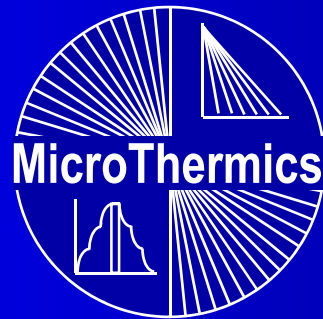


IFTPS 2012

**Aseptic Process Design Considerations-
Lessons Learned From The Pharmaceutical
Industry**



John J. Miles, Ph.D.
President

MicroThermics®

Some House Keeping

- Thank you to the IFTPS for allowing me to speak again this year.

Something Very Special

- MicroThermics received IFT Industrial Achievement Award for 2011.
- This is awarded for significant advancement in the application of food science and technology to food production.

IFT
2011
IAA



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Direct Indirect Processor-W

QuickTime™ and a
decompressor
are needed to see this picture.

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IFT 2011 Industrial Achievement Award

- Our goal has always been to put the process to the hands of the researcher.
- Thermally processed products have come a long way in the last few years.
- Thermal processing has never been more popular. Or reliable.
- MicroThermics® is delighted to be a part of this, and to have this recognized by the IFT.

Our Staff



MicroThermics®

The IFTPS Plug...



MicroThermics®

Some House Keeping

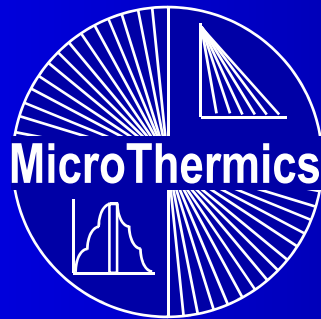
- The IFT Industrial Achievement Award
- Thank you to our clients...!
 - It is a privilege to do this work.
 - Facilitate learning and enabling development.
- What this means to us as thermal process specialists...

What Does This Award Mean To Us In The IFTPS?

- We often work at the technical forefront...
- The award draws attention to the need for our technical challenges to be properly considered.
- Obstacles that hamper our abilities also hamper our organizations.

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General Comments

- In my work with NC State, and MicroThermics, I have the luxury of exposure to a great deal of technologies.
- There are individuals with considerably more expertise in some of these areas, so I am sorry if I am preaching to the choir.
- My goal is to convey this information to help establish perspective and show opportunities for our technologies.
- Why? Because there are a lot of opportunities for our technologies and we need to understand that. MicroThermics®

Presentation's Purpose

- Broadly compare food and pharmaceutical aseptic technologies, and better understand
 - The basis for the differences,
 - The methods of sterilization
 - Standards of performance,
 - Where technology can be transferred.

Food Aseptic Technology (FAT)

- We are all pretty familiar with this...
- Largely limited to virtually the last step in manufacture. It's the final packaging step.
- Primarily uses thermal processes because food does not filter well.
- Primarily continuous flow thermal processes.

Pharmaceutical Aseptic Technology (PAT)

- Is a more general application of aseptic technologies across many more manufacturing operations.
- Part of the packaging operation.
- Not limited to packaging.
- Continuous Flow Thermal Processes (CFTP) are not as common as in the food industry.
 - Often an early process in the manufacturing plan.
- CFTP may be used in addition to filtration sterilization to inactivate viruses. (esp. For tissue and mammalian cell cultures)

PAT Compared to FAT

- For PAT, the focus is on small particle contamination as well as viable or microbial contamination.
- Even if a fluid has been sterilized, it still must contain no particle contaminants.

PAT Compared to FAT

- More extensive use of particle control using
 - HEPA filtration (remove 99.97% of particles ≥ 0.3 microns)
 - ULPA filtration (remove 99.999 particles ≥ 120 microns)
- Entire manufacturing areas may be class 100 or better.
- Influences the design of the building's structure to maintain 1"WC pressure differential.

PAT Compared to FAT -Materials-

- Pharmaceutical Aseptic Technology:
 - All 316SS contact surfaces
 - Highly finished surfaces, primarily electropolished.
 - Elastomers are all USP Class VI
 - Extremely low levels of extractables
- Food Aseptic Technology:
 - 316SS is prevalent
 - Wider assortment of contact materials.
 - Many of our elastomers are not required to be UPS Class VI.
 - Wider assortment of elastomers.

Product Assortment And Use

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Food Product Assortment And Use

- Foods (Fluids):
 - High Acid
 - Low Acid
 - Particulates (high acid then low acid)
- Most often eaten
 - Enters the body via the alimentary canal.
 - Protects the body.

Pharmaceutical Product Assortment And Use

- Very broad range
 - Topical
 - Optical
 - Nasal
 - Oral
 - Enteral
 - Parenteral
- Each involves risk factors associate with the body's normal protective mechanisms.

Pharmaceutical Product Use Considerations

Use	Sensitivity
Topical	-
Optical	High sensitivity to particles
Nasal	High sensitivity to particles
Oral	-
Enteral	-
Parenteral	High sensitivity to particles and pyrogens

Why Are The Use Considerations Of Pharmaceutical Products Important?

- Because they point out where opportunities exist.
- Example:
 - Suspensions of insoluble active agents are often used for optical and nasal treatment which have sensitivity to particles.
 - These cannot be filter sterilized because they are suspensions.
 - Autoclaving often contributes to particle enlargement.
 - Requires considerable secondary handling for correction
 - Continuous flow processing provides sufficiently short exposure times to maintain proper particle size.

Location Of A Continuous-Flow Sterilization Process In The Manufacturing Operation

- Food Aseptic Technology
 - Usually “Late Process”
 - Exceptions may be some high acid products.
- Pharmaceutical Aseptic Technology
 - Can be located anywhere in the manufacturing operation.
 - Early process locations tend to work with “dirtier” materials that will undergo many other purification steps. This may include another sterilization step.
 - Late process locations of CFTP are unusual.

Comparing Methods Of Sterilization

- Food Aseptic Technology
 - Thermal process
 - Continuous flow
- Pharmaceutical Aseptic Technology
 - Filtration for particles and sterilization
 - Autoclaving and filtration for particles
 - CFTP are becoming more popular but in carefully defined locations.

Standards Of Sterilization

- Food Aseptic Technology
 - Defined as the product being free of microorganisms capable of reproducing under the conditions of normal distribution.
 - 12D process requirement
 - Built-in assurance level of the 12D process
 - Designed-in assurance measures
 - Commissioning standard for failures of $<1/10,000$

Standards Of Sterilization

- Pharmaceutical Aseptic Technology
 - Difficult to find a defined process requirement like 12D.
 - Most commonly used performance standard is that of a 10^6 assurance level.
 - Identification of bio-burden which is usually very low.
 - Design the process to deliver the assurance level and validate that it does that.
 - Extensive validation and BI challenges before and after processing.
 - Commissioning standard for failures of $<1/10,000$

Sterility Validation Vs. Parametric Release

- Validation Release:
 - Requires that the process be challenged either during process or before and after to demonstrate that it has been effective.
- Parametric Release:
 - When a product is released as sterile, based on levels of critical process parameters that comply with pre-established conditions that have been demonstrated to be effective. (I.e. Flow rate, hold tube and temperature.)

The Release of Aseptic Foods is Virtually a Parametric Release

- Exception: One to two week storage requirement.
- Why is this used?
 - Summary test.
 - Not testing only the sterilization process but the entire operation.

The Challenge To Adoption of UHT-Style Process For Pharmaceutical Companies

- Continuous flow thermal process design is based on extrapolation in a process environment that excludes validation.
- This is difficult to actually validate because the biological indicator is virtually killed off before it enters the hold tube.
- The understanding of these techniques (UHT/Validation) and their degree of reliability is often a barrier.

Thank You!

For More Information Please Contact Us At:

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