PMF NEWSLETTER

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Lucky Number 13

This is the first issue of the 13th volume of the *PMF Newsletter* - one full year of monthly publications! I want to take this opportunity to thank all of you who have participated and have given your support this past year. Please feel free to write in with articles and ideas.

Important Links:

Information on the PMFList at
http://www.microbiol.org/pmflist.htm

Past Issues of the *PMF Newsletter* at
http://www.microbiologyforum.org/news.htm

This month we have a very interesting article on biofilm and biofouling by Mark Fornalik. He has many years of experience in dealing with this problem in ultra-pure water, and describes the use of in-line witness plates and FTIR analytical tools to get an early and accurate read on the development of biofilm in the water system.

The second article this month deals with determining the best microbial identification system. To save you some time, I will tell you that you will not learn what the best system is by reading the article. That is not what the article's message. The article is actually about the fact that there are many good systems out there, each has strengths and each has weaknesses, and you need to have a clear idea of what you want the system to do and how you want it to do it *before* you go shopping. A strategy is presented to document this decision-making process.

Finally, the 2007 PMF Open Conference on Compendial Issues is almost here. This is going to be a remarkable meeting and an excellent opportunity to meet with regulatory experts. Details are on page 14.

Enjoy the first publication of the 13th volume!

Scott Sutton scott.sutton@microbiol.org

A Practical Approach to Understanding and Controlling Biofouling in Liquid Transfer Equipment

Mark Fornalik
Eastman Kodak Company

Introduction

Biofouling is a ubiquitous problem to a great many industrial processes. While biofouling infrequently makes headline news (note the Alaskan oil pipeline leak, due to microbial-induced corrosion), (1) typically the problem exists with little fanfare, hidden away in liquid transfer lines (pipes, pumps, vessels, etc.). This paper describes a practical approach to detecting, characterizing and fixing industrial biofouling problems.

Many of Kodak's traditional photographic film and paper products involve liquid gelatin-handling processes, as well as other chemicals, including ultrapure water. Over the years, a research effort was put forth to understand the causes and solutions to liquid transfer system fouling, including biofouling. The studies eventually led to a systematic approach to detecting and solving these problems regardless of product or process. This systems approach to cleaning is shown in Figure 1.

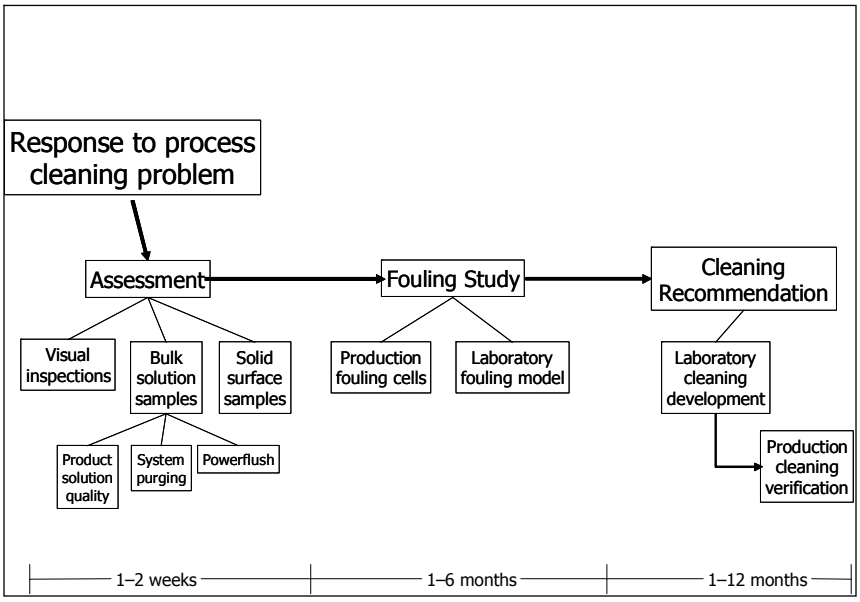

Figure 1. Systems Cleaning Value Stream Map

A key element of this approach is represented by the central portion of this flow chart–the fouling study. The fouling study portion of this chart is the focus of this article, using in this case the special example of biofouling.

Background

Characklis and Marshall (2) defined biofouling as:
Consisting of cells immobilized at a substratum and frequently embedded in an organic polymer matrix of microbial origin;
A surface accumulation, which is not necessarily uniform in time or space, composed of a significant fraction of inorganic or abiotic substances held together by the biotic matrix.

Further descriptions of biofilms can be found in Costerton and Stewart (3), and in Flemming and Geesey (4).

Characklis and Marshall note that the industries that biofilms impact are extensive: food and beverage processing, dairy processing, pharmaceuticals manufacturing, water treatment and distribution, petrochemical processes, marine and freshwater ship fouling, power generation plants (including nuclear), and chemicals manufacturing and processing plants. Biofouling is also a principal problem in a variety of biomedical environments.

Biofouling is but one form of surface fouling (the other forms including, according to Bott (5), organic fouling, inorganic fouling, particulate fouling, crystallization/scale fouling, and combination fouling). Typically, biofilm problems impact manufacturing processes in a variety of ways, generating waste in these processes: increased downtime attributed to cleaning, corrosion of pipelines, increased run lengths to make up for unexpected process downtime, loss of product flow caused by pipelines occluding from biofilm growth, and chemical contamination of the product flowing through the fouled pipelines. These problems are usually discovered before product is released from the plant, and can also lead to elevated process downtime and cost.

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These problems are well documented in academic papers. Biofouling is the focus of many major research programs (Montana State University's Center for Biofilm Engineering, the University of Calgary's Biofilm Research Group, the University of Southern California's Center for Biofilms, and the Biofilm Club in the UK are some examples). The results from these efforts are generally focused on microbiology biofilm molecular genetics. Less obvious are findings that are of immediate value to industry.

The approach in this article marries two simple concepts: surface analytical measurements and manufacturing-worthy coupons or witness plates. A typical example of witness plate technology may be found in Gilbert and Herbert (6). An example of the surface measurement technology may be found in Baier *et al.* (7) and Schmitt and Flemming (8). This combination enables analytical surface chemical measurements to be applied to detecting and characterizing surface chemical fouling as well as biofouling, the rate of fouling/biofouling, and to quantitatively determine the best cleaning methods.

Theory

Biofouling follows a sequence of events (Characklis and Marshall (2), Baier *et al.*(7), Gilbert and Herbert (6)). When an engineering material is placed in contact with flowing biological solutions (including ultrapure water), the initial fouling is usually macromolecular: glycoproteins, proteoglycans, humic acids, etc. This macromolecular fouling phase is known as the induction period (5). Generally, these macromolecules are irreversibly adsorbed to the surface, that is, they require physical abrasion to remove them from the surface. Induction period fouling is not typically a problem for most industrial processes, and it is uneconomical to try to remove induction period fouling with process cleaning.

The next phase of biofouling is the rapid fouling phase (see Figure 2). At this point, the macromolecular fouling begins to attract organisms–microbes concentrate on the walls of transfer lines in part because of the macromolecular nutrient present and in part because of the stagnant or low-flow conditions found at the pipe wall. As cells start to colonize the surface, the film thickness builds up quickly. It is at this stage that the organisms begin to generate and concentrate contaminants: the cells themselves metabolize the nutrient around them and produce chemical waste products (enzymes, ionic species, organic materials), and the new biofilm produces exopolymers (Characklis and Marshall)2 that act to trap and concentrate insoluble particles from the flowing product solution.

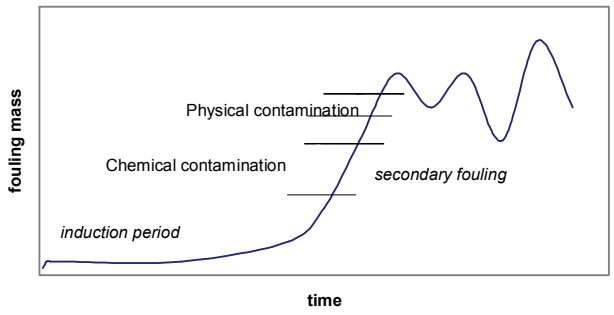

Figure 2. Fouling Sequence

If the fouling is allowed to continue, the final phase of the fouling curve may occur: the biofilm thickness continues to grow until the fouling becomes unstable in the fluid flow. Here, the biofilm may slough off in chunks, regrow, slough off once again, and continue

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Internet Address	Description
http://www.microbeworld.org/	MicrobeWorld explores the world of microbes with vivid images and descriptions. Learn about microbiology, what microbiologists do, how they do it, and current topics in the news.
http://student.ccbcmd.edu/~gkaiser/goshp.html	Dr. Kaiser's microbiology course and laboratory manual are fantastic for anyone wanting to know more about microbes. Good source for training materials.
If you have found an Internet site that contains information of relevance to professional microbiology in the industrial sector, please let us know.	

How Do You Decide Which Microbial Identification System is Best?

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Introduction

Microbial identification plays a central role in the cleanroom control program (24). The method of identification, however, must be wedded to the need. For example, any organism isolated from the critical aseptic processing area must be identified to great detail, while those from class D/ISO 8/100,000 areas might only be characterized to the genus level. The key concern is providing sufficient detail to assist in the tracking of the state of control of the facility.

Most identification schemes still rely on the Gram stain, a differential staining technique developed in the late 1800's by Christian Gram (15). This differential counterstaining technique is very good at distinguishing a real difference in cellular morphology. Unfortunately, this method is prone to a significant level of operator error, which has encouraged the development of alternate methods for showing the difference in cell structure (17, 23). Traditional methods of identification also consider a variety of phenotypic characteristics.

Phenotypic Methods

Phenotypic methods typically incorporate reactions to different chemicals or different biochemical markers. The API strip is basically a prepackaging of the standard method that required racks of test tubes into a convenient bubble-wrap. This method was further refined in the Vitek automated system which miniaturized the process (2, 20). This system has recently been enhanced to provide greater resolution of microorganisms (9, 10).

A second phenotypic system is offered by Biolog, Inc. The fundamental unit in this system is a 96-well plate that has different carbohydrate sources in each well, with a tetrazolium redox dye. If the microorganism is capable of utilizing the carbohydrate the well turns dark indicating reduction of the dye (14, 19). The end-result is a pattern of wells (a "metabolic fingerprint") that allows the user to identify the unknown microorganism. This method has recently been extended to include the identification of molds and filamentous fungi with a proprietary software package.

The use of cellular fatty acid (FA) composition to identify the genus and species has been popular for several years (1, 5). The fatty acids are extracted from the cell cultures and then the patterns of fatty acid esters are determined by gas chromatography (22).

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There are some new methods under development for the pharmaceutical QC lab. These include Fourier-Transform Infrared (FTIR) microscopy (16) and Matrix-Assisted Laser Desorption Ionization–Time of Flight (MALDI-TOF) mass spectroscopy (8, 18). However, these have not seen widespread use in the QC lab as of yet.

Genotypic Methods

The FDA has recently elevated the use of genotypic identification methods with the release of the revised aseptic processing guidance document late in 2004 (6).

The Riboprinter is fundamentally an automated Southern Blot apparatus using labeled ssDNA probe from the 16sRNA codon. The resulting pattern is then used to identify the unknown microorganism (4, 12). If the initial banding pattern is inconclusive, then the restriction endonuclease can be changed to provide an extraordinary level of strain discrimination (3).

Another genotypic identification system on the market is the MicroSeq 500 16S rDNA Bacterial Sequencing Kit which is offered by Applied Biosystems. As the name implies, it provides the materials needed to sequence the first 500 basepairs of the unknown microorganism's 16s ribosomal RNA codon (7). The technology involves amplification of the 16S codon by PCR, followed by automated sequencing.

A final genotypic method that is being marketed into the QC pharmaceutical laboratory is the Bacterial Barcodes system (11). This system is also based on PCR technology, using as a primer a sequence homologous to a repetitive sequence in the bacterial genome. The amplified sequence is then separated by gel electrophoresis and visualized to give the "barcode" specific to that strain.

Qualicon markets the BAX system to the food industry that contains primers for Salmenolla, Listeria or E. coli O157:H7 (13). This system has promise for determination of the absence of specified organisms in the product.

Other genetic methods have been published in the literature, although few are available to the pharmaceutical market (21).

How to Choose?

There are a variety of identification technologies available. When choosing one for the lab you must bear in mind the strengths, and weaknesses, of the various methodologies. For example, the recently released aseptic processing guidance document (FDA 2004) strongly recommends the use of genotypically based methods. However, if you choose PCR based methods or DNA sequencing, there is potentially an associated cost in facilities, labor (highly skilled technicians) and maintenance that is not present with the more traditional methods.

The most direct approach to deciding the appropriate technology is to research the choices fully based on an understanding of what your requirements may be. I recommend the development of a User Requirements Specification (URS) document to drive this process. This is a formal Quality document, similar in concept to a Design Qualification document. Different companies will have different formats for these documents, but the essential features of the document will be that it has the essential requirements and that it has upper management sign-off (for a variety of reasons it is a good idea to document upper-management commitment).

A partial list of topics to be covered in any URS designed for an identification system should include:

- Assay Throughput
  How many samples a day?

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in this pattern of growing/sloughing. If the fluid flow is low enough in Reynolds number, the biofouling may completely occlude the pipe, blocking product flow.

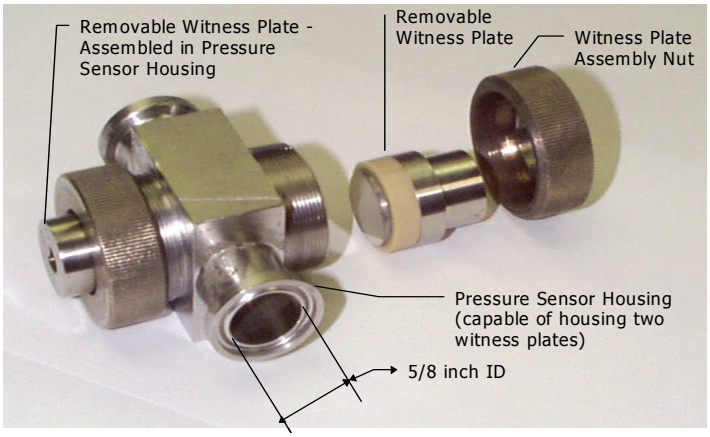
The goal of process cleaning is simple: return the process to the induction level of fouling before there is either a process or product problem. The efficiency of the cleaning process depends very heavily on the chemistry of the biofilm and the chemistry and frequency of the cleaning process.

Practical Approach

Two sets of tools enable the industrial researcher to find, understand, and fix process biofouling problems: in-line witness plates and surface analytical chemistry measurements. These two sets of tools are generally inexpensive, and when used properly can lead to long-lasting improvements in process cleaning.

An example of an in-line witness plate–or fouling cell–is shown in Figure 3. Here, the device is a modified pressure sensor housing designed for a sanitary process. The pressure sensor has been removed and replaced with a pair of mirror-polished stainless steel discs. In practice, discs of any material of interest may be used (stainless steel, titanium, Teflon, various plastics, etc.), but mirror-polished stainless steel is best for initial measurements.

Figure 3. Fouling Cell Discs and Housing



The fouling cell housing and discs are placed in a manufacturing process and removed after some specified time interval. The discs are taken out of the housing and then analyzed by a variety of techniques.

The principal technique is Fourier Transform Infrared (FTIR) spectroscopy. FTIR is a chemical "fingerprinting" technique–generating information on the organic functional groups of a fouling film (see Figure 4). In addition, peak height in the IR is related to mass of the fouling film–the higher the peak, the more fouling mass.

Once FTIR is measured on a fouling cell disc, the disc may be submitted for other nondestructive measurements: atomic force microscopy (AFM, for quantitative fouling film morphology), X-ray fluorescence (inorganic analysis), and X-ray photoelectron spectroscopy (XPS or ESCA). Destructive measurement techniques (that is, techniques that will alter the fouling film) include epifluorescence optical microscopy (for detecting stained organisms), scanning electron microscopy (SEM), standard microbiological culturing techniques, and other chemical analyses.

For industrial biofilm analysis, the most useful tech-

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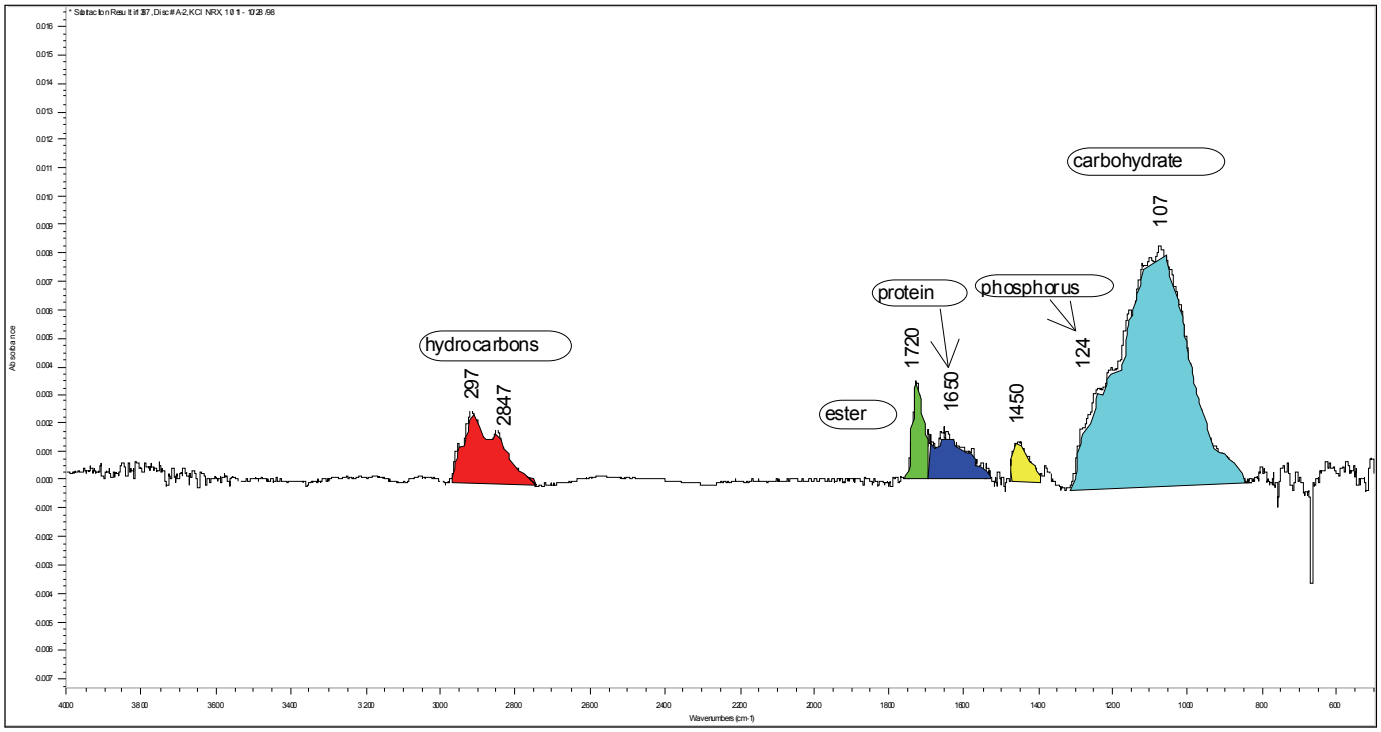

Figure 4. Fourier Transform Infrared Spectrum of Saltwater Biofilm

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niques are FTIR and epifluorescence optical microscopy. The following section describes how this approach was used to solve a biofilm problem.

Saltwater System Biofouling

Production personnel complained of finding a black sludge in a concentrated saltwater transfer system. Problems also included occlusion of manufacturing equipment further down the process, as well as chemical contamination issues.

Fouling cells placed in the salt system revealed the spectrum shown in Figure 4 (above). Note the lack of proteinaceous material 1650 cm-1), the large amount of carbohydrate (1100 cm^{-1}), and a lesser amount of hydrocarbon (2950 cm^{-1}). Cleaning in this system at the time was a simple ambient temperature ultrapure water flush. The materials found on the fouling cells were insoluble compounds that resisted the high-shear, turbulent water flush. Lack of protein-based fouling indicated that bleach cleaning would not be effective.

Further work with a series of fouling cells showed the changes in chemistry as the fouling grew over time (see Figure 5). The bottom spectrum was the fouling

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Upcoming Events

January 2007

- 21st - 23rd **RMUG Conference**
  Location: Arlington, VA, USA
  WebSite: RMUG Registration Forms

February

- 7th - 9th **EM Database and Trending**
  Location: PDA-TRI
  WebSite: www.pdatraining.org
- 19th - 21st **PMF Open Conference on Compendial Issues**
  Location: Baltimore, MD, USA
  WebSite: www.highpeaks.us

March

- 5th - 6th **PMF Conference on Water Systems Microbiology**
  Location: Philadelphia, PA, USA
  WebSite: www.highpeaks.us

April

- April 1st - 4th **Annual Conference of the Association for General and Applied Microbiology (VAAM 2007)**
  Location: Osnabrück, Germany
  WebSite: www.conventus.de/vaam2007

Offering In-House Courses on Microbiology/Aseptic Processing:

- The Microbiology Network/High Peaks Associates http://www.highpeaks.us/in-house.htm
  Experienced in custom-designed courses for the lab or the manufacturing facility, including
  - GMP for the Microbiology Lab
  - Microbiology for Manufacturing
  - Microbiology for Management
  - Auditing the Microbiology Function
  - Investigating Microbiological Data Deviations
- USP
  Contact Steven Paul (stp@usp.org) for information on the course "Fundamentals of Microbiological Testing"

USP Corner

Any questions concerning USP documents should be sent to Radhakrishna (Radha) Tirumalai, Ph.D. You can reach Dr. Tirumalai at: (706) 353-4514, via mail at United States Pharmacopeia, 126 Twinbrook Parkway, Rockville, MD 20852 or via e-mail at RST@USP.org. You can write representing your company, or as an individual scientist.

RMUG™ Meeting

The Rapid Micro Users Group ™ (**RMUG ™**) will host its 5th Annual Conference at the Hilton Crystal City in Arlington, VA January 21-23, 2007. "Crossing The Finish Line-Achieving Rapid Micro Approval" is this year's headline theme. The conference is a rewarding educational experience with new and comprehensive Technology Workshops, Exhibits and Seminars covering hot industry topics such as: Process Analytical Technology (PAT), Rapid Biological Indicators, Recovery of Organisms for Identification, New USP and EP Publications, Real-Time PCR and Real-Time Immuno-PCR. Every year RMUG ™ attracts about 120 attendees, including Laboratory Scientists, Microbiologists, QA and QC Managers, Biology and Scientific Regulatory Affairs Managers from both large and small corporations, as well as a strong FDA presence.

Your registration fees include a beautiful Monday night Gala dinner at the National Geographic Museum, Cocktail Reception, Two Day Conference, access to all Exhibits and Technology Workshops, Breakfast and Lunch during the conference and two or three night hotel accommodations.

If you would like more information or have any questions, please contact a RMUG ™ representative at (800)966-8832 or rmug@vectech.com.

Discussion List Update

PMFList:
Number of Subscribers: 2,066
Number of Countries: 64
Number of Messages Last Month: 133

PSDGList (Pharma Stability Discussion Group):
Number of Subscribers: 885
Number of Countries: 23

Membership is FREE. To **join the PMFList**, visit http://microbiol.org/pmflist.htm and register.

A sister Email is devoted to topics in the **stability testing** of pharmaceuticals, medical devices and personal products. To **join the PSDGList**, visit http://microbiol.org/psdglist.htm and register.

You can ask, answer, or read questions and comments from your colleagues. Archives of the lists are available at:

- http://lists.microbiol.org/archives/PMFLIST.html
- http://lists.microbiol.org/archives/PSDGLIST.html

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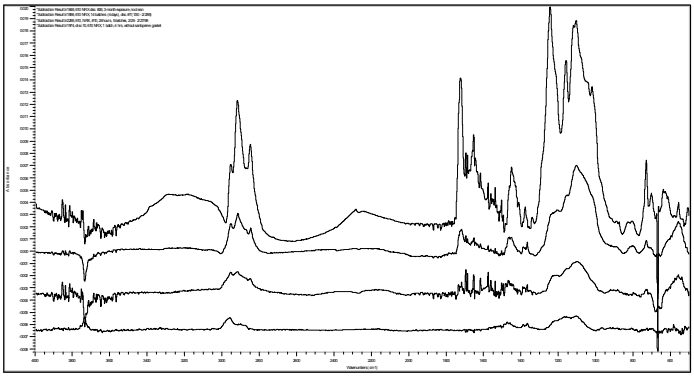
found after a single production run of about 6 hours. The next spectrum up was the fouling after 24 hours of production. The third spectrum up was the fouling after a week of production, and the top spectrum was the fouling after about 6 months of production.

Figure 5. FTIR Analysis of Biofilm Growth as a



Function of Time in Saltwater System

Through this sequence, changes in the fouling film can be seen. Initially, the fouling comprised primarily carbohydrate with a small amount of hydrocarbon. As the fouling grows, however, phthalated ester (1740 cm-1) begins to appear. By the end of six months, there is a small amount of proteinaceous material beginning to appear.

Epifluorescence optical microscopy at two weeks of exposure (Figure 6) shows minute, sub-micrometer-sized organisms and a great deal of exopolymer. It would appear that the harsh, high ionic strength environment in this transfer line led to the generation of a biofilm of uncultivable organisms and a thick insulating layer of polymer protecting the microbes.

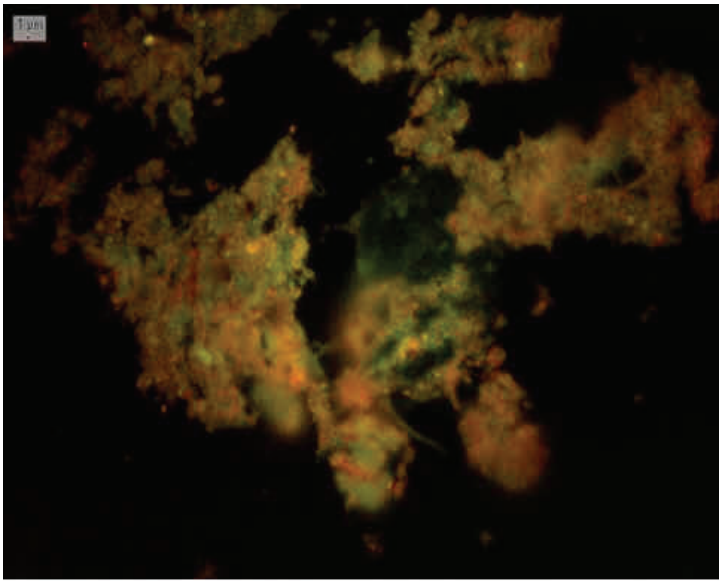


Figure 6. Epifluorescence Optical Photomicrograph of 2-Week Saltwater Biofilm on Stainless Steel (2000X magnification, acridene orange stain)

The functional groups found in the infrared spectra do not lend themselves to cleaning with bleach. Indeed, months of research discovered that the carbohydrate moiety was best controlled with high-shear water flush (see Figure 7). High-shear water flush reduced the carbohydrate peak by about 90%–this suggests that the exopolymer was a vertically oriented, three-dimensional film rising from the fouling cell surface.

The ester peak and the hydrocarbon peak were only 60% removed by the high-shear water flush. The epifluorescence image of this high-shear-cleaned biofilm can be seen in Figure 8. We concluded that water flush cleaning basically reduced the slope of the fouling curve, but did not return the system to the induction level of

Figure 7. High-Shear Water Flush Cleaning of 2-

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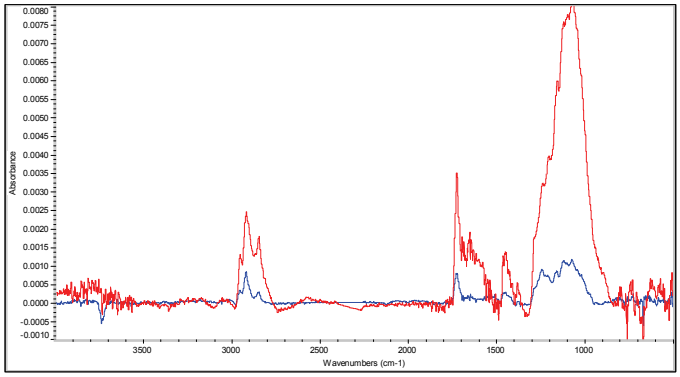
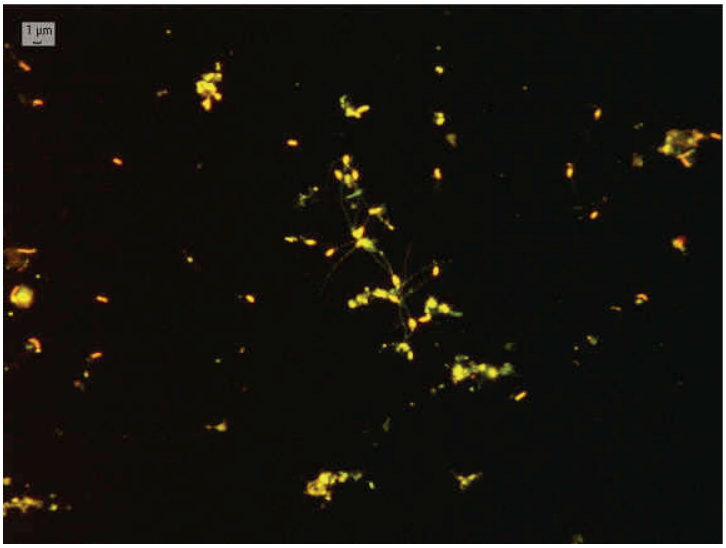


Week Saltwater Biofilm

fouling. This meant work had to be done on developing a chemical cleaning technique.

In the end, it was found that a strong inorganic acid was necessary to eliminate the ester and hydrocarbon functional groups, and an additional chemical treatment with sodium hydroxide was needed to fully eliminate the carbohydrate functional group.

Figure 8. Epifluorescence Optical Photomicro-



graph of 2-Week Saltwater Biofilm on Stainless Steel after High-Shear Water Flush Cleaning (2000X magnification, acridene orange stain)

The fouling cells also revealed (when correlated to product quality data) that this two-step chemical cleaning was needed only on a quarterly basis (data not

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Ideas and Topics for next year's PDA Global Conference on Pharmaceutical Microbiology

Fellow QC Microbiologists:

Last October over 300 professionals, involved in microbial testing, gathered in Bethesda, MD for the Parenteral Drug Association's (PDA) 1st Annual Global Conference on Pharmaceutical Microbiology. The program included sessions discussing Risk Analysis in Microbiology, Disinfectant Qualification, Industrial Practice in Microbial IDs, USP / EP / JP Updates, EM Data Management, and an "Ask the Experts" Panel Discussion.

I have been invited to participate on the Program Planning Committee for the 2007 meeting and I hoped you could provide me with your ideas and topics of interest that I can bring to our next committee teleconference as we design next year's meeting program.

Hopefully, this meeting can become one of the premier conferences for Pharmaceutical QC Microbiologists and the other professionals that support microbial testing activities. It can only become a success if we have program topics that are current, relevant and stimulating for the audience. We can only do this with your help and suggestions.

Thank you, in advance, for taking the time to provide your input. Hopefully, our program will encourage you to attend the PDA's 2nd Annual Global Conference on Pharmaceutical Microbiology in 2007.

Respectfully,
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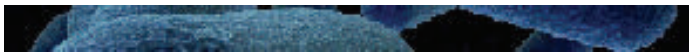


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shown). Further, the study found that the order of cleaning chemicals mattered. It is a simple task to use these tools to determine the effect of order of cleaning chemicals, as well as chemical concentration, temperature, and contact time.

Conclusions

This witness plate and surface analysis approach was developed to a very practical level at Kodak. Fouling cells were used to benchmark cleaning at Kodak's global sites, quantitatively documenting cleaning effectiveness for each site. Fouling cells were used in processes ranging from photographic emulsion manufacturing, film and paper photographic coating, to support manufacturing in both aqueous and solvent-based environments, and pure chemical transport systems (ultrapure water, pure solvents, strong acids and bases, etc.).

The result of this is the knowledge that fouling–including biofouling–can be detected, characterized and controlled using inexpensive tools. Fouling cells can:

- Determine the chemical fingerprint of biofilms and chemical fouling
- Determine the rate of biofilm formation
- Provide direction on how to best clean the process, physically and chemically
- Determine the most cost-effective frequency of cleaning

This process is practical for businesses with analytical capabilities, but can also be within reach of companies who contract out analytical services. Fouling cells can generally be designed to fit into nearly any manufacturing process. The combination of fouling cells and analytical measurements makes for a powerful means to control biofouling problems.

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About the Author

Mark Fornalik has been with the Eastman Kodak Company for 21 years, and headed up a systems cleaning/process contamination research team for 5 years. The team solved major production contamination problems at nearly all of Kodak's global manufacturing sites, and worked in both aqueous and solvent environments. Mark's current assignment at Kodak is as a product development team leader. Mark has also recently launched his own biofouling consulting business, Industrial Biofouling Science, LLC. Mark Fornalik has a master's degree in biophysics from SUNY/Buffalo, where he studied the surface chemical properties of protein and bacterial adhesion to surfaces. Mark can be reached at 585-750-8785 or markfor@rochester.rr.com

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- Assay Time-to-Completion
  How quickly?
- Cost of Consumables
  How much? Frequently the cost of consumables can soon dwarf the capital expense.
- Labor requirements
  Including the technological sophistication of the operators—can your technicians actually operate the equipment reliably?
- Size of microorganism identification database
  A major consideration. If you purchase two systems to cover identifications of unknowns, it is imperative to ensure that the databases are large and complementary; that is they both don't have the same organisms in them, but that they include many different ones as well.
- Facility requirements
  Obvious stuff like electrical and plumbing, but also less obvious concerns about RNA/DNA contamination and cleanroom issues.
- Compatibility with existing systems
  LIMS, workflow, *etc.*
- Need for physiological information
  Do you need to know if the organisms are capable of degrading your product components? You may want to use a system that will help determine this.
- Purpose
  - Routine ID
  - Investigations

  The use of the system may be different for different systems. A good system for routine work may not be the best for investigations, and vice versa.

In short, there are a wide variety of choices available to help with the identification of unknown organisms. It is important to define your specific requirements and to purchase the appropriate system to meet those needs.

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USP Discontinues Use of "Intent to Comment" Form

Beginning with the Jan/Feb 2007 issue of *Pharmacopeial Forum*, the "Intent to Comment" form has been removed from the back of the publication. Previously, the comment period for each issue of PF was 60 days. In 2005, the comment period was increased to 90 days. With this expansion in the comment period, it was no longer viewed as necessary or appropriate to routinely allow further extensions of time to comment through the "Intent to Comment" form. In order to ensure that comments on a proposed revision will be considered by the Expert Committee in determining whether and how a proposed revision should proceed, comments should be received within the 90-day comment period.

The 2007 Open Conference on Compendial Issues

PMF is starting the year with a strong conference. USP, JP and Pharm Eur have harmonized (almost) the Microbial Limits Tests; there are new water chapters underway, and this past summer saw 7 new chapters for microbiology in the USP.

Come to the PMF Open Conference on Compendial Issues to be held February 19-21 in Baltimore Inner Harbor (http://www.highpeaks.us/2007/openconf/) to discuss these changes with the people responsible for drafting the chapters and opinon leaders in the industry.

ABOUT THE CONFERENCE

The Compendia play a pivotal role in the activities of the qc laboratory, and industry input into their discussions is of enormous benefit to both their deliberations and the quality of the documents that result. PMF is providing an opportunity for the membership to meet in small groups with international representatives of the Compendia and Regulatory Agencies to discuss issues relating to laboratory operations (GMP) and the microbiological quality of finished products.

This is an unparalleled opportunity to benchmark your practices not only against other companies in the industry, but also against current regulatory expectations.

WHO SHOULD ATTEND

The meeting will be of particular interest to pharmaceutical microbiologists and microbiology laboratory managers, contract laboratory microbiologists and managers, pharmaceutical manufacturers, and individuals concerned with the regulatory aspects of microbial control.

All attendees will receive conference proceedings.

THE FACILITATORS

The conference facilitators will be drawn from the USP Committee of Experts in Microbiology and Sterility Assurance, the FDA (invited), the European Pharmacopoeia Microbiology Committee of Experts and thought leaders in the industry. Each discussion session (Feb. 20th) will provide an opportunity to bring your issues and concerns to the attention of the people who can make changes in the regulatory climate.

A partial list of facilitators includes:

- James Akers, Ph.D. - Chairman of the USP MSA; Akers and Associates
- Scott Sutton, Ph.D. - Vice Chair of USP MSA; Vectech Pharmaceutical Consultants
- David Porter, Ph.D. - Past Director, USP; Vectech Pharmaceutical Consultants
- David Hussong, Ph.D. - Chief Microbiology Reviewer, FDA/CDER; member USP MSA (invited)
- Dennis Guilfoyle, Ph.D. - Lab Chief, FDA/CDER; member USP MSA (invited)
- Sylvie Guyomard - Sanofi-Aventis, Pharm Eur, Microbiology Committee of Experts
- Radhakrishna Timuralai, Ph.D. - USP Staff Liaison to USP MSA
- Donald Singer - GlaxoSmithKline; member USP MSA
- TC Soli, Ph.D. - Solipharma Solutions; USP Water Committee member
- Ed Balkovic, Ph.D. - Genzyme
- Dona Reber - Wyeth Pharmaceuticals
- Len Mestrandrea, Ph.D. - Pfizer; member USP MSA
- Carole Genovesi - Genentech, Inc.
- Ken Muhvich, Ph.D. - Micro-Reliance LLC
- James Agalloco - Agalloco & Associates; member USP MSA