A Review of Reported Recalls Involving Microbiological Control 2004-2011 with Emphasis on FDA Considerations of "Objectionable Organisms"

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Abstract

An analysis was conducted of 642 microbiologically-related recalls over the years 2004-2011. This analysis was conducted using publically available enforcement reports as presented on the US FDA website. The microbiologically-related recall activity shows a decided increase in recent years. Most of the reported recalls involved sterile products, and of these medical devices accounted for the majority. The reasons given for sterile product recalls were varied, but the majority cited "Lack of Sterility Assurance" with sterile packaging clearly identified as the main culprit.

There was significant information in the recall data for non-sterile products as well. The majority of the recalls came from OTC and personal care products, with "Objectionable Organisms" as the most prevalent reason for recall by a wide margin. These recalls are further analyzed to provide indication of the FDA policy on what is an objectionable organism, along with a review of current regulatory guidance. Finally, recommendations are presented in determining an "Absence of Objectionable Organism" policy for a manufacturer.

Introduction

In a previous report, one of the authors presented information on recalls in the US market that had a microbial basis [1]. A review of enforcement activity is important, as in addition to the Agency's written policy on GMP there is a great deal of "corporate culture" to CGMP that is not written in official guidance documents but is nonetheless strictly enforced. By studying enforcement patterns we can deduce policy.

This report is an update on this topic, covering the years 2004 - 2011, with particular attention paid to non-sterile recalls. There will be some discussion of the sometimes confusing concept of "objectionable organisms" and what the analysis of product recalls can teach on this subject.

A note on the methodology used in this study is important. The source information is listed on the FDA web site, listing recalls by "Enforcement Reports." These enforcement reports, while a valuable source of information, do have several limitations. First of all, the recalls are listed (on the Enforcement Report) by Recall Identification Number. This recall may include one batch, or several hundred batches. A single recall may also cover many different, but related products (and multiple batches of

each product). The reader is urged to avoid the mistake of confusing the number of recalls with the eventual impact of that number on a particular company or on the industry. Secondly, there seems to be a significant and variable period of time between the actual event (the recall) and the appearance of the recall in the enforcement report. Therefore the dates of the enforcement reports should be viewed only as identification of the report, not necessarily as dates of recalls. For the purposes of this article we will, however, refer to the date of the enforcement report and the date of the recall interchangeable for simplicity's sake.

The Enforcement Report lists several different categories of recalls. This review does not consider the differences among class 1, class 2 and class 3 recalls (refer to 21 CFR 7.41). The Enforcement Report format also catalogs the recalls by product type. With some slight variability over the years, the main product categories used in the Enforcement Reports include:

- Food (including personal care products)
- Drugs (OTC and prescription)
- Biologics
- Devices
- Veterinary

This review focuses on personal care products, drugs (pharmaceutical and OTC), and medical devices. The category of Biologics recalls was deliberately omitted despite its obvious interest to the readership because of the extraordinarily large number of recalls in virtually all weekly Enforcement Reports dealing with irregularities in the blood supply. Inclusion of this data would skew the results for the entire review.

Overview

The years 2004-2011 saw 642 recalls that involved a microbiological component, with a clear increase evident in 2010 and 2011 (Figure 1). This increase in microbiologically-related recalls reflects an increase in overall enforcement activity by FDA. In fact, 2009 might have also shown an increase in overall recalls however but the Agency was consumed by enforcement activities involving peanuts and pistachios. The evident dip in enforcement activity in 2009 for microbiologically-related issued might be due to a limitation of resources within the Agency.

Figure 1. Microbiologically-related Recalls by Year. Total number of microbiologically-related recalls as described in FDA weekly enforcement reports for the product categories included.

As we look deeper into the microbiologically-related recalls we can see some distinct preferences in terms of types of products involved in these situations (Figure 2). Most of these recalls involve Medical Devices, followed by Pharma and OTC products. Dietary Supplements and Probiotics are the least, but this may be an artifact of the recent implementation of 21 CFR111, and the fact that with all the enforcement opportunities offered by the dietary supplements industry microbiological concerns are relatively low on the list.

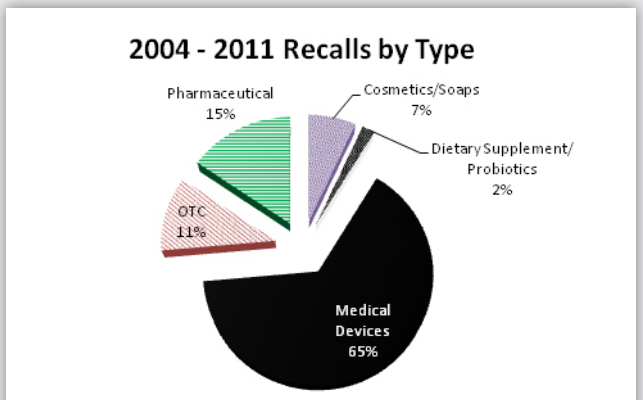

Figure 2. Microbiologically-related Recalls by Product Category. The authors determined the type of finished product involved in the microbiologically-related recall. Much of this information was supplied in the Enforcement Report (Food/Cosmetics, Drugs, Medical Device) and the authors used this information to assign these categories.

Sterile Product Recalls

If we look at the data from a different perspective we can evaluate FDA concerns for Sterile vs Non-sterile products. Over ¾ of the recalls during the years 2004-2011 involved sterile products (Figure 3). Of these sterile product recalls, approximately 80% were due to "Lack of Sterility Assurance" (Figure 4) with remaining due to "microbial contamination", a failed finish product test (BET or antimicrobial efficacy), or was an issue with a diagnostic test (usually involving media or microbial ID kits) (Figure 5). The finding "Lack of Sterility Assurance" is frequently discussed at conferences and in publications, it is useful to look at what this really means from the perspective of enforcement activities.

Looking at the underlying causes of "Lack of Sterility Assurance" we can see that most of them are the result of packaging concerns (incomplete or weak seals, pinpricks in the sterile barrier, transport issues, etc). Of the remainder, almost all are either undetermined GMP issues or frank manufacturing errors (incomplete sterilization, non-sterile components added to sterile products, etc). Relatively few of these "Lack of Sterility

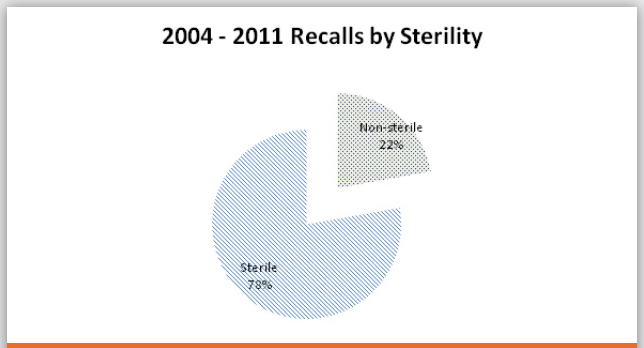

Figure 3. Microbiologically-related Recalls by Product Sterility. Distribution of the included recalls based on the required state of sterility for the finished product.

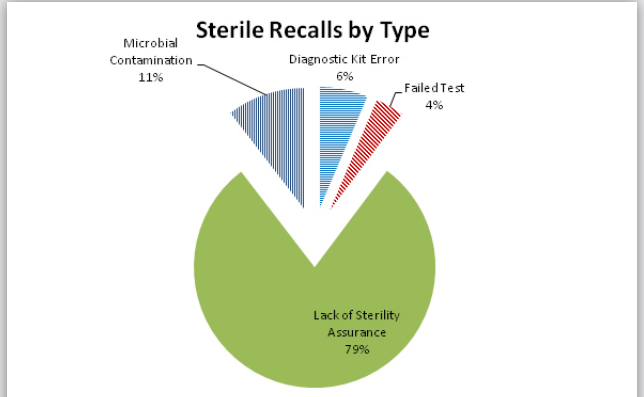

Figure 4. Microbiologically-related Recalls of Sterile Products by Recall Category. One of five recall categories were assigned to the product recalls for sterile products. Recalls for "microbial contamination" may or may not have a contaminating microorganism identified; "Failed test" is either a failed sterility test, a failed antimicrobial preservative effectiveness test or bacterial endotoxin test (BET) associated with the recall; "Diagnostic kit error" is a broad category which includes media issues, biological indicator issues and microbial identification kit issues (as well as others). Finally a recall would be placed in the "Lack of sterility assurance" if this is the cited reason on the enforcement report, or if the cited reason mentions product sterility but the recall (of the sterile product) does not fit into any other category.

Assurance" recalls actually showed contamination. It is more common to issue the recall on the basis of "contaminated product" (see Figure 4) rather than cite "Lack of..." for these situations. From this, it seems apparent that "Lack of Sterility Assurance" means either that there is a potential problem with the product or packages, or that the manufacturer cannot document that the product was manufactured and sterilized in a state of control. If the product is obviously contaminated, that is the cited reason for the recall (in the vast majority of cases).

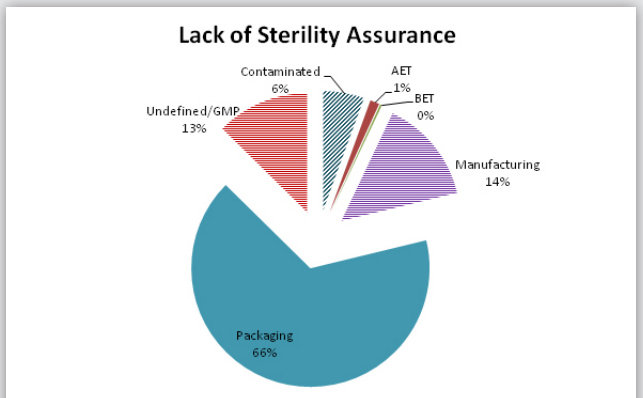

Figure 5. Underlying reason for "Lack of Sterility Assurance" citation in recalls. Those sterile product recalls were examined to determine the basis for a recall reason involving "Lack of Sterility Assurance." Most were packing issues (pinpricks, defective seals, damage to the sterile barrier during transport, etc).

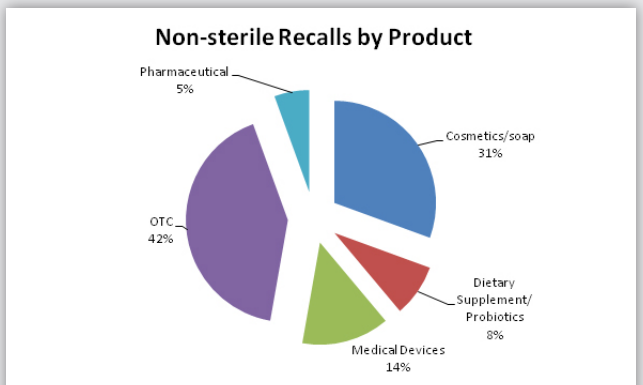

Figure 6. Non-Sterile Recalls by Product Type. Non-sterile product recalls were most commonly either OTC or personal care products.

Non-sterile Product Recalls

An area of particular interest to the authors is the regulation of non-sterile medications. Looking at the enforcement reports for the non-sterile products, approximately ¾ of the recalls are due to either OTC products or personal care products during this period (Figure 6). The reasons for the non-sterile recalls are presented in Figure 7.

Figure 7 draws our attention to the topic of Objectionable Organisms. The issues facing non-sterile manufacturers are peculiar in that the finished product is intended to be contaminated (non-sterile). The challenge is to manufacture a non-sterile finished dosage form that does not have too high a level of contamination, and is not contaminated with the wrong type of organisms (objectionable ones). The Code of Federal Regulations provides some guidance:

- 21 CFR 211.84(d)(6) "Each lot of a component, drug product container, or closure with potential for microbiological contamination that is objectionable in view of its intended use shall be subjected to microbiological tests before use."

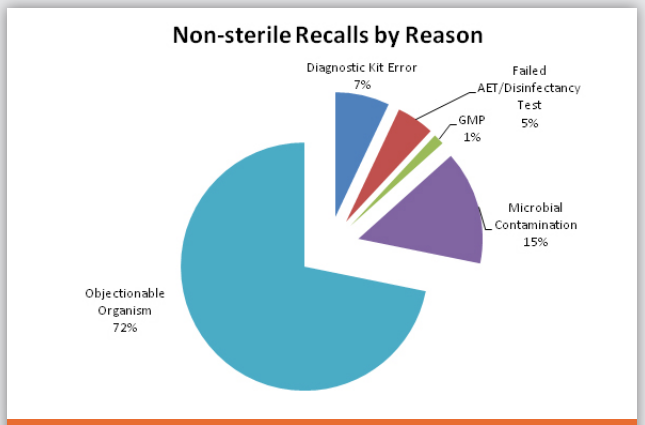

Figure 7. Non-sterile Product Recalls by Reason.

- 21 CFR 211.113(a) "Appropriate written procedures, designed to prevent objectionable microorganisms in drug products not required to be sterile, shall be established and followed."
- 21 CFR 211.165(b) "There shall be appropriate laboratory testing, as necessary, of each batch of drug product required to be free of objectionable microorganisms."

However, it must be noted that this does nothing to help determine what an objectionable organism might be.

Further guidance is provided by USP in the harmonized informational chapter <1111> [2]. It must be noted that the compendial Microbial Limits Tests are not intended to serve as a test for objectionable organisms [3] nor were they ever intended to do so [4,5].

Bringing this academic discussion into the real world, FDA has a solid track record of enforcing the requirement for absence of objectionable organisms in raw materials and finial, non-sterile products. In the previous review of recalls from 1998 through 2006 [1] 134 recalls listed on the FDA website for this time period were identified. Of these, only 14 were due to organisms listed in the Microbial Limits Tests - the others were "objectionable" but not "specified." In this review, 144 recalls were identified for non-sterile products, only 8 of these recalls cite organisms listed in USP <62>.

However, returning to USP chapter <1111> we read:

"In addition to the microorganisms listed in Table I, the significance of other microorganisms recovered should be evaluated in terms of the following:

- The use of the product: hazard varies according to the route of administration (eye, nose, respiratory tract).
- The nature of the product: Does the product support growth?
- Does it have adequate antimicrobial preservation?
- The method of application.
- The intended recipient: risk may differ for neonates, infants, the debilitated.
- Use of immunosuppressive agents, corticosteroids.
- The presence of disease, wounds, organ damage.

Where warranted, a risk-based assessment of the relevant factors is conducted by personnel with specialized training in microbiology and in the interpretation of microbiological data. For raw materials, the assessment takes account of the processing to which the product is subjected, the current technology of testing, and the availability of materials of the desired quality."

This compendial guidance provides the basis for an evaluation of potentially objectionable organisms by a competent, trained, professional microbiologist. It should also be noted that a risk assessment approach is encouraged. The first consideration should be total numbers of microorganisms present. An unfortunate fashion has arisen that argues immunocompromised patients are at increased risk for oral drugs, such that extremely tight total aerobic counts (10 CFU/G for tablets) must be established for the specification [6]. This argument completely ignores the fact that these same patients may each a pound of food a day (10^5-10^7 cfu/g, or $5x10^7$-$5x10^9$ cfu/lb) without harm. It is important to have total bioburden limits set, but they must be defensible. The true concern with high levels of bioburden would be that they may well indicate a manufacturing process out of control, or that a spoilage organism is proliferating in your product. If the numbers of organisms in the product are not large, the question remains to determine if those organisms present are "objectionable".

The two methods currently in use to determine objectionable organisms both use some form of risk analysis. The first is to determine all organisms (or families) that might cause a problem (using science, regulatory policy or both). The basic goal here is to form a list of "objectionables" – if the organism is not on the list, it is defined as acceptable. The problem with this approach is that if a new organism arises that was not initially considered, or that the inspector feels is objectionable that your list failed to include, there may be several batches of product placed at risk.

The second approach to determination of the absence of objectionable organisms is to analyze all microbial isolates found and determine if they fit a criteria for "objectionable." The difficulty with this method is that it is extremely labor intensive. Perhaps a blending of the two would be most productive, with organisms categorized as either "objectionable" or "benign" based on the product presentation and target population. The placement of the organism into either category would require research, but this research would then be retained for future use.

Table 1 provides a summary of recalls, with information on the product involved, Recall Category and Specific Reasons for the recall (both deduced by the authors), the date of the enforcement report and a reproduction of the reason cited by FDA in the enforcement report. Based on the review of recalls, both numbers of organisms and the objectionable nature of some organisms have been responsible for FDA participation in "voluntary" (voluntary in the sense that the company accedes to the FDA recommendation) as well as enforced recalls. Of the 142 non-sterile recalls during the period 2004-2011 listed in Table 1, 103 were for objectionables and 22 for "microbial contamination" (Figure 7). As might be expected, the breakdown of the organism types is as follows:

Table 1. Non-sterile Recall Summary 2004-2011

Product	Recall Category	Specific Reason	Date	Reason (as described in Enforcement Report)
Biological Indicators	Diagnostic Kit Error	Diagnostic Kit Error	1/21/2004	The XXXXX Biological Indicators of ETO sterilization contain a microbiological contaminant which can affect the performance of the positive control and the indicators to some limited extent. The color on a positive control may revert to negative after 24 hours of incubation.
Aloe vera lotion, in 2 oz. containers, packaged as part of various hospital and amenity kits.	Objectionable Organism	Burkholderia cepacia	2/11/2004	Lotion may be contaminated with the organism Burkholderia cepacia.
Medicated hand wash	Objectionable Organism	Pseudomona spinosa	4/7/2004	Microbial Contamination: Medicated handwash may be contaminated with Pseudomonas spinosa
XXX Dietary Supplement Tablets	Objectionable Organism	Mold	5/19/2004	XXX Tablets are contaminated with mold.
Antiseptic mouthwash	Objectionable Organism	Fungal	6/16/2004	Microbial contamination (yeast and mold)
XXX Natural Sinus Relief	Objectionable Organism	Mold	7/28/2004	Microbial Contamination; product contains mold and yeast.
12 Hour Nasal Spray	Objectionable Organism	Burkholderia cepacia	8/4/2004	Microbial contamination; Burkholderia cepacia.
Baby Lotion	Objectionable Organism	Burkholderia cepacia	9/1/2004	Private lab analysis detected Burkholderia cepacia in the product.
Acne cream	microbial contamination	Unidentified Bacteria	9/8/2004	Bacterial contamination.
XXXX brand Sheer Blonde Curvaceous Blonde Curl-Defining Styler, Curls Swirls Brightens Blond Hair	Objectionable Organism	Burkholderia cepacia	9/15/2004	The product may be contaminated with Burkholderia cepacia.
XXXXX SLS-1 Sublingual System	Objectionable Organism	Burkholderia cepacia	9/15/2004	The product is contaminated with Burkholderia cepacia (formally known as Pseudomonas cepacia), based on the Texas Health Department analysis and also firm's analysis.
Multiple Kits containing Baby Lotion	Objectionable Organism	Burkholderia cepacia	10/13/2004	Lotion may be contaminated with Burkholderia cepacia
Purified Water (Distilled Water) USP	Objectionable Organism	Burkholderia cepacia	10/20/2004	Microbial contamination; Burkholderia cepacia.
Gram Crystal Violet	Diagnostic Kit Error	Reagent QC	10/27/2004	Reagent for microbiological testing may cause inconsistent staining characteristics and subsequent misidentification of bacteria in patient samples.
Multiple Water Products	Objectionable Organism	Burkholderia cepacia	10/27/2004	Microbial contamination; Burkholderia cepacia.
XXXX, Frizz Ease 5-Minute Manager Blow Dryer Styling Spray	Objectionable Organism	Yeast and Mold	12/22/2004	Product is contaminated with yeast and mold.
12 Hour Nasal spray	Objectionable Organism	Burkholderia cepacia	12/22/2004	Microbial Contamination; Burkholderia cepacia.
XXXXX Oral Suspension (megestrol acetate)	Objectionable Organism	Fungal	2/23/2005	Product contains microbial contamination; mold and yeast
Tattoo Ink: XXXX brand Black Magic Color	Objectionable Organism	Acremonium mold and P. aeruginosa	3/23/2005	The product is contaminated with Acremonium mold and Pseudomonas aeruginosa.
Multiple Lotions and oils	Objectionable Organism	Burkholderia cepacia	3/23/2005	Lotions and oils are contaminated with Burkholderia cepacia, and fungus respectively.
Extra Strength Antigas plus Antiacid	Objectionable Organism	Staphylococcus aureus	5/4/2005	Microbial test specification failure; (Staphylococcus aureus).
XXXX oral swabsticks	Objectionable Organism	Aspergillus and Penicillium	5/18/2005	Contaminated with Aspergillus and Penicillum molds.
Lubricating Skin Lotion	Objectionable Organism	Enterobacter cloacae	6/1/2005	One lot of Original Lubricating Skin Lotion was tested and found to be contaminated with Enterobacter cloacae.
Tablets	Objectionable Organism	Mold	7/20/2005	Mold growth on PRODUCT
Disinfectant sprays	Failed Disinfectant Efficacy	Failed Disinfectant Efficacy	8/31/2005	Failed EPA required efficacy testing; may not perform as intended.
Furosemide Tablets	Objectionable Organism	Mold	9/28/2005	Mold Growth was found on tablets.
Baby Wipes	Objectionable Organism	Mold	10/5/2005	Products are contaminated with mold.
Self Contained Biological Indicator	Diagnostic Kit Error	D-value	11/30/2005	The certified Ethylene Oxide D-values of the lots cannot be confirmed to be within specification.
Aspirin & Ibuprofin Tablets	microbial contamination	Unidentified Bacteria	11/30/2005	Microbial contamination of a non-sterile product.
XXXXX Liquid,a Pyrantel Pamoate	Failed AET	AET Failure	12/7/2005	USP Antimicrobial Effectiveness Failure (12 month stability)
Retin-A Cream	microbial contamination	Unidentified Bacteria	12/7/2005	Microbial Contamination
Glutaraldehyde Sterilizing & Disinfecting Solution	Failed Disinfectant Efficacy	Failed Disinfectant Efficacy	12/14/2005	The product, XXXXXX, a reusable sterilizing and disinfecting solution, is likely to be ineffective for its intended use because testing found it failed testing for sporicidal use.
XXX Grape Suspension	microbial contamination	Unidentified Bacteria	12/21/2005	Product intended for destruction due to microbial contamination was possibly diverted to retail stores.
Dishwashing Liquid Antibacterial hand soap	Objectionable Organism	Pseudomonas aeruginosa	12/28/2005	Microbial contamination: Contaminated with the bacteria Pseudomonas aeruginosa.
Calcium Carbonate Gelcaps	Objectionable Organism	Pseudomonas aeruginosa	2/8/2006	Microbial Contamination: product intended for destruction due to Pseudonomas aeruginosa found in water port was possibly diverted to retail stores.

Table 1. Non-sterile Recall Summary 2004-2011 (cont.)				
Product	**Recall Category**	**Specific Reason**	**Date**	**Reason (as described in Enforcement Report)**
Teethers	Objectionable Organism	Pseudomonas spp.	2/15/2006	Liquid filled infant teething ring contaminated with Pseudomonas aeruginosa and Pseudomonas putida.
Shampoo caps	Objectionable Organism	Serratia marcescens	2/22/2006	Shampoo caps may be contaminated with Serratia marcescens.
Furosemide Tablets	Objectionable Organism	Mold	2/22/2006	Mold Growth
Alcohol-Free Mouthwash	Objectionable Organism	Burkholderia cepacia	3/29/2006	Alcohol-free mouthwash is contaminated with Burkholderia cepacia and is associated with an illness outbreak.
XXXXXX Personal Hygiene Hospital Admission Kits	Objectionable Organism	Burkholderia cepacia	3/29/2006	The kits contain XXX Alcohol-Free Mouthwash that is being recalled for contamination with Burkholderia cepacia bacteria. The mouthwash is associated with an illness outbreak/
XXXX Miracle Skin Moisturizer	Objectionable Organism	Stenotrophomonas maltophila and Staphylococcus warneri	4/5/2006	The product contains Stenotrophomonas maltophila and Staphylococcus warneri.
Body Gels and Lotions	microbial contamination	Unidentified Bacteria	4/12/2006	Microbial contamination
Aspergillus niger Microbial Suspension	Diagnostic Kit Error	Diagnostic Kit Error	4/26/2006	Aspergillus niger microbial suspension, found to be contaminated with yeast, was distributed.
XXXX Mouthwash; an all natural, fluoride-free oral rinse	Objectionable Organism	Enterobacter gergoviae	5/10/2006	A breakdown in the product's preservative system allowed the growth of Enterobacter gergoviae bacteria in the mouthwash
XXXX brand brilliant brunette, Starlit Waves, Wave Enhancing Spray	Objectionable Organism	Pseudomonas spp.	5/10/2006	Hair Spray is contaminated with Pseudomonas
Acetaminophen 500 mg Tablets	Objectionable Organism	Mold	6/14/2006	Firm received a complaint of spotted (discolored) tablets due to mold contamination.
XXXXX Triple Boosting Serum	Objectionable Organism	Enterobacter gergoviae	7/5/2006	Triple Boosting Serum is contaminated with Enterobacter gergoviae.
Liquid potassium supplement	Objectionable Organism	Aspergillus sydowii	7/5/2006	Dietary supplement may be contaminated with Aspergillis sydowii and yeast
Multiple Lots of Oral Anticavity Rinse	Objectionable Organism	Pseudomonas aeruginosa and Burkholderia cepacia	7/19/2006	Microbial Contamination -- Pseudomonas aeruginosa and Burkholderia cepacia
Personal Cleansing Perineal Care Washcloths, Dimethicone 3%	Objectionable Organism	Burkholderia cepacia	8/16/2006	Microbial contamination; Burkholderia cepacia
XXX Baby Butter Massage Lotion	Objectionable Organism	Enterobacter gergoviae	11/15/2006	Product is contaminated with Enterobacter gergoviae.
XXX Prompt Inoculation System-D	Diagnostic Kit Error	Inocula inaccurate	12/13/2006	Product does not meet performance specifications through its standardized inocula for XXXX Dried Gram-Negative and Gram-Positive Overnight panel testing.
XXXX Diabetic Skin Care Therapy Hand & Body Treatment	Objectionable Organism	Pseudomonas aeruginosa	1/3/2007	Hand & Body Cream is contaminated with Pseudomonas aeruginosa.
XXX Oral Moisturizer	microbial contamination	Unidentified Bacteria	3/28/2007	Microbial Contamination. Certain lots of product failed USP <61> Microbial Limits Testing for total aerobic count during 6 month stability testing.
Baby Wipes	Objectionable Organism	Burkholderia cepacia	4/4/2007	The product may be contaminated with Burkholderia cepacia.
New Alpine Xtreme Evergreen Forest Body Wash	Objectionable Organism	Enterobacter gergoviae	5/16/2007	The product is contaminated with Enterobacter gergoviae.
XXXX, Nature's Miracle for the Total Body	microbial contamination	Unidentified Bacteria	6/13/2007	This is an extension of a recall initiated in January 2006 due to microbial contamination. Because these products have no code number, but have similar labeling, they cannot be distinguished from product having microbial contamination.
XXXXX Instant Line Relaxing Formula	Objectionable Organism	Pseudomonas aeruginosa	7/11/2007	Product is contaminated with Pseudomonas aeruginosa and is promoted for use in the eye area
XXXXX Retexturinzing Cleanser; a creamy, exfoliating lotion that helps dissolve make-up and remove dead surface skin cells while cleansing	Objectionable Organism	Mold	7/25/2007	The cleanser was found to be contaminated with mold
XXXX Oral Electrolyte Solution	Objectionable Organism	Burkholderia cepacia	8/1/2007	Products may be contaminated with Burkholderia cepacia.
XXXX Shark Cartilage	Objectionable Organism	Salmonella spp	8/1/2007	Testing performed recently at NBTY, Inc. (the manufacturer) shows that the recalled capsules have the potential to be contaminated with Salmonella
Multiple Products -Topical Anesthetic Skin Refrigerant	Objectionable Organism	Mold	8/1/2007	Mold contamination
Shark Cartilage Capsules	Objectionable Organism	Salmonella spp	8/8/2007	Shark Cartilage Capsules may be contaminated with Salmonella.
XXXXX Sensitive Skin Moisturizing Body Wash and Shampoo	Objectionable Organism	Klebsiella oxtoca	9/5/2007	XXXXX might be contaminated with bacteria including Kiebsiella oxytoca.
XXX Vitamin B12 Liquid, hypo-allergenic dietary supplement	Objectionable Organism	Mold	9/19/2007	Product may be contaminated with mold
XXX Ultra Mild Antibacterial Skin Cleanser, Triclosan 0.30%	Objectionable Organism	Pseudomonas aeruginosa	10/31/2007	Microbial contamination of Non Sterile Product; the product is contaminated with Pseudomonas aeruginosa.

Table 1. Non-sterile Recall Summary 2004-2011 (cont.)

Product	Recall Category	Specific Reason	Date	Reason (as described in Enforcement Report)
Group B Streptococcus Culture Identification Test	Diagnostic Kit Error	Manufacturing	12/26/2007	Mispackaging: Kits may contain Haemophilus Influenza probe pouches in addition to Group B Streptococcus probe
Folic Acid Liquid, 120 ml, dietary supplement packaged in a plastic container with dropper	Objectionable Organism	Mold	2/20/2008	Product may be contaminated with mold.
Various XXXX QC Sets for H influenza	Diagnostic Kit Error	Manufacturing	2/20/2008	Incorrect micro-organism-- .Quality control In-vitro diagnostic test was manufactured with Cryptococcus neoformans (ATCC 76484) instead of Haemophilus parainfluenzae (ATCC 7901).
Gas Relief Drops - Simethicone	Objectionable Organism	Fungal	3/12/2008	Microbial Contamination of Non Sterile Product; Yeast
PreOperative Skin Solution	Objectionable Organism	Burkholderia cepacia	8/13/2008	Microbial contamination of a non-sterile product. The alcohol-free mouthwash was found to be contaminated with Burkholderia cepacia bacteria
Alcohol-Free Mouthwash	Objectionable Organism	Burkholderia cepacia	8/13/2008	Microbial contamination of a non-sterile product. The alcohol-free mouthwash was found to be contaminated with Burkholderia cepacia bacteria
Alcohol-Free Mouthwash	Objectionable Organism	Burkholderia cepacia	8/27/2008	CGMP Deviations. The mouthwash was manufactured under conditions where by it may be contaminated with the bacteria Burkholderia cepacia
2% Chlorhexidine Gluconate Cloth (wipes)	Objectionable Organism	Burkholderia cepacia	9/10/2008	Microbial Contamination of Non-Sterile Product; cloths found to be contaminated with Bulkholderia cepacia
XXXXs Cosmetic Set, body glitter	Objectionable Organism	Mold	10/8/2008	The product was found to be contaminated with mold
Hemmorhoidal suspension	microbial contamination	Fungal	10/29/2008	Product exceeded microbial limit for Total Aerobic Count, Total Yeast and Mold Count
Bacitracin ointment	microbial contamination	Unidentified Bacteria	10/29/2008	Product exceeds microbial specifications
XXXX All Body Wash	Objectionable Organism	Achromobacter xylosoxidans	11/12/2008	This product is being recalled due to microbial contamination with Achromobacter xylosoxidans, a gram-negative organism
Benzoyl peroxide gel	Objectionable Organism	Burkholderia cepacia	12/10/2008	Product may contain the bacteria Burkholderia cepacia.
XXXX Microbial Suspension - Candida albicans CA1	Diagnostic Kit Error	Inocula inaccurate	4/8/2009	Candida albicans microbial suspension, certified to deliver less than 100 organisms per dose, was found to have a population count which exceeded 100 organisms per dose, following distribution
Face Paints	High microbial and Yeast/ mold counts	Unidentified Bacteria	5/13/2009	The face paints have been associated with reports of skin irritation (rashes, itchiness, burning sensation and swelling). Additionally, FDA analyses of the products found they had APC (aerobic plate counts) and yeast/mold counts substantially above industry guidelines
XX Foam, for wraps, setting & styling	Objectionable Organism	Burkholderia cepacia	8/5/2009	The product may be contaminated with Burkholderia cepacia
XXXXX brand Liquid Coral Calcium Dietary Supplement	Failed AET	AET Failure	8/5/2009	Product may not have sufficient preservative levels to inhibit growth of bacteria if organisms introduced post-pasteurization
XXX Locion Perfumada	Objectionable Organism	Pseudomonas putida	8/12/2009	Product is contaminated with Pseudomonas putida and Pseudomonas fluorescens
Multiple Children's XXXX	Objectionable Organism	Burkholderia cepacia	9/30/2009	The raw material used to manufacture the finished product may have been contaminated with B cepacia
XXXX Detox Spa Foaming Sea Salt Scrub	Objectionable Organism	Pseudomonas aeruginosa	10/28/2009	Routine testing discovered the presence of Pseudomonas aeruginosa bacteria
XXXXX Soothing Facial Cosmetic Mud Mask	Objectionable Organism	Pseudomonas putida	11/11/2009	The product is contaminated with Pseudomonas putida
Antimicrobial lotion	microbial contamination	Unidentified Bacteria	11/18/2009	Antimicrobial skin sanitizers and hand protectant products may contain high levels of bacteria
XXX, a homeopathic liquid, oral suspension	Objectionable Organism	Fungal	12/2/2009	Yeast contamination
Oil-free Eye Make-up Remover pads, with Aloe, Cucumber, and Green Tea	Objectionable Organism	Mold	1/20/2010	Product may contain mold
Oral Electrolyte Solutions	Objectionable Organism	Pseudomonas fluorescens and Serratia fonticola.	1/27/2010	Pediatric Electrolyte Solution is contaminated with Pseudomonas fluorescens and Serratia fonticola
XXXXX Strengthening Conditioner with Satin Finishers	Objectionable Organism	Burkholderia cepacia	3/10/2010	Product is contaminated with the microorganism, Burkholderia cepacia
XXXX (Oxymetazoline HCl) Nasal Spray 0.05%	Objectionable Organism	Burkholderia cepacia	3/10/2010	Microbial Contamination of Non-Sterile Product: Product may be contaminated with bacteria Burkholderia cepecia. A stability sample had failed microbial content testing. The microbial content was 8560 cfu/ml for total aerobic count (specification maximum is <100 cfu/ml)
XXXX Lotion SPF 15	Failed AET	Failed AET	3/24/2010	Error with Regard to Preservative: The lotion has the potential for preservative failure, which would allow mold growth to occur
XXX (Triclosan), anti-bacterial foaming soap	microbial contamination	Unidentified Bacteria	4/14/2010	The product will not meet its normal shelf life of two years due to the presence of spoilage organisms

Table 1. Non-sterile Recall Summary 2004-2011 (cont.)

Product	Recall Category	Specific Reason	Date	Reason (as described in Enforcement Report)
Hand Sanitizer Gel	Objectionable Organism	Burkholderia cepacia	4/28/2010	Microbial contamination of Non-Sterile products. FDA samples showed contamination with Burkholderia cepacia (a.k.a. Pseudomonas cepacia)
New Chapter Organics Probiotic Colon	Objectionable Organism	Eschericia coli	4/28/2010	Product may be contaminated with E. coli
Hair Conditioners	microbial contamination	Unidentified Bacteria	5/12/2010	Micro results above specification limits of less than 10 cfu/gram. Results range from 32 cfu/gram to 28,000 cfu/gram
Shark Cartilage Powder	microbial contamination	Unidentified Bacteria	5/19/2010	Possible microbial contamination
XXXX Wipes; a disinfectant medical device, active ingredient Sodium hypochlorite 0.525%; a single 9" x 9" towelette, pre-moistened with 0.525% - 0.656% sodium hypochlorite	Failed Disinfectant Efficacy	Failed Disinfectant Efficacy	7/21/2010	The disinfectant wipes were found out of specifications for the disinfectant activity prior to the expiration date
Various lotions and creams	Failed AET	Failed AET	8/11/2010	The cosmetics have sporadic failure of the preservative system, which allows mold growth to occur
Alcohol-Free Hand Sanitizer Foam	Objectionable Organism	Burkholderia cepacia	11/10/2010	Product may be contaminated with Burkholderia cepacia
Instant Hand Sanitizer	Objectionable Organism	Pseudomonas putida	11/17/2010	Microbial Contamination of Non-Sterile Products: FDA testing results identified gram negative bacteria Pseudomonas putida
XXX EZ Large Incubation Container, a component of the XXX EZ Gas Generating Container System	Diagnostic Kit Error	Reagent QC	12/22/2010	In vitro diagnostic reagent containers may be defective and could cause incorrect test results in patient samples
XXX Patient Starter Kits	Objectionable Organism	Bacillus cereus	3/9/2011	the Kits are being recalled because the alcohol prep pads have the potential to be contaminated with Bacillus cereus
Various Kits	microbial contamination	Unidentified Bacteria	3/9/2011	Microbial Contamination of Non-Sterile Products: Kits were manufactured using a recalled component (alcohol pads).
Alcohol free sanitizer foam	Objectionable Organism	Burkholderia cepacia	3/23/2011	Microbial contamination of additional brand named Non-sterile Products: Non-Alcohol Foaming Hand sanitizer may be contaminated with Burkholderia cepacia.
Somatropin (rDNA origin) injection pen	Objectionable Organism	Bacillus cereus	3/23/2011	Microbial contamination of non-sterile products: XXX kits contain alcohol wipes that have been recalled by XXX due to Bacillus cereus.
Dietary Supplement, Organic Tart Cherry	microbial contamination	Unidentified Bacteria	5/18/2011	Bottles were reported as bulging or misshaped and in some instances the seals have popped off.
Device Kits	microbial contamination	Unidentified Bacteria	6/8/2011	Product package contains alcohol prep pads recalled by XXX because the prep pads have the potential to be contaminated with an objectionable organism.
Povidone iodine Pads	Objectionable Organism	Staphylococcus warneri, Stenotrophomas maltophilia and Elizabethkingia meningoseptica	6/8/11	Microbial Contamination of Non-Sterile Products: The recall of all lots of Povidine Iodine Prep Pads was initiated due to results of analytical testing showing the presence of objectionable organisms, namely showing the presence of objectionable organisms, namely Staphylococcus warneri, Stenotrophomas maltophilia and Elizabethkingia meningoseptica
Pure Cocoa Plum Fruit Pigmented Eye Shadow	Objectionable Organism	Pseudomonas luteola	6/22/2011	FDA samples confirmed the presence of Pseudomonas luteola in Cocoa Plum colored eye shadow.
XXXX Make-up Design Sketch Book	Objectionable Organism	Staphylococcus spp (warneri and intermedius)	6/22/11	The recall was initiated due to potential contamination of the products with certain microorganisms, namely Staphylococcus warneri and Staphylococcus intermedius.
Multiple Baby Wipes	Objectionable Organism	Enterobacter gergoviae	6/29/2011	Product has the potential to be contaminated with Enterobacter gergoviae.
XXX Starter Kits	Objectionable Organism	Bacillus cereus	6/29/11	Recalling the alcohol prep pads due to potential contamination with the bacteria, Bacillus cereus, which could result in life threatening infections, especially in at-risk populations, including immune suppressed and surgical patients.
XXXXX Patient Electrode Sensor Test Kit	Objectionable Organism	Bacillus cereus	7/6/11	Kits contain a product component (XXXX Alcohol Prep Pads) recalled due to potential Bacillus cereus contamination.
Alcohol wipes	Objectionable Organism	Bacillus cereus	7/13/11	The recall of the XXX alcohol prep products is due to potential contamination of these products with the bacteria Bacillus cereus, which could lead to life-threatening infections.
XXXX, Three Benzalkonium Chloride Swabsticks	microbial contamination	Unidentified Bacteria	7/13/11	Microbial contamination of non-sterile products.
Povidone Iodine pads in First Aid Kits	Objectionable Organism	Elizabethkingia meningoseptica	7/27/11	Microbial Contamination of Non-Sterile Products: XXXXX has initiated the recall due to a recall being conducted for the XXX Povidone Iodine Prep Pads manufactured by XXXX. Concerns were expressed by the Food and Drug Administration regarding the potential contamination of XXXX Povidone Iodine Prep Pads. The XXXXX Povidone Iodine Prep Pads are potentially contaminated with an objectionable organism, Elizabethkingia meningoseptica. The XXX Povidone Iodine Prep Pads have an NDC number of 50730-3201-1 and are the only defective material in the First Aid Kits.

Table 1. Non-sterile Recall Summary 2004-2011 (cont.)				
Product	**Recall Category**	**Specific Reason**	**Date**	**Reason (as described in Enforcement Report)**
Skin-Prep wipes	microbial contamination	Unidentified Bacteria	8/4/11	These products were manufactured by XXXX who has initiated a recall of products manufactured in their facility for potential microbial contamination.
Simethicone Emulsion	Objectionable Organism	Burkholderia cepacia	8/10/11	Microbial Contamination of Non-Sterile Products: Certain lots of the product were confirmed to have exceeded the USP specification for maximum microbial content (microbial type, Burkholderia cepacia).
First Aid Kits	Objectionable Organism	Burkholderia cepacia	8/24/11	Lack of Assurance of Sterility: These kits are being recalled because they contain individually wrapped Triad alcohol pads which were recalled under the Triad Group recall because of potential contamination with the bacteria, Bacillus cereus.
Levetiracetam Oral Solution	microbial contamination	Unidentified Bacteria	8/24/11	Out of specification results were observed in stability sample testing for microbiological limits in three lots of Levetiracetam Oral Solution
Simethicone Emulsion	Objectionable Organism	Burkholderia cepacia	8/31/11	Microbial Contamination of Non-Sterile Products: Certain lots of the product were confirmed to have exceeded the USP specification for maximum microbial content (microbial type, Burkholderia cepacia).
Multiple First Aid Kits	Objectionable Organism	Bacillus cereus	9/3/11	Kits containing Alcohol Prep Pads recalled by XXXXX due to contamination with Bacillus cereus.
Blood Specimen Collection Kit	Objectionable Organism	Elizabethkingia meningoseptica	9/7/11	Microbial Contamination of Non-Sterile Products: This is a sub-recall of XXX Povidine Iodine Prep Pads; The Kits under recall contain Povidine Prep Pads recalled by XXXX due to the potential contamination with an objectionable organism, Elizabethkingia meningoseptica.
Povidone-iodine solution	microbial contamination	Unidentified Bacteria	9/21/11	CGMP Deviations: Products were manufactured without having in place a system for microbial testing at the time of release, without having a system for testing of incoming components, and without having procedures designed and established to prevent objectionable microorganisms in drug products.
Infant's Simethicone Drops	Objectionable Organism	Burkholderia cepacia	9/21/11	Microbial Contamination of Non Sterile Product; product may be contaminated with Burkholderia cepacia.
First Aid Kits	Objectionable Organism	Bacillus cereus	10/5/11	Microbial Contamination of Non-Sterile Product: North Safety Kits contain a product component (XXX Alcohol Prep Pads) recalled due to potential Bacillus cereus contamination.
Non-Sterile Alcohol Prep Pads/Swabs, saturated with 70% v/v Isopropyl Alcohol	Objectionable Organism	Bacillus cereus	10/5/11	Microbial Contamination of Non-Sterile Products: The non-sterile alcohol prep pads/swabs were found to be contaminated with Bacillus cereus based on FDA sampling and analysis.
Simethicone Emulsion USP	Objectionable Organism	Mold	10/5/11	Microbial Contamination of Non Sterile Product; mold found in gasket area of drum lid.
XXX Nasal Decongestant	Objectionable Organism	Burkholderia cepacia	10/19/11	Microbial Contamination of Non-Sterile Product: This product is being recalled due to the presence of Burkholderia cepacia
XXXXX Highlight Activating Enhancing Conditioner for Lighter Shades	microbial contamination	Unidentified Bacteria	11/2/2011	Product erroneously shipped to customers during transfer for destruction. Product had been rejected, quarantined, and blocked by Quality Services due to microbial contamination. Micro results were above specification limits of: Less than 100 cfu/grams. Results range from 120 cfu/gram to 210 cfu/gram.
Mouthwash	Objectionable Organism	Burkholderia cepacia	11/9/11	Microbial Contamination of Non-Sterile Products: The mouthwash component of the kit was found to be contaminated with Burkholderia cepacia.
First Aid Kits	Objectionable Organism	Elizabethkingia meningoseptica	11/9/11	Microbial Contamination of Non-Sterile Products: The products contain povidone iodine prep pads which were recalled by the supplier.
First Aid Kits	Objectionable Organism	Elizabethkingia meningoseptica	11/16/11	The first aid kits are recalled because the kits contain Iodine Prep Pad single use wipes which were recalled by XXXX.
Povidone Iodine Swabsticks	GMP	Lack of Micro Testing	11/16/11	CGMP Deviations: This kit is being recalled because a component, povidone iodine swabstick, was recalled by the manufacturer because they were manufactured without having in place a system for microbial testing at the time of release, without having a system for testing of incoming components, and without having procedures designed and established to prevent objectionable microorganisms in drug products.
Povidone Iodine Swabsticks	GMP	Lack of Micro Testing	11/30/11	CGMP Deviations: This kit is being recalled because a component, povidone iodine swabstick, was recalled by the manufacturer because they were manufactured without having in place a system for microbial testing at the time of release, without having a system for testing of incoming components, and without having procedures designed and established to prevent objectionable microorganisms in drug products
Multiple Specimen Collection Kits	Objectionable Organism	Bacillus cereus	12/21/2011	XXXX is recalling certain Specimen Collection Kits that contain Triad brand non-sterile alcohol prep pads which have been recalled by XXXXX due to Bacillus cereus, microbial contamination

Table 1. Non-sterile Recall Summary 2004-2011 (cont.)				
Product	**Recall Category**	**Specific Reason**	**Date**	**Reason (as described in Enforcement Report)**
Infants', Gas Relief, Liquid Drops	Objectionable Organism	Burkholderia cepacia	12/21/2011	Microbial Contamination of Non-Sterile Product: Various brands of Infant Gas Relief Drops may have microbial contamination with Burkholderia cepacia due to a raw material that was used to manufacture the product.
MANY First Aid Kits	Objectionable Organism	Elizabethkingia meningoseptica	12/21/2011	Microbial Contamination of Non-Sterile Products: The products contain povidone iodine prep pads which were recalled by the supplier.
Vitamin E Oil	Microbial Contamination	Yeast and Mold	12/28/2011	Vitamin E Oil was recalled as it did not meet the specifications for microbial limits, specifically for yeast and mold
XXX Nasal Decongestant	Objectionable Organism	Burkholderia cepacia	12/28/2011	Microbial Contamination of Non-Sterile Product; product found to contain Bulkholderia cepacia

- Gram Negative Bacilli – cited in 77 recalls
- Yeast/Mold – cited in 23 recalls
- Gram Positive Cocci – cited in 3 recalls

Figure 8 provides details on the types of organisms cited in FDA enforcement reports for this period. From this analysis it is clear that the pseudomonads are the most frequently cited of the "objectionables" in recalls of this type. Table 2 provides detail on the cited identity of microorganisms in these recalls.

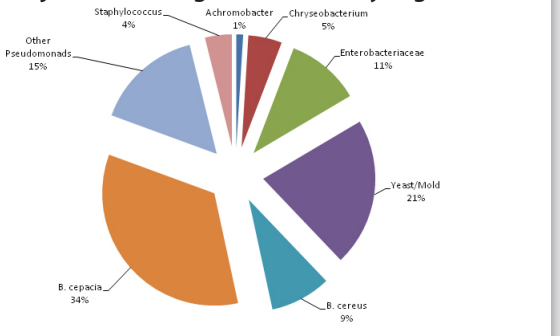

Figure 8. Objectionable Organism Recalls by Organism for Non-sterile Products

One of the immediate impressions from Table 2 is the prevalence of recalls that specifically cite *Burkholderia cepacia* as the objectionable organism in non-sterile products. In fact, *B. cepacia* alone is cited in 34% of the non-sterile recalls from the years 2004-2011. This extends a trend reported for the years 1998-2006 where *B. cepacia* was the cited cause for non-sterile recalls in 22% of the cases [1]. The recalls involving *B. cepacia* in the 2004-2011 timeframe have ranged from mouthwashes (alcohol-free mouthwash packaged both independently and in hospital hygiene kits), moist wipes, soaps and sanitizers, nasal products to hair dyes.

As discussed above, *B. cepacia* holds a special place in the corporate culture of FDA. This dates back to a tragedy in the early 1980s when an inhalant was marketed contaminated by *Pseudomonas cepacia (Burkholderia cepacia)*. This product had passed USP tests (which are not capable of recognizing *B. cepacia* – see USP 1982 for more details). However, this event caused the death of several cystic fibrosis patients and lead to the realization that this organism had the capability to cause disease in a susceptible population and also to survive in preserved

Table 2. Identity of Objectionable Organisms Cited in Recalls for "Objectionable Organisms" 2004 – 2011

Microorganism	Number of Cited Recalls
Achromobacter xylosoxidans	1
Acremonium mold and P. aeruginosa	1
Aspergillus and Penicillium	1
Aspergillus sydowii	1
Bacillus cereus	9
Burkholderia cepacia	34
Elizabethkingia meningoseptica	5
Enterobacter cloacae	1
Enterobacter gergoviae	5
Escherichia coli	1
Fungal (Yeast and/or Mold)	19
Klebsiella oxtoca	1
Pseudomonas spinosa	1
Pseudomonas aeruginosa	6
Pseudomonas aeruginosa and Burkholderia cepacia	1
Pseudomonas fluorescens and Serratia fonticola	1
Pseudomonas luteola	1
Pseudomonas putida	3
Pseudomonas spp.	2
Salmonella spp	2
Serratia marcescens	1
Staphylococcus aureus	1
Staphylococcus spp (warneri and intermedius)	1
Staphylococcus warneri, Stenotrophomas maltophilia and Elizabethkingia meningoseptica	1
Stenotrophomonas maltophila and Staphylococcus warneri	1
Unidentified Bacteria	1

solutions [7,8]. This also led to the establishment of a requirement that aqueous-based inhalants must be sterile (21 CFR 200.51) [9].

Recently a rationale was published discussing the intense concern that the Agency continues to feel towards *B. cepacia* as an objectionable organism in a wide range of non-sterile products [10]. This article has raised additional questions from the field [11]. However, there is a real argument that can be made for concern over *B. cepacia* in non-sterile products that enter the nasal passage or the lungs, particularly in those populations susceptible to pneumonia. These patient populations at risk might include neonates, advanced elderly and cystic fibrosis patients (among others) and products marketed to those populations, or likely to be used on those populations, should not contain *B. cepacia*.

Table 3. "Wipes" Recall Summary 2004-2011

Product	Recall Category	Specific Reason	Date	Reason (as described in Enforcement Report)
Baby Wipes	Objectionable Organism	Mold	10/5/05	Products are contaminated with mold.
First Aid High Performance Gauze Pad	Lack of Sterility Assurance	Manufacturing	7/26/06	After reviewing manufacturing records it has been determined that these lots inadvertently were not sterilized after packaging in individual boxes labeled as sterile product.
Baby Wipes	Objectionable Organism	Burkholderia cepacia	4/4/07	The product may be contaminated with Burkholderia cepacia.
2% Chlorhexidine Gluconate Cloth (wipes)	Objectionable Organism	Burkholderia cepacia	9/10/08	Microbial Contamination of Non-Sterile Product; cloths found to be contaminated with Burkholderia cepacia
Oil-free Eye Make-up Remover pads, with Aloe, Cucumber, and Green Tea	Objectionable Organism	Mold	1/20/10	Product may contain mold
XXX Wipes; a disinfectant medical device, active ingredient Sodium hypochlorite 0.525%; a single 9" x 9" towelette, pre-moistened with 0.525% - 0.656% sodium hypochlorite	Failed Disinfectant Efficacy	Failed Disinfectant Efficacy	7/21/10	The disinfectant wipes were found out of specifications for the disinfectant activity prior to the expiration date
XXXX {somatropin (rDNA origin) injection} XXXX pen	Objectionable Organism	Bacillus cereus	3/23/11	Microbial contamination of non-sterile products: XXX kits contain alcohol wipes that have been recalled by XXX due to Bacillus cereus.
I.V. PREP (Isopropyl Alcohol 70% v/v) Antiseptic Wipe,	Lack of Sterility Assurance	Contaminated	4/20/11	This action is being taken "due to an abundance of caution" as this product is manufactured by XXX in the same location which manufactures various sterile alcohol wipes/swabs and swabsticks that are currently being recalled for suspected bacterial contamination.
I.V. PREP (Isopropyl Alcohol 70% v/v) Antiseptic Wipe,	Lack of Sterility Assurance	Contaminated	4/20/11	This action is being taken "due to an abundance of caution" as this product is manufactured by H&P Industries dba The Triad Group in the same location which manufactures various sterile alcohol wipes/swabs and swabsticks that are currently being recalled for suspected bacterial contamination.
Povidone iodine Pads	Objectionable Organism	Staphylococcus warneri, Stenotrophomas maltophilia and Elizabethkingia meningoseptica	6/8/11	Microbial Contamination of Non-Sterile Products: The recall of all lots of Povidine Iodine Prep Pads was initiated due to results of analytical testing showing the presence of objectionable organisms, namely showing the presence of objectionable organisms, namely Staphylococcus warneri, Stenotrophomas maltophilia, and Elizabethkingia meningoseptica
Multiple Baby Wipes	Objectionable Organism	Enterobacter gergoviae	6/29/11	Product has the potential to be contaminated with Enterobacter gergoviae.
Disposable, Convenience Tray	Microbial Contamination	Burkholderia cepacia	7/6/11	Kits contain protective wipes that may be contaminated with Bacillus cereus.
Alcohol wipes	Objectionable Organism	Burkholderia cepacia	7/13/11	The recall of the Triad Group alcohol prep products is due to potential contamination of these products with the bacteria Bacillus cereus, which could lead to life-threatening infections.
XXX Catheters	Microbial Contamination	Unidentified Bacteria	7/13/11	A component of the XXX device recalled the Skin-Prep, a protective wipe due to bacterial contamination.
Povidone Iodine pads in First Aid Kits	Objectionable Organism	Elizabethkingia meningoseptica	7/27/11	Microbial Contamination of Non-Sterile Products: XXX has initiated the recall due to a recall being conducted for the Triad Povidone Iodine Prep Pads manufactured by XXX. Concerns were expressed by the Food and Drug Administration regarding the potential contamination of Triad Povidone Iodine Prep Pads. The XXX Povidone Iodine Prep Pads are potentially contaminated with an objectionable organism, Elizabethkingia meningoseptica. The XXX Povidone Iodine Prep Pads have an NDC number of 50730-3201-1 and are the only defective material in the First Aid Kits.
Sure Seal Golden Drain, One Piece Urinary Incontinence Device	Lack of Sterility Assurance	Contaminated	7/27/11	The Kit contains Skin-Prep protective wipes that were manufactured by the XXX and are being recalled by XXX, due to possible bacterial contamination.
Skin-Prep wipes	Microbial Contamination	Unidentified Bacteria	8/4/11	These products were manufactured by XXX who has initiated a recall of products manufactured in their facility for potential microbial contamination.
Non-Sterile Alcohol Prep Pads/Swabs, saturated with 70% v/v Isopropyl Alcohol	Objectionable Organism	Burkholderia cepacia	10/5/11	Microbial Contamination of Non-Sterile Products: The non-sterile alcohol prep pads/swabs were found to be contaminated with Bacillus cereus based on FDA sampling and analysis.
First Aid Kits	Objectionable Organism	Elizabethkingia meningoseptica	11/16/11	The first aid kits are recalled because the kits contain Iodine Prep Pad single use wipes which were recalled by XXX.

Given that the organism is a concern for severely compromised individuals if presented to the lungs, is this an argument for the elimination of *B. cepacia* from all non-sterile products? The Agency has stated from the podium that it is FDA policy to "regulate to the most susceptible population." This policy strikes the authors as ill-advised. First of all, it is imprecise. The most susceptible population is that portion completely devoid of a functioning immune system (regulating to Bubble-boy is unworkable). Since this is clearly not what the Agency means, we are left to divine its intent based on clues. Secondly this policy is illogical, "regulating to the most susceptible population" might be as well expressed as "everyone in the family must eat strained carrots because the baby cannot eat steak." In no other area of life or business

would this philosophy be followed. It is far more reasonable and efficient to control the access to, and use of, products by the user, based on the risk posed to that user. There are those allergic to shellfish –yet the sale of shellfish continues. However, it is clearly the policy of the FDA that *B. cepacia* is a severe threat to the health of the nation and will be viewed as sufficient reason to encourage a "voluntary" recall if seen in a product (despite the paucity of scientific data supporting its hazardous nature in most situations). The large number of non-sterile product recalls during this period citing *B. cepacia* underscores the importance of this discussion.

Another troubling area for this analysis of non-sterile recalls is the large number (15%) that only cite "microbial contamination" as the cause for a non-sterile product recall. One must assume that many of these are due to extremely large numbers of microorganisms present, but this should properly have been cited for the record. Having these large numbers of microorganisms is objectionable in and of itself as it might either indicate slovenly manufacturing practices or the presence of a spoilage organism that is growing in the product. In either case, given the widespread availability of microbial identification systems [12] the failure to note (or to identify) the causative microorganism(s) is regrettable.

A final point of interest is the prevalence of *Bacillus cereus* in the listing. All of the 2011 recalls of this product category are linked to the recall of product ("sterile" and non-sterile alcohol prep pads) from a single manufacturer. There are two points here. The first is the enormous impact this recall had on many different products – both sterile and non-sterile (mainly kits). The second consideration is that FDA is clearly concerned with the current safety of moist wipes on the marketplace. A summary of recalls involving moist wipes is presented in Table 3. Perhaps the sterility requirements for this product category – moist wipes – needs to be reconsidered. Is there a place for non-sterile moist wipes in the marketplace? If so, should procedures that require sterile wipes (for example, preparation of an injection site) be clearly described to prevent the misuse of labeled non-sterile wipes?

Where does this leave us in terms of generating an understanding of "objectionable organisms"? Much depends on your company's scientific sophistical and tolerance of risk. Using the previous recall review with the data presented in this review and available regulatory documents one might put together a list of "objectionables". This is probably the best course of action for those least tolerant of risk or desirous of engaging the Agency in scientific debate. For those who would have a rationale for this risk assessment, the authors urge a risk assessment strategy based on the rationale presented in USP chapter <1111>.

Conclusions

An analysis was conducted using publically available enforcement reports as presented on the US FDA website. The microbiologically-related recall activity shows a decided increase in recent years. Most of the reported recalls involved sterile products, and of these medical devices accounted for the majority. The reasons given for sterile product recalls were varied, but the majority cited "Lack of Sterility Assurance" with defects and weaknesses of sterile packaging clearly identified as the most common source of contamination potential.

There was significant information in the recall data for non-sterile products as well. The majority of the recalls came from OTC and personal care products, with "Objectionable Organisms" as the most prevalent reason for recall. Information on FDA policy in terms of "objectionable organisms" was apparent from the data.

This review demonstrates that analysis of enforcement reports, freely available from the FDA web site, provides insightful and actionable information on CGMP. A review of this kind also makes one extremely grateful for the diligence of the FDA in safeguarding the regulated industries.

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This article was printed in the January/February 2012 issue of *American Pharmaceutical Review*, Volume 15, Issue 1, pages 42-57.