce unless it is the subject of an approved new drug application."

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https://www.fda.gov/drugs/developmentapprovalprocess/developmentresources/over-the-counterotdrugs/statusofotcrulemakings/ucm070821.htm#Consumer_Antiseptic

CONSUMER ANTIBACTERIAL WASHES



- Antiseptic products **no longer allowed to be marketed OTC:**
 - Triclosan, Triclocarban, Povidone-iodine, Cloflucarban, Fluorosalan, Hexachlorophene, Hexylresorcinol, multiple Iodine complexes, Methylbenzethonium chloride, Phenol, Secondary amylicresols, Sodium oxychlorosene, Tribromsalan, Triple dye
- Action Deferred until March 2018:
 - Chloroxylenol
 - Benzalkonium chloride
 - Benzethonium chloride

- Status report due in January each year
- FDA publishes decision to continue deferral annually in March

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[https://www.regulations.gov/docket?D=FDA-1975-N-0012;](https://www.regulations.gov/docket?D=FDA-1975-N-0012)
<https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm538131.htm>

CONSUMER ANTIBACTERIAL WASHES



- Data gaps:

- Safety

TABLE 6—SAFETY STUDIES AVAILABLE FOR CONSUMER ANTISEPTIC WASH ACTIVE INGREDIENTS¹

Active ingredient	Human pharmacokinetic (MUsT)	Animal pharmacokinetic (ADME)	Oral carcinogenicity	Dermal carcinogenicity	Reproductive toxicity (DART)	Potential hormonal effects	Resistance potential
Benzalkonium chloride			✓				✓
Benzethonium chloride		✓		✓	✓		✓
Chloroxylenol	✓				✓		✓

- Efficacy

- Requiring disease reduction studies – Protocols must be designed:
 - Staph/MRSA Family Intervention
 - E. coli Foodborne Illness Intervention

- Support Groups:

- American Cleaning Institute (ACI) Submission Plan:
 - Efficacy 2024
 - Safety >2018-2022
 - Expect FDA final decision no sooner than 2025 unless suppliers pull support or insufficient action occurs

CONSUMER ANTIBACTERIAL RUBS



- Use without water by general population in home or public settings on a frequent or daily basis

- Status

- June 2016 Proposed Rule
Comment period closed 2016
 - April 2019 Final (AI) Rule
 - April 2020 Effective Date



- Expect FDA to remove products by April 2020** if they contain:

- Benzethonium chloride, Chloroxylenol, Triclosan, Triclocarban, Cloflucarban, Fluorosalan, Hexachlorophene, Hexylresorcinol, multiple Iodine complexes, Methylbenzethonium chloride, Phenol, Secondary amyltricsresols, Sodium oxychlorosene, Tribromsalan, Triple dye

https://www.fda.gov/drugs/developmentapprovalprocess/developmentresources/over-the-counterotdrugs/statusofotcrulemakings/ucm070821.htm#Consumer_Antiseptic

CONSUMER ANTIBACTERIAL RUBS



- *Expect* FDA to defer the following in the 2019 Rule:
 - 60-95% Ethanol
 - 70-91.3% Isopropyl Alcohol (*Industry proposed 60-61.3%*)
 - Benzalkonium chloride
 - Povidone-iodine (*Industry request Mar 2017*)
- Support Groups:
 - ACI Submission Plan for Ethanol & BZK:
 - Efficacy 2019-2021
 - Safety \geq 2018
 - Expect FDA final decision (unless suppliers pull support or insufficient action occurs)
 - Ethanol: 2020-2021
 - Benzalkonium: No sooner than 2022
 - Povidone-iodine
 - IPA

<https://www.regulations.gov/docket?D=FDA-1975-N-0012>

CONSUMER ANTIBACTERIAL RUBS



- Data gaps:
 - Safety:

Table 6--Safety Studies Available for Consumer Antiseptic Hand Rub Active Ingredients¹

Active Ingredient	Human Pharmacokinetic (MUsT)	Animal Pharmacokinetic (ADME)	Oral Carcinogenicity	Dermal Carcinogenicity	Reproductive Toxicity (DART)	Potential Hormonal Effects	Resistance Potential
Alcohol	◦	•	•	•	•	•	•
Benzalkonium chloride		◦	•		•	•	◦
Isopropyl alcohol	◦	◦		◦	•	◦	•

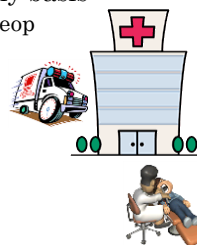
¹ Empty cell indicates no data available; "◦" indicates incomplete data available; "•" indicates available data are sufficient to make a GRAS/GRAE determination.

- Efficacy:
 - No disease reduction study required
 - ASTM studies:
 - MIC/MBC: 900 strains
 - Time Kill: 99.9% reduction in 18 strains
 - ASTM *In vivo* (E1174 or E2755):
 - Meet FDA statistics/control/vehicle requirements
 - 2.5LR after a single application

HEALTHCARE ANTIBACTERIAL WASH/RUBS



- Use with/without water by healthcare professionals in a hospital or other healthcare situation on a frequent or daily basis
 - Healthcare Personnel Handwash, surgical scrub, Preop
- Status
 - April 2015 Proposed Rule
 Comment period closed 2016
 - Jan 2018 Final (AI) Rule
 - Jan 2019 Effective Date
- Expect FDA to remove products by **Jan 2019** if they contain:
 - Triclosan, Triclocarban, Cloflucarban, Fluorosalan, Hexachlorophene, Hexylresorcinol, multiple Iodine complexes, Methylbenzethonium chloride, Phenol, Secondary amyltricsresols, Sodium oxychlorosene, Tribromsalan, Triple dye



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https://www.fda.gov/drugs/developmentapprovalprocess/developmentresources/over-the-counterdrugs/statusofotcrulemakings/ucm070821.htm#Healthcare_Antiseptic

HEALTHCARE ANTIBACTERIAL WASH/RUBS



- Expect/Action Deferred until Jan-Mar 2018:
 - **Rub:**
 - 70-91.3% Isopropyl Alcohol (Expected?)
 - 60-95% Ethanol (March 2018)
 - Benzalkonium chloride (March 2018)
 - **Support Groups:**
 - *ACI Plan (Ethanol/BZK)* : Eff. 2019-21; Safety \geq 2018 \rightarrow FDA Decision \geq 2022
 - IPA Preop – Medtronic
 - Ethanol – DFB Technology Limited
 - **Wash:**
 - Benzalkonium chloride (March 2018)
 - Benzethonium chloride (March 2018)
 - Povidone iodine (March 2018)
 - Chloroxymenol (PCMX) (March 2018)
 - **Support Groups:**
 - *ACI Plan*: Eff. 2019; Safety >2018-2022 FDA Decision \geq 2022
 \rightarrow

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<https://www.regulations.gov/docket?D=FDA-1975-N-0012>



HEALTHCARE ANTIBACTERIAL WASH/RUBS

- **Data gaps:**

- **Safety:**

TABLE 10—SAFETY STUDIES AVAILABLE FOR HEALTH CARE ANTISEPTIC ACTIVE INGREDIENTS¹

Active ingredient ^a	Human pharmacokinetic (MUST)	Animal pharmacokinetic (ADME)	Oral carcinogenicity	Dermal carcinogenicity	Reproductive toxicity (DART)	Potential hormonal effects	Resistance potential
Alcohol	○	●	●	●	●	●	●
Benzalkonium chloride	○	○	○	○	○	○	○
Benzethonium chloride	○	○	○	○	○	○	○
Chloroxlenol	○	○	○	○	○	○	○
Povidone-iodine	4○	4●	4○	4●	4○	4○	4○
Isopropyl alcohol	○	○	○	○	○	○	○

- **Efficacy:**

- No disease reduction study required
 - ASTM studies:
 - MIC/MBC: 1200 strains
 - Time Kill: 99.9% reduction in 24 strains
 - ASTM *In vivo* (E1174, E 2755, E1115, E1173):
 - Meet FDA statistics/control/vehicle requirements
 - HCPHW: 2.5LR after a single application in 5mins;
 - **Surgical Scrub:** 2LR in 1min; No baseline increase at 6hrs
 - **Preop Prep:** 2LR dry and 3LR wet site in 30sec; No baseline increase at 6hr



FOODHANDLER ANTIBACTERIAL WASH/RUB

- Use with or without water by food professionals in institutional/industrial settings on a frequent or daily basis
 - Private homes for family consumption are not included
- **Status:**
 - Await Proposed Rule
 - Consent Decree does not cover this use
 - Expect FDA to take similar approach
 - Will suppliers support AI beyond those already discussed?



CURRENT REALITY



- ❖ What are you doing to prepare?
 - ❖ Review your Product line:
 - ❖ Sort products into monograph categories
 - ❖ If AI are not being supported.....
 - ❖ Prepare to leave the market
 - ❖ Consider reformulation
 - ❖ File an NDA
 - ❖ Consider relabeling
 - ❖ If AI are supported....
 - ❖ Monitor to assure ongoing support
 - ❖ Compare current efficacy data to new criteria
 - ❖ Beware extensive testing on end products as testing/ criteria may still change
 - ❖ Review your Market:
 - ❖ Look for opportunities created by discontinuations

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CURRENT REALITY - SUMMARY

- ❖ OTC antiseptics are at *risk* in all markets!
- ❖ FDA will ban active ingredients if not supported by acceptable safety and efficacy data
- ❖ Will end formulations pass future efficacy and safety criteria?
- ❖ Market Disruption may create opportunities!

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NEXT WEBINAR: OCT. 24 @ 11 A.M.

- CA Prop 65 Revisions and CA Safer Consumer Products Regulations
 - Revisions to Prop 65 Warning Requirements
 - Safer Consumer Products Regulations
 - Implications for commercial, institutional cleaning products
- Presenters
 - Gary Whitmyre, Senior Director of Exposure and Risk Assessment, toXcel
 - Jon Benjamin, Partner, Farella Braun + Martel
- www.issa.com

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THANK YOU FOR ATTENDING!

QUESTIONS?

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