



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Nashville District Office

6/15/98  
418496

297 Plus Park Boulevard  
Nashville, TN 37217

*Quayle 6/8/98*  
*JEA*

June 8, 1998

CERTIFIED-RETURN RECEIPT REQUESTED

Mr. Harry Boon  
Chief Executive Officer  
Ansell International  
Two Industrial Way West  
Eatontown, NJ 07724

WARNING LETTER - 98-NSV-16

Dear Mr. Boon:

During an inspection of your firm located at 1500 Industrial Road, Dothan, Alabama, on January 27 - February 12, 1998 our investigators determined that your firm manufactures a variety of spermicidally and plain lubricated, and non-lubricated natural latex condoms. Latex condoms are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above-stated inspection revealed that these devices are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Current Good Manufacturing Practice (CGMP) requirements of the Quality System Regulation (QSR), as specified in Title 21 Code of Federal Regulations (CFR), Part 820. The 1978 Good Manufacturing Practices (GMP) for Medical Device Regulations were superseded on June 1, 1997 by the Quality System Regulation. Since some of the records reviewed were dated prior to June 1, 1997, the deficiencies noted during the inspection are cross referenced to the 1978 GMP.

The inspection revealed the following deviations from 21 CFR Part 820:

1. You have failed to assure the preparation of a device master record to control the manufacture of the "Lifestyles \* X-tra Pleasure™ " condom, otherwise referred to as the "baggy" or "baggy" condom. Elements of the device master record, such as approved and complete design drawings and specifications, and

manufacturing specifications specific to this condom were completely absent from the established Ansell Incorporated Policies/Procedures Specifications.

2. The Corrective and Preventive Action - Level 2 Procedure, Number 0914 which you have established did not clearly require the implementation of corrective actions for significant process failure, or even specify what constitutes a significant process failure. Furthermore, reports prepared under this procedure, specifically condom dipping non-conformances, failed to include required information such as:

- a. the exact nature of the identified problem,
- b. the probable cause(s) of the failure,
- c. what corrective actions were taken, and
- d. whether or not the corrective actions were effective.

In fact, records related to dipping failures on condom machine 10, sides 1 and 4, and machine 24, side 2 during April through May 1997, and December 1997 through January 1998, respectively, disclose that Ansell, Inc. continued to process condoms on these machines in the face of continuing original and aged air inflation failures over extended periods of up to a month with no resolution of the problems. Furthermore, it is not evident from the records that the exact nature of the problems was even completely reported to the firm's senior managers in a timely manner.

3. Your firm has used the process of "skip lot" testing for original and aged air inflation, and tensile testing of condoms since on/about June 19, 1995. Using this procedure, only one of five lots of condoms are routinely subjected to air inflation and tensile testing after five lots in a row of the product have passed. You have failed to substantiate the validity of this test procedure by reference to any statistically valid body of historical testing data that would have justified its use. In fact, the F52 "baggy" condom, which entered manufacture in November 1997, was placed on the skip lot testing program after only 5 production lots had been manufactured. Furthermore, your firm's records show that, in at least one instance, a major change in the nature of the product being dipped (a change of product to F52 Black on machine 10 side 4 on May 26, 1997) did not result in testing of the next five lots as required by the procedure.

4. Your firm failed to follow its ~~own~~ complaint review procedures in five identified instances by not conducting and reporting a complaint history search of the subject lot to determine if

five or more complaints had been received. For lots # 50803000, 610700100, 408021100, 412028200, and 606254500, five or more complaints had been received, but no report of this fact was recorded to the Quality Assurance Manager, Regulatory Affairs manager, or Director Consumer Products Operations North America, as required by Revision #10 of the Complaint Management System procedure, # 9012.

5. Complaint investigation and reporting procedures at Ansell, Inc. are further deficient in that:

a. Three complaints (EOC060/9480, EOC060A/9481, and ASC108-/9391) were not fully investigated to include review of the pertinent device history records, despite the fact that the samples of product returned with each complaint demonstrated defective latex and a high water testing failure rate. The reported decision in each case was no corrective action.

b. Complaint # ANC219/9066 remained open with no reported activity since August 29, 1997. The Complaint Management System procedure effective at the time required issuance of a request for information to the evaluator if no activity was reported within 30 days. No such request was issued.

6. You have allowed continued condom manufacture without appropriate established production and process controls to assure that condoms manufactured at Ansell, Inc. conformed to the established specifications. The following are some examples which were observed by our investigators of inadequate control of condom manufacturing:

a. There was no established procedure for manually controlling the initial heat conditioning of latex in the compounding process if the process line controller (PLC) failed.

b. The record used to report the compounding of latex failed to include the date the Phase II compounding procedure starts. Because the hold time for latex before it is used for dipping is dependent on the beginning of the Phase II procedure, and can extend over multiple days, the lack of a beginning date in the record creates potential ambiguity in the allowable hold time.

c. Latex lots which did not meet the firm's specifications for chemical stability, among other things, were nevertheless used to compound latex for production without any clear explanation in the device history record of why this practice was acceptable. In fact, two such lots (3261 from ~~XXXXXXXXXX~~, and NNT10 from ~~XXXX~~ and ~~XXXXXXXXXX~~), both of which had high numbers for chemical stability, were used together to blend latex for multiple finished condom lots

despite the fact that the Materials Review Board review for lot NNT10 had specifically stated that it would be blended with a lot of low chemical stability to achieve the necessary specification. This action was not explained in the record.

d. Shift supervisors did not enter information regarding process deviations and on-the-spot corrective actions into the shift journal at the time these activities occurred. Nor were shift journal entries specific for each condom line or machine side when a general failure resulted in multiple problems across several or all production lines. The information related to process deviations was not incorporated into the device history record for each affected lot.

e. There were no established procedures to govern restarting either the dip lines or the electronic test machines in the event of a complete power failure as happened on the first day of the inspection. In each instance, there are a number of tasks required to be performed to assure that potentially defective product doesn't escape control, and that the restarted equipment is performing properly.

f. The Preventive and Corrective Action - Level 2 procedure did not require or provide guidance for when to initiate reporting of ongoing known process deviations that do not result in Quality Control test failures. This was exemplified by a packaging machine failure, on the ~~XXXXXX~~ #4 machine, brought to the attention of our investigators on February 5, 1998. The deviation, which caused seal failures and scrapped product, and ultimately required engineering intervention, had not been reported, other than by minimal entries in the machine log, after persisting for three operating days.

7. You have failed to establish appropriate procedures to assure that computerized processing control systems and data storage systems used in the production and quality systems at Ansell, Inc. are secured and managed to assure the integrity of processes and data that could effect the conformance of the condoms to established specifications. Examples of such failure include the following:

a. You have failed to establish management approval procedures for software installed on PLC's which control major process functions throughout the plant including compounding, condom dipping, and electronic testing.

b. You have failed to assure the retention and security of captured processing data from the compounding PLC in that no backup power supply was provided for the desktop computer used to capture, store and process the data.

c. The PLC controlling compounding had neither physical nor password access controls to prevent unauthorized access to set point changes.

d. The master programs for each PLC are not clearly named or otherwise related to the pertinent PLC's, either as stored on the engineering computer hard drive or by any other listing, to assure they can be properly retrieved to evaluate system problems or to prepare updates. Ansell, Inc. had no established procedure to control the secure retention of these master programs, or to identify and retain all versions as updates are written.

8. You have failed to establish procedures to assure that computerized documents which form part of the device master record and/or the quality system record are prepared and approved as required by document control provisions of the Quality System Regulation at 21 CFR 820.40. Examples of such failure are as follows:

a. Primary engineering drawings for manufacturing equipment used in condom production, and for the devices themselves are stored in AutoCAD form in a desktop computer. These drawings are not stored in approved hard copy, or otherwise approved form. The storage device was not protected either mechanically or by password control from unauthorized access and modification of the drawings.

b. Changes to engineering drawings and specifications were not approved or otherwise controlled.

c. Ansell, Inc. Procedure number 9003 for Writing, Approving, Distribution and Control of Procedures and Policies did not specify that electronic copies of procedures, policies and specification must be verified against the approved hard copy before being placed on the ~~network~~ network for general floor distribution. Nor did any procedure specify the task necessary for controlling this distribution to assure the documents were properly installed in the secured hard drive for read only distribution.

- We acknowledge that Mr. Lon McIlvain of your firm has submitted to this office responses dated February 25, March 13, and April 1, 1998 concerning our investigator's observations noted on the form FDA 483. We have reviewed your responses and have concluded that they are inadequate. You need to further address the specific inadequate items which we have cited below:

Your response to Item #1 of the Inspectional Observations is incomplete. The Ansell procedure #9028, revision 04, Design Drawing Control System will not adequately address the problems

cited in that, it does not specify that either all drawings will be approved in hard copy, or otherwise explain how drawings stored only in electronic format will be approved, i.e. electronic signature, approval code, etc.. Nor do the backup and storage procedures specifically assure that a copy of each approved version of a design drawing is retained either in hard copy or in the CDROM backup storage system.

We do not agree with your response to Item #4. The skip lot air inflation testing procedure, as implemented by your firm, remains unacceptable. You have failed to submit any evidence of statistically valid data relative to the compliance of your specific products. Valid data should take into account the physical and manufacturing differences of each significant product group. We have, to date, not been presented with such evidence. For this reason, we find that those lots which have not been subject to the full complement of quality assurance air inflation tests are in violation of the law.

Furthermore, current revision #13 of Ansell procedure #6316, Air Inflation Testing, does not adequately correct the problems addressed in Item #5 of the FDA 483 in that the specific hold time required prior to testing is indeterminate. Only the minimum is stated with no iteration of the rationale for shorter or longer hold times, requirements which will certainly impact the success of the testing procedure for any given lot. We also find no provision in the procedure for retention of all results for the testing of all samples, including those which failed.

Additionally, in reviewing the revised procedures submitted with your responses to Items #5 and #33, we noted that there is significant inconsistency in the sample sizes cited in the different versions of procedure #6316 and #4310, Condom Process Control/Classification Procedure For Dipping, Extracting, Drying Process and Lot Formation. Some of the inconsistency with regard to procedure #6316 certainly derives from the different dates of response, as the procedure was revised twice during the response period. However, the differences between the sample sizes cited in Revision #13, procedure #6316 and Revision #19, procedure #4310 remain without explanation. We would expect to see an explanation for variation in cited sample sizes ranging from ~~100~~ pieces to ~~1000~~ pieces for essentially the same battery of tests.

Your response to Item #7b does not appear to answer the inspector's observation, as written. The inspector was addressing the fact that the information on the MDRS Complaint Form was incorrect in that the Complaint Evaluation Form for the same complaint showed that the samples were water tested, not air tested, and the number of failures differed in the record. If, however, the factual substance of your response is correct in that air inflation tests were performed, copies of those results should be

maintained in your MDR files and none were observed during the inspection.

Your response to Item #11 is inadequate in that it violates the intent of the complaint reporting requirements in the QSR. We do not agree with your stated intent to not record complaints from foreign sources which do not initially include complete information for follow-up. Failure to record and conduct reasonable follow-up investigation of all complaints, including from foreign sources, could result in failure to obtain and evaluate information that would reveal product defects with impact not only on lots distributed overseas, but on related domestically sold lots.

In your response to Item #14, Revision #4 of Ansell, Inc. Procedure #2124, Compounding Materials Disposition and Rework, should positively state that the reworked material may be released for further manufacturing only if it complies with the appropriate specifications and is released according to normal release criteria for that material.

Your response to Item #17 is inadequate in that it does not fully explain or illustrate why you believe it is impractical to physically protect the set point controllers by installation of locked covers or other barriers to unauthorized access.

The draft procedure for managing access to the ~~network~~ network, which is cited in your response to Item #28 of the Inspectional Observations do not seem to address the responsibility for notification of the Information Technology Department regarding the change of status of employees requiring review of access rights.

All other completed corrective actions reported to this office in the noted response letters appear to adequately address the Inspectional Observations to which they pertain. The currently proposed schedule of completion for those items reported as incomplete is satisfactory. We will expect additional correspondence to address those items upon their completion.

Additionally, the above stated inspection revealed that your devices are misbranded within the meaning of Section 502(t)(2) of the Act in that your firm failed to submit information to the Food and Drug Administration as required by the Medical Device Reporting (MDR) Regulation, as specified in 21 CFR Part 803.

Ansell, Inc. failed to file seven (7) of the thirteen (13) MDR reportable complaints it submitted to the Food and Drug Administration during Fiscal Year 1997 within the thirty day time limit required for such reports.

Your response to Item #6 does not provide an adequate explanation for the failure to report MDR events within the required 30 day time frame as follows:

(1) "...personnel qualified to assess MDR reports are not aware of the complaint"

Manufacturers are considered to have "become aware" when any employee becomes aware of an event that is required to be reported within 30 days or required within 5 days pursuant to a request from FDA [see 21 CFR 803.3(c)]. The only exception to this are 5 day reports required by 803.53(b).

It is your firm's responsibility to establish and implement procedures to ensure that MDR reports are identified and forwarded to appropriate staff for review/decision making [see 21 CFR 803.17(a)(1)]. The 30 day time frame starts the day after a firm's employees become aware of information reasonably suggesting that a reportable event has been received. Firms cannot wait to start the reporting clock until designated MDR review staff eventually receive or become aware of information that "reasonably suggests."

(2) "...samples for evaluation did not arrive until after complaint receipt"

The availability of samples does not affect when a firm becomes aware of an event that "reasonably suggests" or when the 30 day reporting time frame starts.

(3) "...a decision for MDR reportability potential cannot be made until after extensive investigation"

When a firm is in receipt of information that "reasonably suggests" obtaining samples and "extensive investigations" can be useful in confirming that a "reasonably suggested event" did, in fact, occur. However, the standard for MDR reporting is that the device "may have caused or contributed" to the event and confirmation is not necessary to determine that an event is reportable.

For example, if a firm is in receipt of information that "reasonably suggests" and is also in the process of obtaining or testing samples to confirm, the event MUST be reported before the 30 day time frame has expired; the firm cannot wait for the result if the event "reasonably suggests." The information derived from the samples/investigations would be submitted in a supplement report.

This inspection also revealed that, starting in the fall of 1997, your firm had distributed a new product, the "Life Styles X-tra Pleasure" condom.

The Act requires that manufacturers of medical devices obtain premarket approval for their products from the FDA before they may offer them for sale. This helps protect the public health by ensuring that new medical devices are shown to be either safe and effective or substantially equivalent to other devices already legally marketed in this country.

Our records do not show that you submitted a premarket notification submission [510(k)] before you began offering your "X-tra Pleasure" condom for sale. This was confirmed during the inspection, when responsible individuals at your firm informed the FDA investigators that your firm had not submitted such a premarket notification submission. The Center for Devices and Radiological Health has determined that such notification is necessary because this device is significantly changed in design from devices that your firm previously had in commercial distribution, and this change could significantly affect the safety or effectiveness of the device.

Because you do not have a finding of substantial equivalence from FDA, the "X-tra Pleasure" condom is automatically classified into Class III, and therefore is required to have an approved premarket approval application (PMAA) or an approved investigational device exemption in order to be legally distributed. Therefore your product is adulterated within the meaning of Section 501(f)(1)(B) of the Act because it lacks an approved PMAA. The device is also misbranded within the meaning of Section 502(o) because there has been no submission of the notification required under Section 510(k).

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance system. You are responsible for investigating and determining the cause of the violations identified by the FDA. If the causes are determined to be system problems, you must promptly initiate permanent corrective actions.

Federal agencies are advised of the issuing of all warning letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no request for Certificate For Products For Export will be approved until the GMP violations related to your latex condoms have been corrected.

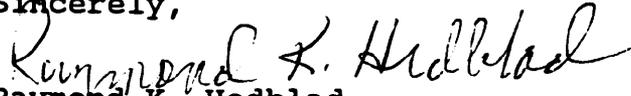
You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in

regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to seizure, injunction and/or civil penalties.

Please notify this office in writing within fifteen (15) working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying system problems necessary to assure that similar violations will not recur. Insofar as the letter responses previously submitted to this office by Mr. Lon McIlvain reflecting the current position of your corporation, your reply to this letter may incorporate them by reference. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the time within which the corrections will be completed.

Your reply should be addressed to the attention of Joseph E. Hayes, Compliance Officer, Food and Drug Administration, 297 Plus Park Boulevard, Nashville, Tennessee 37217.

Sincerely,

  
Raymond K. Hedblad  
Director, Nashville District

RKH/kl

Enclosures:

FDA-483  
21 CFR Part 820  
21 CFR Part 807.87  
21 CFR Part 803

cc: John Gardner  
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