

**PDA Journal of
Pharmaceutical
Science and
Technology**

Technical Report No. 36

**Current Practices in the
Validation of Aseptic Processing—2001**



May/June 2002

Supplement TR36

Volume 56

Number 3

Survey prepared, distributed, and compiled by:

James P. Agalloco, *Agalloco & Associates*

James E. Akers, Ph.D., *Akers Kennedy & Associates*

Russell E. Madsen, *PDA*

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Vol. 56, No. 3, May/June 2002, Supplement TR36

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Introduction

The validation of aseptic processing continues to be a major area of interest within the pharmaceutical industry. Five years have passed since the last PDA survey on this subject. While there have been no new broadly applicable regulations or regulatory guidance since that time, there has been continued controversy over the details of aseptic processing and process simulation practice. Industry practices largely adhere to current regulations and guidelines on aseptic processing by the European Union (1), ISO (2), and FDA (3). The impact of PDA’s TR #22 on “Process Simulation Testing for Aseptically Filled Products” (4) is also apparent.

Over time, industry methods, practices, and limits have been modified to adapt to the changing circumstances. The Pharmaceutical Manufacturers Association (now PhRMA) in 1979 (5) and PDA in 1986 (6), 1992 (7), and 1996 (8) conducted surveys on this subject that have provided a clearer understanding of contemporary industry practice. This survey addresses the continuing need to track industry practices in the validation of aseptic processing as it evolves.

Questionnaires were sent to eighty-eight (88) firms that specifically agreed to participate with PDA in this effort. Forty-three (43) responses were received representing both US and overseas locations. The results were tabulated to provide both raw numerical and percentage of total respondents. Where the respondents provided comments (whether solicited or given voluntarily), these comments are provided after the question. Where more than one respondent provided essentially the same response selection and comment, they have been consolidated and a number appears next to the response indicating the number of comments of that type. The nature and extent of the comments received were extensive, and for this reason, the authors have chosen to combine similar responses. One of the major benefits of surveying on a regular basis is the opportunity to follow the evolution of concepts and practices over time. To that end, this survey instrument used many questions that were nearly identical to those asked in 1992 and 1996.

PDA 2001 Aseptic Processing Survey

1. In what country, or state, is your Aseptic Processing Area (APA) located?

United States - 28 - California, Florida, Illinois, North Carolina, Pennsylvania, Texas (2), Indiana, Kansas, New Jersey, New York (3), US (4)

International - 31 - Australia, Canada, Italy, Spain, Sweden (2), England, France, Germany, Hungary, Indonesia, Ireland, Korea (3)

No answer - 2

2. What types of sterile products do you manufacture at this site? Please mark all that apply.

a. Large volume parenterals	10	23.3%
b. Small volume parenterals	36	83.7%
Solutions	16	37.2%
Suspensions	5	11.6%
Lyophilized	11	25.6%
Powders	9	20.9%
c. Ophthalmic and/or otic solutions	11	25.6%
d. Inhalation solutions	8	18.6%
e. Ointments	3	7.0%
f. Biologicals	14	32.5%
g. Products for veterinary use	5	11.6%
h. Medical devices - liquid based products	6	13.9%
i. Medical devices - non-liquid products	4	9.3%
j. Other - please describe	2	4.6%

Comments

- j. Drugs containing implants, control release devices
- j. Clinical supplies

3. How many different sterile product presentations (all strengths and fill sizes of all products) do you manufacture at this site?

a. 0 – 5	8	19.0%
b. 6 – 49	14	33.3%
c. 50 – 99	6	14.3%
d. 100 – 149	6	14.3%
e. >150	9	21.4%

4. What percentage of your sterile products is manufactured using aseptic processing?

a. Less than 25%	2	4.6%
b. 25% to 50%	5	11.6%
c. 51% to 75%	3	7.0%
d. More than 75%	33	76.7%

5. Is this percentage an increase or a decrease from five years ago?

a. Increase	7	16.3%
b. Decrease	5	11.6%
c. Same	31	72.1%

Comments

a. No production five years ago.

6. At your site, is aseptic processing used for products that could be terminally sterilized? (For the purposes of this response, consider "could be terminally sterilized" to mean a product and container/closure/delivery system that could withstand moist heat sterilization processes with a total accumulated F_0 of 8 or more minutes.)

a. Yes	14	32.6%
b. No	29	67.4%

If yes, what percentage of the aseptically produced products does this represent?

2% (2), 5%, 10% (2), 20% (2), 30%, 35%, 47%, 60%, 75%, 85%

Comments

a. We are manufacturing clinical supplies only, so information is not available at this time.

7. What percentage of your aseptically filled products contains an anti-microbial preservative that complies with pharmacopoeial anti-microbial effectiveness testing requirements?

a. None	14	33.3%
b. Less than 25%	11	26.2%
c. 25% to 50%	5	11.9%
d. 51% to 75%	4	9.5%
e. More than 75%	10	23.8%

Comments

b. The same product may be manufactured with or without preservative; depends upon whether they are for multi-dose markets, i.e., US states a multi-dose product will have a preservative. Single dose of same product -- no preservative.

d. All our products comply with USP but not with A criteria from European Pharmacopoeia; 60% comply with B criteria from *European Pharmacopoeia*.

d. Liquid >75%; Powder, none.

Release/Quarantine Practices

8. If a process simulation* action level is exceeded on a validated production line, what action do you take with regard to products manufactured on the line prior to the media fill failure?

a. Release	3	7.0%
b. Release after investigation	6	13.9%
c. Release only after an investigation indicates good process control and one or more successful additional media fills are conducted	33	76.7%
d. Other action - please describe	4	9.3%

Comments

c. Plus double sterility test.

d. Release only after investigation could assure SAL of products.

d. No formal procedure. Never occurred, therefore, no test case.

d. Normally, release after investigation; however, would depend upon number of contaminated units and types of organisms. Worst case: recall product.

***Note:** In this survey, the terms process simulation test, media fill, and media fill test are used interchangeably.

9. If a process simulation action level is exceeded on a line, what action do you take with regard to products manufactured on the line subsequent to the media fill failure?

a. Release	0	0.0%
b. Release after investigation	1	2.3%
c. Release only after an investigation indicates good process control and one or more successful additional media fills are conducted	39	90.7%
d. Other action - please describe	4	9.3%

Comments

- c. Plus double sterility and stop production.
- d. Release only after investigation could assure SAL of products.
- d. Lots rejected unless assignable cause can be determined that was not present during the processing of the product batches.
- d. Normally, release after investigation; however, would depend upon number of contaminated units and types of organisms. Worst case: recall product.

10. Is positive action taken against a certain number of lots or over a certain time period in the event of a media fill failure?

a. Yes - please specify number of lots involved before and after the failure.	7	17.5%
b. Yes - please specify time period involved before and after the failure.	15	37.5%
c. No - please describe your practice	7	17.5%
d. Other	11	27.5%

Comments

- a. All.
- a. Any product manufactured between filling trials and the date of the failure and subsequent batches must be held in quarantine until the investigation is complete. Aseptic product manufactured on the filling line, and still in company control, should be quarantined until investigation is complete.
- a. All unreleased lots before and after the failures are held until three successive media fills are performed and found to meet acceptance criteria.
- a. Three lots before and after.
- a. All lots after the failure.

- b. Investigation will be conducted on all batches of the last successful media fill; refer to QC for further action.
- b. All before the last media fill and all post.
- b. Before: Back to previous acceptable media fill. After: Lots filled after action limit and prior to obtaining satisfactory results for repeat media.
- b. Six months (2)
- b. Since the last successful media fill on the affected line (3)
- b. From previous media fill to the next media fill (3).
- b. Three months before failure and all lots after media fill are kept in QA.
- b. Depends upon the outcome of the investigation! Worst case scenario: all lots produced since the last approved media fill.
- c. No practice is in place due to manufacturing under development.
- c. Lots filled prior and post the failure will be dispositioned depending upon the outcome of the investigation. Lots filled post media fill are quarantined until investigation results are known.
- c. Hold lots for investigation and draft an action memo for released lots.
- c. Once investigation is concluded and corrective action taken, we return to normal production. Never occurred, therefore, no test case.
- c. Action would be taken on individual batches as far back and forward as necessary to fence in the issue, based upon the individual investigation. This could go all the way back to the previous media fill.
- d. Release only after an investigation indicates good process control and one or more successful additional media fills is conducted.
- d. Dependent upon outcome of investigation (2)
- d. No policy in place for this scenario; no history of failure.
- d. We stop the line until there are three successful media fills.
- d. Investigation reveals the source of failure and depending upon the type of source, the number of lots or time period are considered. If it is needed, recall for certain lots should be performed.
- d. Everything not yet released since the last successful process simulation test is placed on hold until the investigation is complete and a successful process simulation test is completed. (3)

11. Is positive action taken on production during a set period of time before and after a media fill failure?

- | | | |
|---|----|-------|
| a. Yes - please specify time period involved before and after failure | 18 | 45.0% |
| b. No - please describe your practice | 9 | 22.5% |
| c. Other | 13 | 32.5% |

Comments

- a. All periods involved.
- a. All before the last media fill and all post.
- a. Production is on hold pending investigation.
- a. Between current and previous media fill results (2).
- a. Aseptic production ceases on the affected machine until investigation is completed and satisfactory repeat filling trial has been completed. Repeat trial in triplicate on the container size implicated.
- a. Before: Back to previous acceptable media fill. After: Lots filled after action limit and prior to obtaining satisfactory results for repeat media.
- a. Six months.
- a. Going back to the last successful media fill. (3)
- a. Depends upon the outcome of the investigation! Worst case scenario: all lots produced since the last approved media fill.
- b. Depends upon investigation results. (2)
- b. Implement corrective actions based upon the outcome of investigation.
- b. No practice is in place due to manufacturing under development.
- b. Lots filled prior and post the failure will be dispositioned depending upon the outcome of the investigation. Lots filled post media fill are quarantined until investigation results are known.
- b. Once investigation is concluded and corrective action taken, we return to normal production. Never occurred, therefore no test case.
- b. Action would be taken on individual batches as far back and forward as necessary to fence in the issue, based upon the individual investigation. This could go all the way back to the previous media fill.
- b. After the failure only.
- c. Dependent upon outcome of the investigation (3).
- c. We stop the line until there are three successful media fills.
- c. It is difficult to take action before since we do not know that we have a failure.

- c. Hold lots for investigation and draft an action memo for released lots.
- c. If further investigation finds that there is a possible impact from equipment, facility, and/or personnel, re-qualification would be required.
- c. Everything not yet released since the last successful process simulation test is placed on hold until the investigation is complete and a successful process simulation test is completed. (3)
- c. All lots manufactured during the prior six months would be investigated then an appropriate action could be taken by QC, normally.

12. In the event of an unsuccessful* revalidation media fill test, how many consecutive satisfactory tests must be completed before the production line is considered re-qualified for manufacturing operations?

- | | | |
|----------------------------|----|-------|
| a. None | 0 | 0.0% |
| b. One | 1 | 2.3% |
| c. Two | 1 | 2.3% |
| d. Three | 37 | 86.0% |
| e. Other - please describe | 6 | 13.9% |

* The test fails to meet the acceptance criteria.

Comments

- d. If not able to invalidate media fill.
- e. One: In case of identified failure cause after correction action. Two: In case of unidentified cause.
- e. Based upon investigation, 1-3 may be performed.
- e. If reason for failure is known, one. If reason for failure is not known, three. (2)
- e. If cause of failure is known, one only. If cause of failure is unknown or uncertain, three. In all cases, an investigation is also conducted.
- e. One repeat if able to invalidate media fill.

Frequency

13. Do you routinely conduct revalidation media fills on each filling line or machine on a regularly scheduled basis?

- | | | |
|---------------------------------------|----|--------|
| a. Yes | 43 | 100.0% |
| b. No - please describe your practice | 0 | 0.0% |

Comments

- a. We do it quarterly, but the process used is not determined in order to cover all processes.

14. If yes, how often?

a. Weekly	0	0.0%
b. Monthly	0	0.0%
c. Every other month	0	0.0%
d. Quarterly	2	4.6%
e. Semi-annually	36	83.7%
f. Annually	4	9.3%
g. Other - please define	1	2.3%

Comments

- e. At minimum, each line typically has five or six due to new product container closure systems.
- e. At least two media trials per year. However, to validate/re-qualify operators, many lines are performing up to six trials per year.
- g. Every fourth month.

15. If a sterility test failure occurs, does this failure initiate a media fill test on the line that manufactured the product that failed the sterility test?

a. Yes	12	27.9%
b. No - please describe your practice	7	16.3%
c. Sometimes - please explain the decision factors that would lead your firm to require a re-validation media fill test to clear a sterility test failure	24	55.8%

Comments

- b. Initiates investigation and exception reports. (2)
- c. After investigation: lab failure = retest; no lab failure = batch rejected.
- c. Depends upon results of investigation and if additional controls were positive.
- c. Based upon investigation findings. (7)
- c. If the investigation determined the root cause to be a failure in design or practice requiring significant change. (2)
- c. Response to product test failure requires investigation covering sterility testing and production records/environments. Outcome of the manufacturing investigation indicating production environment/procedure may result in a media trial. (2)
- c. Investigate to exclude analytical error or if some obvious event has caused the failure.
- c. Cross-functional team assembled to investigate. Findings would decide if additional media fill necessary.

- c. If no assignable cause found.
- c. QC management would assess the aseptic production area and determine a probable cause. If no assignable cause was found, a media fill would be requested.
- c. EM monitoring data, sterile cleaning practice, sterilizing cycle, DOP, Royco of HVAC, LFs, education, new operators.
- c. Decision to conduct a media fill is based upon the results of the sterility test failure investigation.
- c. If no cause can be identified from lab error or process error, a media fill test may be carried out.
- c. Investigation into failure conducted against machine and batches taken if warranted.
- c. May require that production be stopped on the line. Depends upon results of investigation of sterility test failure.
- c. No revalidation is performed if a lab error is the cause of the failure.
- c. If aseptic processing.
- c. If cause is assigned to line failure.
- c. An investigation will be initiated. If the investigation doesn't show that the failure is due to a lab contamination, all steps in production will be checked. Depending upon the results, an evaluation will be done if a new media fill is necessary to verify that the process is under control. For example, an upward trend of microorganisms in the APA or a recently failed media fill could lead to a revalidation.
- c. Would depend upon type of organism and if any other failures from same line, e.g., two sterility test failures with anaerobic organisms – have investigation and anaerobic media fill.

16. How are your media fill tests distributed among different shifts?

a. Equally distributed across shifts	32	74.4%
b. Distributed according to production volumes	5	11.6%
c. No - please explain	6	14.0%

Comments

- c. There is only one shift. (5)
- c. In some areas, media fills are performed which cover shift changeover. In other areas, because of their design and need for only one operator, we have a rationale that states shift changeover has no impact on integrity of process.

17. Are all aseptic fill and set-up personnel included in the process simulation program?

- | | | |
|--|----|-------|
| a. Yes - on an annual basis | 34 | 79.1% |
| b. Yes - please specify frequency | 7 | 16.3% |
| c. Other - please describe your practice | 1 | 2.3% |

Comments

- a. Vial size on rotating basis.
- b. Semi-annually. (6)
- c. Frequency depends upon type of intervention.

18. Are personnel, including new hires, qualified to operate in the APA through participation in a media fill test?

- | | | |
|--|----|-------|
| a. Yes - using participation in an actual process simulation | 31 | 72.1% |
| b. No - please describe your practice | 12 | 27.9% |

Comments

- c. They are qualified performing the job, but a media fill is not scheduled to complete their qualification. They will participate in the next scheduled media fill if a media fill is not scheduled at completion of their qualification.
- c. Operator certification program for aseptic technique and gowning, as well as GMP training. Due to media fill frequency operators generally participate in media fills within about six weeks of employment.
- c. No practice set up yet. Intention to make them qualified with media fill as one part of the qualification.
- c. Using a "hand fill" simulation.
- c. New hires are trained to work in aseptic processing areas via SOPs and on-the-job-training. They are cycled into media program after initial training has been completed.
- c. We perform a specific training program and final validation in accordance with the SOP.
- c. Qualification of an operator is based upon training for gowning and aseptic practices. The operator can then operate in the aseptic processing area and participate in the next media fill.
- c. New operators are scheduled for the first available media fill.
- c. Prior to entering the APA, employees must pass a "broth test" in a lab environment demonstrating

good aseptic technique, then successfully participate in a process simulation study.

- c. Process uses barrier technology, therefore, personnel participate in the media fills, but they are not qualified.
- c. Gowning certification only.
- c. Gown qualification, personnel monitoring, media fill within six months.

19. How many media fill tests must a new hire participate in to be considered qualified to work on a specific validated process?

- | | | |
|-----------------|----|-------|
| a. None | 13 | 30.9% |
| b. One | 28 | 66.7% |
| c. Two | 0 | 0.0% |
| d. Three | 2 | 4.8% |
| e. Four or more | 0 | 0.0% |

Comments

- b. All training related to aseptic behavior.
- b. But must perform all critical activities.
- b. Plus micro training, aseptic training, and repetitive (3x) gowning assessment.

20. If different filling set-ups and/or closure systems are utilized on a filling line, will your process simulation program address all combinations?

- | | | |
|---------------------------------------|----|-------|
| a. Yes | 30 | 71.4% |
| b. No - please explain your rationale | 12 | 28.6% |

Comments

- a. On a rotating basis according to product.
- b. Initial qualification would be yes, but routine re-qualification would be about largest and smallest.
- b. Worst case conditions will be investigated.
- b. One simulation trial to one filling line.
- b. Bracket the largest/smallest vial/closure combinations. (2)
- b. Different lines have different combinations to bracket all.
- b. Because we are in research, it is changing all the time.
- b. We only do the minimum and maximum fill, based upon line speed.
- b. All formats are covered; not all stoppers.
- b. Worst case, large vial openings – most difficult fill set-up.

21. Does your firm employ a minimum time duration for media fill tests?

a. Yes - not less than 1 hour	4	9.3%
b. Yes - not less than 2 hours	1	2.3%
c. Yes - not less than 3 hours	2	4.6%
d. Yes - four hours or more	1	2.3%
e. Yes - duration of fill process	16	37.2%
f. Yes - minimum number of filled containers	24	55.8%
g. No - please describe your practice	6	13.9%

Comments

- d. Typically, 8-16 hours.
- e. Including all worst cases.
- e. "Start-Stop" Approach: Actual minimal fill time is not more than three hours.
- f. 6,800 units
- f. Would normally fill for length of typical production shift. $\leq 6,300$ units processed to cover all production intrusions.
- g. Both: minimum number of units to fill and the whole duration of the process.
- g. NLT to 60% of filling process duration.
- g. Duration of the longest filling time.
- g. Simulate 1-1/2 hours of empty running during some of the challenge.
- g. Plus necessary time for simulations.

Methods

22. Is the fill volume of media employed the same as that utilized in production?

a. Yes	18	45.0%
b. No - container size is too large	2	5.0%
c. No	20	50.0%

Comments

- c. Half volume of a vial. (4)
- c. Volume of media is greater than product fill (2).
- c. Vial volume sufficient to promote growth.
- c. Sufficient media is added to ensure one-half of the vertical surface of container is covered. Units inverted during incubation.

23. Do you utilize the same filling line speed for process simulations as that utilized in production for that container?

a. Yes	20	46.5%
b. No - speed equal to slowest normal fill speed on that line	15	34.9%
c. No - speed equal to the highest normal speed on that line	2	4.6%
d. No - other speed - please explain	9	20.9%

Comments

- b. Re-qualifications.
- b. Majority of cases slowest (longest dwell time).
- c. On certain high-speed fillers, >300/minute (highest) is deemed worst case; units fall over and there are more interventions.
- d. The line speed is lower than the standard speed due to the necessary equipment to dose the media and represent worst case.
- d. Process simulations require at least 25% of fill at minimum speed, 25% normal/routine speed, 25% maximum speed.
- d. Currently, slower than normal production speed is used. In the future, this process and normal production speed will be used.
- d. Initial Performance Qualification utilizes minimum speed and approximate production speed.
- d. Slowest filling speed and at the end of test, highest speed.
- d. Combination of B and C.
- d. Slowest speed for largest container and fastest speed for smallest container.
- d. Slower and faster speeds are used during the challenge.
- d. The speed that is considered as worst case for each container size.

24. Do your process simulation trials include inert gassing if used in production?

a. Yes - using Fluid Thioglycollate medium and nitrogen	3	7.0%
b. Yes - using Soybean Casein Digest medium and nitrogen	4	9.3%
c. Yes - other method - please explain	15	34.9%
d. No - please explain	23	53.5%

Comments

- c. Using Soybean Casein Digest medium and compressed air. (3)
- c. Using compressed air in place of N₂ with SCDM.
- c. Compressed air. (4)
- c. Sterile filtered air as part of production process.
- c. Soybean Casein and oxygen.
- c. Soybean Casein Digest medium and nitrogen.
- c. TSP medium and nitrogen.
- c. SCDB and compressed air to simulate inert gas. (3)
- c. Inert gas is exchanged with air.
- d. Not used. (3)
- d. Soybean Casein Digest medium without nitrogen.
- d. Is considered worst case using air.
- d. Compressed filtered air.
- d. Inert gas is not used.
- d. SCD broth.
- d. Purge needles, tubing, etc., installed; no gas used.
- d. Inert gassing is not used in production.
- d. During media fills that simulate processes utilizing nitrogen, sterile filtered air is utilized due to inhibitory microbial nature of nitrogen.
- d. Inert gas replaced with air for duration of media fill(s).
- d. Pressurized air is used instead of nitrogen, as our production lines apply both techniques (air and nitrogen).
- d. No gassing.
- d. Replace N₂ with compressed air to increase the challenge for growth.
- d. Inert gases are not used to prevent product degradation or exposure in our process.
- d. Sterile filtered pressurized air instead of nitrogen.
- d. Use SCD and compressed air.

25. Will the number of samples used in a process simulation vary from line to line?

- | | | |
|-------------------------|----|-------|
| a. Yes - please explain | 15 | 34.9% |
| b. No | 28 | 65.1% |

Comments

- a. >6,300 units
- a. Only one line. (3)
- a. NLT 6,000 vials.
- a. Depends upon batch size.
- a. One of four lines fills at a faster speed.

- a. Depending upon the speed of the machine.
- a. Depending upon challenge time and production complexity.
- a. Conventional: NLT 10,000; high speed: NLT 30,000; FFS: NLT 15,000.
- a. In order to respect the minimum one-hour fill, high-speed line tends to have more samples filled.
- a. Minimum of one-hour filling and 3,000 units, whichever is greater for each shift.
- a. Depends upon commercial batch size.
- a. Actual number attained is dependent upon line speed with a minimum yield targeted.
- a. Higher speed lines are challenged with higher numbers of units.
- a. If aseptic fill is validated for two days, the amount is doubled.
- b. Normally >6,300; exception is high-speed ampoule m/c – 10,000 units.

26. Which media do you utilize for process simulation trials on a regular basis?

- | | | |
|---------------------------|----|-------|
| a. Soybean Casein Digest | 39 | 90.7% |
| b. Fluid Thioglycollate | 3 | 7.0% |
| c. Other - please specify | 1 | 2.3% |

Comments

- c. SCD with HEC or HPMC for ointment or gel lines

27. Do you use exactly the same compounding and filtration equipment in conducting a media fill test that you use in actual production?

- | | | |
|----------------------------|----|-------|
| a. Yes | 33 | 76.7% |
| b. No | 6 | 14.0% |
| c. Other - please describe | 4 | 9.3% |

Comments

- c. Additional pre-filters are used.
- d. The same fill line equipment used, however, additional equipment is necessary for the media fill dosing.
- d. Same compounding equipment and filter housings, but no filters.
- d. Filtration is the same; compounding as close as possible.
- d. The same filling equipment is used, but not the solution preparation equipment. (2)

28. When performing process simulation trials, do you retain sterile media in sterile holding vessels to simulate standard manufacturing holding times prior to filling?

a. Yes	30	69.8%
b. No	13	30.2%

Comments

- a. Annually.
- a. Overnight approach.
- b. Yes, during the initial qualification of new product.
- b. Separate ventilation.
- b. No sterile vessels.

29. Do you inspect the filled containers prior to the end of the full incubation period (14 days)?

a. Yes - once after seven days of incubation	25	58.1%
b. Yes - once, please specify number of days of incubation	1	2.5%
c. Yes - twice, please specify number of days of incubation	3	7.5%
d. Yes - three times, please specify number of days of incubation	6	15.0%
e. No	8	20.0%

Comments

- a. Eye drops.
- b. 14 days
- c. 7 days and 14 days (2)
- c. 3 days and 7 days
- d. 1, 4, 7, 10, 14 on a routine basis.
- d. 2 or 3, 6 or 7, 14 (2)
- d. 3, 7, 14 (2)
- d. 3, 5, 14
- e. If containers are opaque.
- e. Ophthalmic ointments.
- e. Only in cases of special problems, an additional inspection after seven days is performed.
- e. Inspected prior to incubation and after 14 days.

30. Does your process simulation program include the following routine interventions?

a. Weight/fill volume adjustment		
Yes	38	88.4%
No	4	9.3%
N/A	0	0.0%
b. Component replenishment		
Yes	34	79.1%
No	4	9.3%
N/A	0	0.0%
c. Filter change		
Yes	21	48.8%
No	16	37.2%
N/A	4	9.3%
d. Filling needle change		
Yes	30	69.8%
No	7	16.3%
N/A	3	7.0%
e. Operator breaks		
Yes	40	93.0%
No	2	4.6%
N/A	0	0.0%
f. Change in filling vessel		
Yes	21	48.8%
No	19	44.2%
N/A	2	4.6%
g. Component change		
Yes	20	46.5%
No	16	37.2%
N/A	3	7.0%
h. Powder can changes		
Yes	12	27.9%
No	16	37.2%
N/A	12	27.9%
i. Dosing wheel, dosing disc changes		
Yes	13	30.2%
No	18	41.9%
N/A	10	23.2%
j. Powder hopper changes		
Yes	6	13.9%
No	21	48.8%
N/A	12	27.9%
k. Operator change		
Yes	40	93.0%
No	1	2.3%
l. Other - please specify		
Yes	17	39.5%
No	5	11.6%