PROCESS VALIDATION FOR SAFETY

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A more elaborate version of this article, with pictures, can be found at http://www.ifis.org/forum/sept_2002/validation.html

Food processors have long been accustomed to complying with safety regulations which define, for example, when cooking, pasteurisation or sterilisation procedures have been successfully achieved, with respect to inactivation of common foodborne pathogens. In these situations, process validation has already been performed and the role of food processors is restricted to showing regulatory bodies that the processing conditions known to ensure safety are strictly adhered to. Here, meeting the legal requirement for safety is achieved through *process control.*

Process validation, in contrast, is a new development. The emergence of new pathogens and the development of novel processing technologies, among other factors, have prompted regulatory agencies around the world to put in place comprehensive and powerful safety assurance strategies, based on HACCP, and requiring a more active participation of food manufacturers. As part of these strategies, food processors will be increasingly required to demonstrate that the processes they use are safe. This demonstration, referred to as *process validation*, is needed when a potential risk for the consumer has been identified and when appropriate operating conditions for processing safely are not precisely known.

Process validation generally requires access to specially designed facilities

Process validation generally involves introducing the target pathogen at specific stages of manufacturing and following its inactivation as further processing is carried out. In addition, regulatory agencies recommend that process validation be performed on substantial quantities (15-20 kg batches) of products, using industrial type equipment such as that found in pilot plants.

Because pathogen handling is required, special precautions need be taken to protect personnel involved in process validation studies, and to avoid spread of the organisms into the surrounding environment. These precautions are defined in government publications such as Laboratory Biosafety Guidelines, published by Health Canada (http://www.hc-sc.gc.ca/pphb-dgspsp/ols-bsl/lbg-ldmbl/index.html).

The level of protection required is dictated by classification of the pathogen concerned within the four biosafety risk levels (BSL1 to BSL4). In practice, virtually all foodborne pathogens are classified under BSL2. A few foodborne pathogens, however, have been classified in the BSL3 group, because of the low numbers of cells required to produce an infection (*Escherichia coli* O157:H7 in Europe, not in North America) or the high potency of their toxins (*C. botulinum*, during toxin production experiments).

In addition to standard handling practices required in a regular microbiology laboratory, special procedures are necessary to guarantee safety during process validation. Supervision must be carried out by a competent scientist or professional microbiologist and the personnel carrying out process validation must be aware of potential hazards and demonstrate proficiency in pathogen handling and decontamination procedures.

There is no official description of how a pilot plant for process validation should be designed. However, it should possess at least the following features, which are required in BSL2 microbiological laboratories:

- location separate from public areas
- biosafety warning signs
- incoming air flow which is not re-circulated to adjacent rooms
- availability of a large capacity autoclave nearby for disinfection of solid wastes.

Additional features normally required in a BSL3 laboratory environment should also be present, such as:

- use of double door entry
- limited access at all times
- covering of walls and floor (and ceiling, if possible) with water resistant material to withstand industrial type cleaning and sanitation procedures
- filtration of the outgoing air by a microbiological filter (e.g. HEPA)
- working area kept under negative pressure.

Finally, an effluent treatment system should be installed to prevent leakage of pathogens into the environment.

The whole room and the processing equipment it contains should ideally be dedicated to pathogen work and should be thoroughly cleaned and sanitized when production is complete, using adequate equipment.

Finally, an elaborate protective gear (such as heavy duty rubber boots, disposable paper coveralls with head covers, several layers of gloves, disposable mouth covers, and facial masks) is required in a pilot plant environment, in which the personnel in charge of product manufacture is in direct contact with heavily contaminated raw food, equipment and work surfaces.

A methodology that needs to be constantly refined

The method used in process validation studies is called *microbial challenge testing* and has already been critically reviewed (Notermans *et al.* 1993). Specific factors that have been found to affect the test results generally relate to the organisms selected for the test, the product manufacturing procedure, the inoculation procedure, and the manner in which results are evaluated. All these factors must be adequately controlled in order to avoid underplaying or overestimating the risk associated with a given process.

The choice of organism is generally simple. When known incidents of toxi-infections related to the process being investigated have occurred, the strains isolated from the contaminated food or patients affected should be the first choice material, along with similar strains from the same species, strains frequently isolated from the raw material entering the process, or from the typical work environment.

The procedure used to maintain the cultures is of the utmost importance. Pathogens isolated from contaminated food or from a processing environment may have developed a resistance to the specific combination of stresses to which they have been routinely submitted. In contrast, repeated culturing may result in loss of the acquired resistance. It is therefore recommended that cell viability and retention of characteristic properties be checked prior to undertaking process validation.

Preparation of the inoculum is also critical. Exposure to stress during preparation may result in subsequent loss of viability or an extended lag phase. In contrast, cells collected from a rich laboratory medium may be loaded with nutrient reserves, essential cofactors and enzymes involved in active growth, which may not have been present in the food processing environment. The effect may be minimised if cells are

grown in a product homogenate or in a synthetic broth with similar characteristics.

The appropriate inoculum concentration should be carefully chosen after initial trials, since concentration effects have been reported in the literature (Stiebing *et al.*, 1998). Whenever possible, the concentration normally expected in the raw product should be used, even though this may require using more sensitive, thus more demanding microbiological enumeration techniques, such as ISO-GRID or MPN, in order to detect the surviving cells.

The method of inoculation should also be carefully selected. We have shown that inoculating *E. coli* O157:H7 cells at the surface of beef trimmings 1 wk prior to manufacture of Genoa sausages (mimicking the state in which the pathogen likely enters the process under real manufacturing conditions) resulted in a greater extent of pathogen inactivation (approximately 1 $\log_{10}$ cfu/g more) than inoculation of the raw batter, as recommended by FSIS.

There is presently no rule on how process validation studies should be carried out with regard to product manufacture. Clearly, more research is needed in this area and only practice will indicate how to select a production scale that is large enough to be representative of a true industrial process, but small enough to avoid unnecessary costs and unmanageable experimental constraints.

Finally, greater attention should be paid to the manner in which validation results are evaluated. In general, assessment of process safety is based on the number of cells that can grow to form colonies on standard laboratory agars, with or without prior resuscitation on nutrient-rich media. This reveals little about the real ability of the pathogen to survive the human digestion process, to colonise the intestine, and to cause a disease. These considerations should be addressed by scientists involved in process validation studies.

Requirements for a better use of process validation

Unfortunately, while the need for pilot scale process validation is now recognised by regulators and food scientists, at the present time, very few facilities are available to carry out validation studies in the right environment and new facilities must be built in the near future to adequately answer a growing demand. Because process validation requires a good level of exchange and communication between the scientists involved and their industrial partners, the new facilities will have to be located in regions where food processors are most concentrated.

Process validation is expensive. Carrying out a process validation for fermented sausages with regard to *E. coli* O157:H7, following strictly the FSIS guidelines, takes about 2 months per process (including follow-up analyses) and has been estimated to cost around 8000 to 10 000 CDN $, essentially for labour fees; this excludes depreciation costs of infrastructure and processing equipment. This estimate closely matches the value calculated at the US National Center for Food Safety and Technology, i.e. 5000 to 6000 US $ (Dr. Chuck Sizer, personal communication). If process validation is to become increasingly frequent as a safety assurance tool, mechanisms have to be found to ensure that the cost involved does not become prohibitive.

Finally, clear, precise, and specific guidelines should be written for process validation. This will necessitate a major collaborative effort on the part of food scientists, food processors, and food regulators. New research may be required, as current knowledge of bacterial inactivation kinetics, measured in a laboratory environment, cannot be assumed to be always adequate to describe or predict the behaviour of pathogens in a processing environment.

References

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