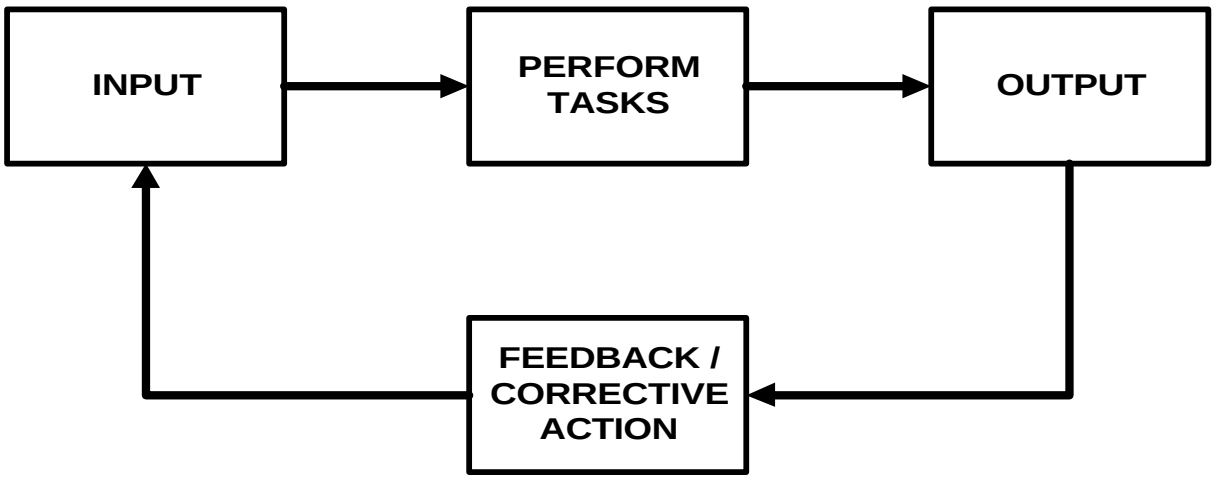
10 QUALITY SYSTEM REGULATORY REQUIREMENTS AS APPLIED TO MEDICAL GLOVES

INTRODUCTION[1]

Manufacturers of medical gloves are required to meet the Good Manufacturing Practices (GMP) regulation for medical devices in 21 CFR 820. The GMP regulation requires that every manufacturer of finished medical devices shall prepare and implement a quality system that is appropriate to the specific device manufactured and meets the requirements of the regulation. Because of the requirement for a quality system, the GMP is called a Quality System regulation.

A network as shown in the diagram below is based on input, functions or tasks to be performed, output, and feedback. A network becomes a system only when it is correctly established, managed and operating, the paths are connected, and information is fed back and used to correct any problems in the system or the output. Thus, a system is self-correcting and is called a dynamic system because it functions as if alive.

DYNAMIC SYSTEMS



The medical device good manufacturing practices regulation requirements for a quality system covers objectives and policies for management and continues with the review of the quality system, quality related activities and corrective and preventive action. The required quality system contains several general elements or tools, particularly in §§820.05 to 820.25, to guide management and support the system. These management elements/tools are outlined next so that their extent can easily be seen.

Management Responsibility and Related QS Elements

[1] The illustrative examples, procedures and forms included in this manual are for educational purposes only. They show one method, but not the only method, for performing a quality system function. Do not use these examples, procedures and forms without first modifying them to meet your specific requirements, operations and devices. Please see the disclaimer on page iv.

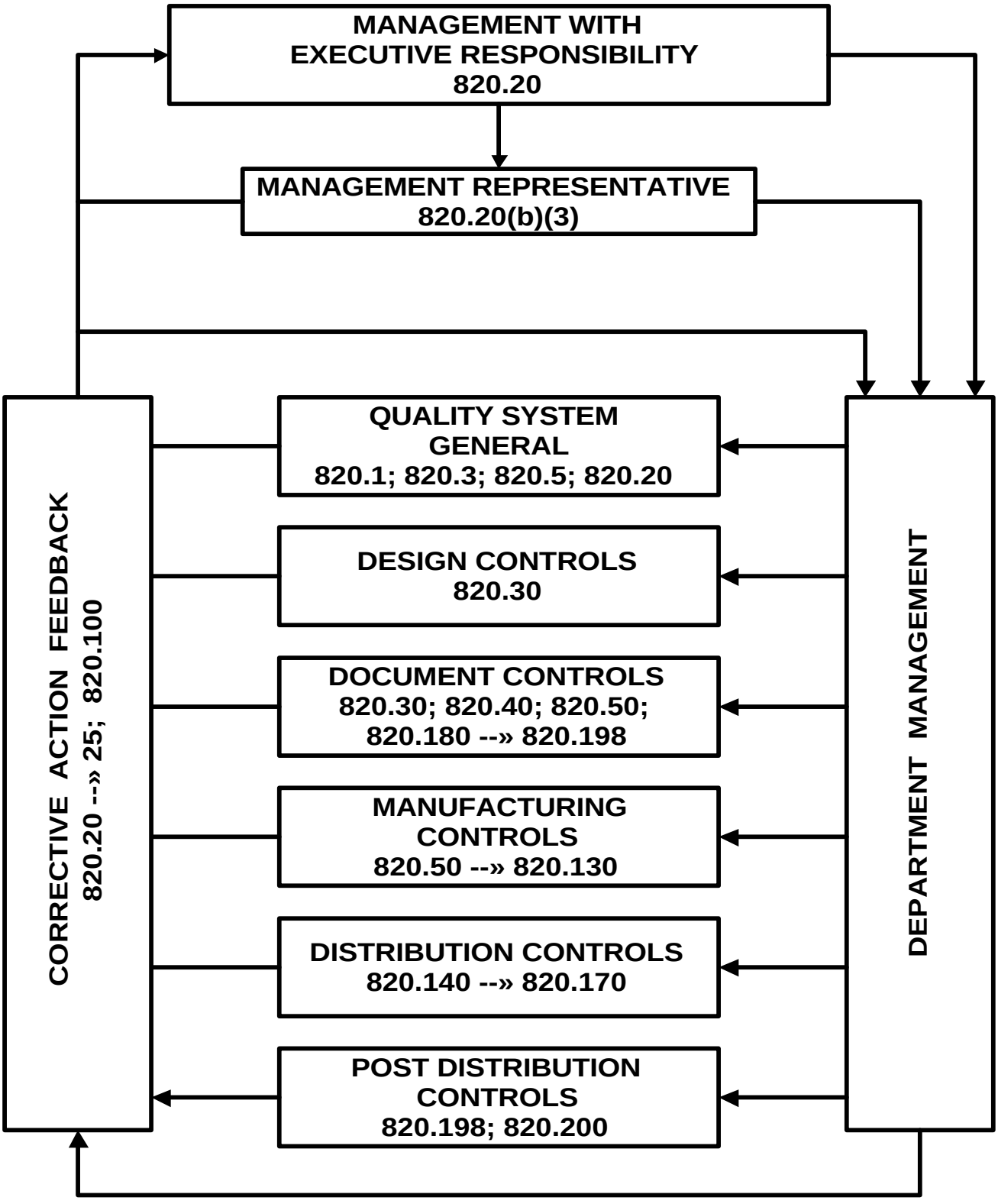
820.20(a)	Quality Policy
820.20(b)	Organization
820.20(b)(1)	Responsibility and Authority
820.20(b)(2)	Resources
820.20(b)(3)	Management Representative
820.20(b)(3)(i)	QS Established and Maintained
820.20(b)(3)(ii)	Report QS Performance to Management With Executive Responsibility
820.20(c)	Management Review
820.20(d)	Quality Planning
820.20(e)	Quality System Procedures

An overview of the required quality system is shown below in the diagramed FDA Quality System Regulation. (This is the same type of dynamic system as diagramed above. Note that a system diagram becomes more complex as the functions in each box are detailed.) The QS diagram below clearly shows the role played by all levels of management and by feedback and corrective action. For example, an audit may be directed by management or be triggered by data flowing through the corrective action path. Briefly, the QS requirements, as diagramed from top to bottom, cover:

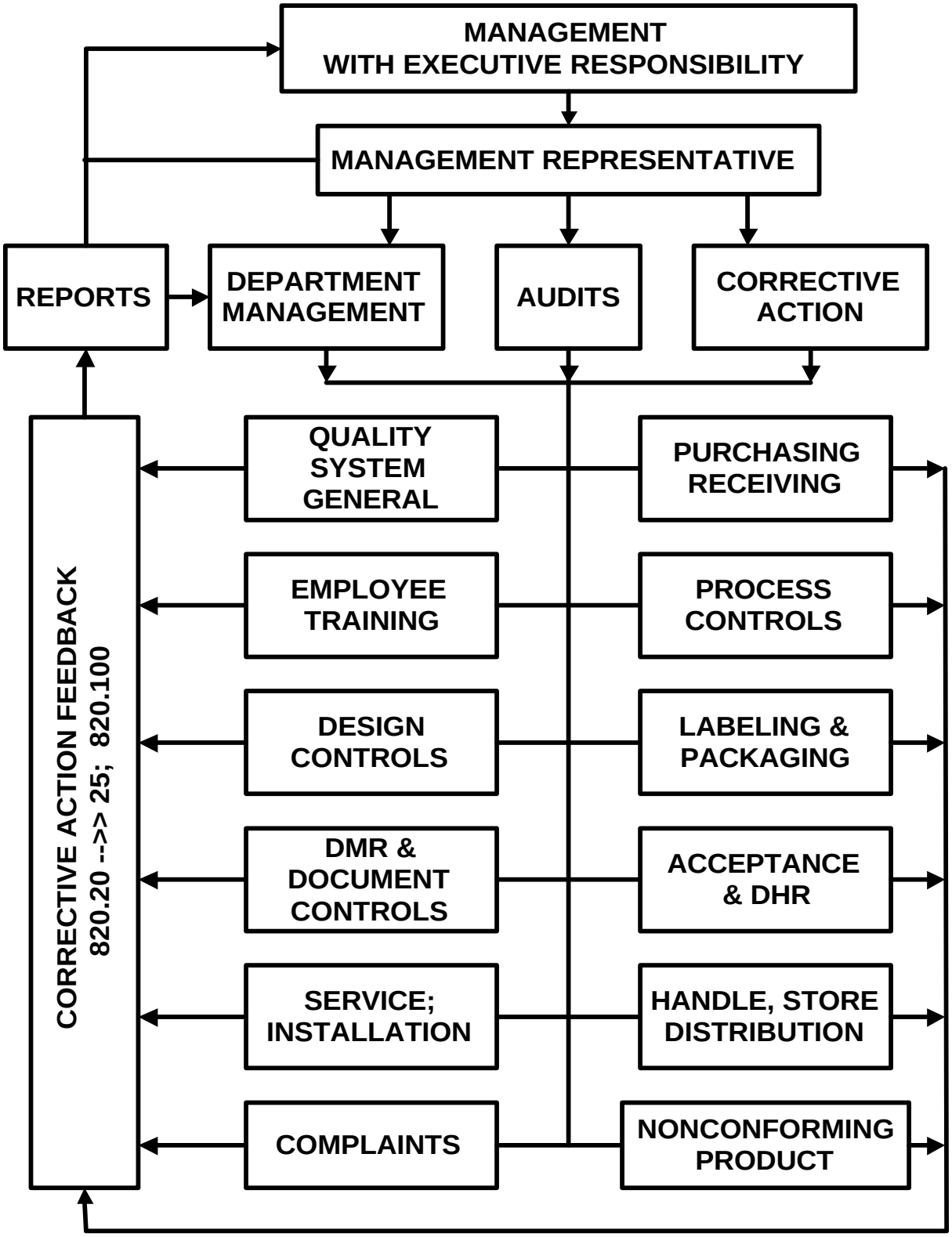
- adequate management controls to assure the continual management oversight of the system. FDA recognizes that management with executive responsibility may need assistance in managing the system. Therefore, the GMP requires in §820.20(b)(3) that a Management Representative be appointed. In a very small firm, the manager with executive responsibility and the management representative may be the same person.
- supporting definitions and additional general controls such as employee training;
- design controls to help assure the design of gloves that are safe and effective, correctly labeled, correctly packaged, and meet the needs of the user and/or patient;
- documented design output, design history files, device master records, purchasing data, quality system records, production procedures, production records, and change controls;
- manufacturing/production controls to assure that finished gloves meet the documented design output;
- storage and distribution controls to maintain the quality of the gloves during production, storage and movement until they are delivered into commercial distribution; and
- internal system controls and post-distribution controls to collect and analyze any problem information and take corrective and preventive action, including management time.

In day-to-day activities, the QS functions are interconnected as needed to design, produce and distribute safe and effective gloves and to take any needed corrective or preventive action (CAPA). The next diagram, Quality System and QS Audits, expands the overall system diagram to show most of the broad functions covered by the QS regulation. This diagram shows many paths between the various functions. For example, 14 paths are shown into, and 12 paths out of, employee (personnel) controls to other areas. (Please note that it is not feasible for such diagrams to show all possible functions and interconnecting paths.)

FDA QUALITY SYSTEM REGULATION



QUALITY SYSTEM & QS AUDITS



Quality System Documents

assure that a formally established and documented quality system is implemented. "Established" means defined, documented, and implemented (per 820). Meeting the system requirements and this definition requires an obvious commitment to quality by management as shown by policy statements; assignment of responsibilities and authorities; and actions that define and support the quality system. Manufacturers must have the records required by the QS regulation such as:

- personnel training records,
- general quality system records or files (QSR or QSF),
- design history files (DHF),
- device master records (DMR),
- device history records (DHR),
- maintenance schedules and records,
- complaint files,
- distribution records, and
- audit reports, supplier evaluation/audit reports and management review reports.

EMPLOYEE TRAINING

Employee training is described in more detail in Chapter 5, *Personnel*, of the *Medical Device Quality Systems Manual: A Small Entity Compliance Guide* available at: http://www.fda.gov/cdrh/qsr/05prsnl.html Training requirements apply to all employees that perform any function covered by the Quality Systems regulation.

It is not unusual for FDA investigators to conduct factory inspections and see employees who are unaware of situations that can result in poor product quality. An example is glove strippers who are not paying attention to the condition of the formers. They have not been properly instructed to identify formers with charred latex, cracks, or chips; and give the former number to the line supervisor. These employees have not been properly advised that formers with these conditions can cause defects in gloves.

FDA employees have also seen compounders who have not been instructed on the importance of thorough ball milling to prevent particles with incorrect sizes from entering the dipping tanks. The ball milling master record may state to grind for 20-24 hours or 28-32 hours; but has the important nature of this operation been told to the compounders to assure that they follow the written instructions? Employees have been seen **sweeping floors near coagulant and latex dipping tanks**. We have seen employees handling gloves while wearing sharp-edged rings or other jewelry. We are always advised that it is the manufacturer's policy not to allow jewelry or to require finger cots over ringed fingers**;** but are employees periodically reminded of the reason for the no ring requirement and why dipping tank solutions and formers must be kept clean?

QS Employee Requirements

The QS regulation requires in §820.25 that each manufacturer have sufficient personnel with the necessary education, background, training and experience to assure that all operations are

correctly performed. Employees must be made aware of glove defects which may occur from improper performance of their specific jobs. Also, quality assurance or other verification personnel must be made aware of defects and errors likely to be found in defective components, gloves. Some defects are not visible such as micro-holes, high bioburden, excessive moisture, adverse chemical residues and high protein levels.

Personnel who perform verification and validation activities must be made aware of defects and errors that may be encountered as part of their job functions.

Proper job performance by employees in accordance with the QS regulation requires management that has a good knowledge of the QS regulation. Therefore, management including marketing managers who may receive complaints or review corrective action and preventive action (CAPA) should also have appropriate education, background, training and experience.

Quality assurance employees should meet the QS personnel requirements stated above for manufacturing employees and should be made aware of defects and errors likely to be found in defective components and gloves. Also, appropriate QA employees should be made aware of defects that can result from contaminants such as manufacturing materials, debris, charred starch, and moisture. Usually it is easier to teach all of the QS personnel requirements to all employees.

Training Indicators

In order to meet the proactive requirements in §§820.25 and 820.100, management should diligently look for factors that indicate a need for additional training or retraining. This information is derived from management observations, analysis of device history records, analysis of complaint records, and quality assurance audits. Some of these factors are:

- incorrect compounding,
- debris and grease in the dipping tanks,
- excessive product defects,
- line down time,
- dirty or defective formers on the line,
- improper labeling or packaging,
- employee confusion,
- employees ignoring environmental control requirements, and
- customer complaints.

DESIGN CONTROLS

Design controls cover the practices and procedures that are used to help assure that the design of a glove is safe and effective, and meets the intended use, user/patient needs, applicable regulations, and applicable standards. The details of design control systems vary depending on the complexity of the product or process being designed. However, manufacturers of surgeon's gloves are expected to define, document and implement design control procedures as required by the QS regulation. FDA has proposed that patient examination gloves be reclassified as class II. If patient examination gloves are reclassified, then design controls would also apply to them. Design Controls are in §820.30 and are listed below:

(a) General,
(b) Design and development planning,
(c) Design input,
(d) Design output,
(e) Design review,
(f) Design verification,
(g) Design validation,
(h) Design transfer,
(i) Design changes, and
(j) Design history file.

These design controls are shown below in the diagram, "Design Control System Outline." This diagram is an expansion of one element, design controls, from the system diagram shown earlier. (This overview design control diagram cannot show all paths nor show the number of times each path is used.)

Manufacturers may establish one design control procedure to cover the various design control sections; or, they may use one or more procedures for each topic. Multiple procedures may be easier to develop, update and implement. General design control procedures may be part of the quality system records or files noted in §820.186.

Personnel training in §820.25 applies to employees that perform any activity covered by the QS regulation including design. Most technical employees need various amounts of training in device regulations, safety, risk analysis, labeling, human factors, verification, validation, design review techniques, etc. Manufacturers are required to establish procedures for identifying training needs and making certain that all personnel are trained to adequately perform their assigned responsibilities. Design personnel must be made aware of glove defects which may occur from the improper performance of their specific jobs. In particular, personnel who perform verification and validation activities must be made aware of defects and errors that may be encountered as part of their job functions.

Design and Development Planning

Developing and producing a new glove are very complex tasks. Without thorough planning, program control, and design reviews, these tasks are virtually impossible to accomplish without errors or leaving important aspects undone. Planning and execution of the plans are complex because of the many areas and activities to be covered. Some key planning activities are:

- determining and meeting the user requirements;
- meeting regulations and standards;
- developing input requirements and subsequent specifications for the glove;
- selecting colors, odorants, and a donning lubricant;
- developing, selecting and evaluating components and suppliers;
- developing and approving labels and user instructions;
- developing packaging;

- developing specifications for manufacturing processes;
- developing manufacturing facilities and utilities;
- developing and validating manufacturing processes;
- verifying safety and performance of prototype and final gloves;
- verifying compatibility with the environment (water, saline, blood, etc.,) and lubricants;
- verifying biocompatibility of the finished glove;
- training employees; and
- documenting the details of the glove design and processes.

Each manufacturer shall establish and maintain plans that describe or reference the design and development activities and define responsibility for implementation. The plans shall identify and describe the interfaces with different groups or activities that provide, or result in, input to the design and development process. The plans shall be reviewed, updated, and approved as design and development evolves.

The plans should be consistent with the remainder of the design controls. For example, the design controls require a design history file (DHF) per §820.30(j) that contains or references the records necessary to demonstrate that the design of the glove was developed in accordance with the approved design plan and regulatory requirements.

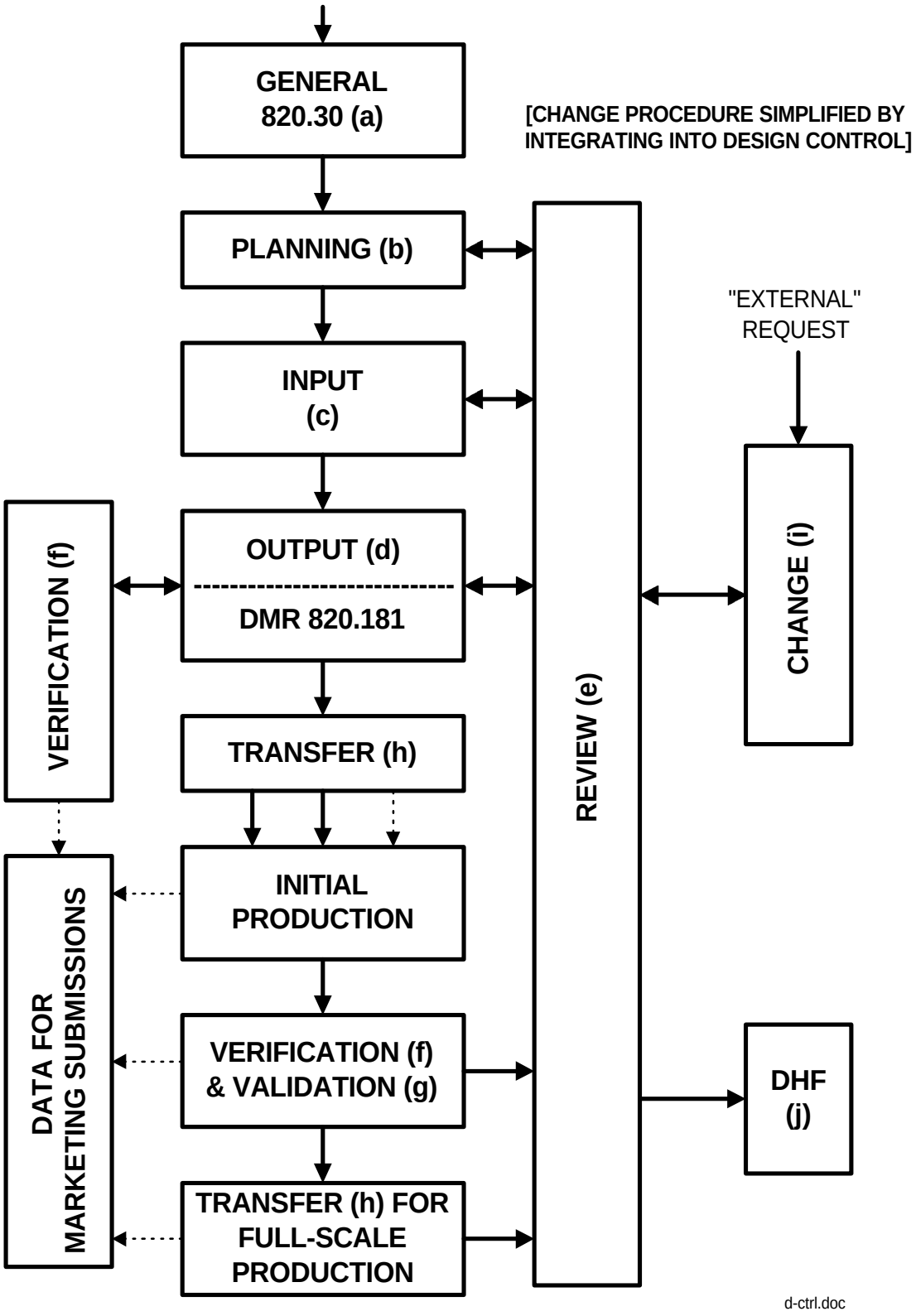
One of the first elements in each design plan should be how the manufacturer plans to meet each of the design control requirements for the specific glove the manufacturer plans to develop; that is, the design plans should support all of the required design control activities. Such plans may reference quality system procedures for design controls in order to reduce the amount of writing and to assure agreement. Each design control plan should be broad and complete rather than detailed and complete. Broad plans:

- are easier to follow;
- contain fewer errors;
- have better agreement with the actual activities; and
- will require less updating than detailed plans.

Regardless of the effort in developing plans, they usually need updating as the ongoing development activities dictate. Thus, the QS regulation requires in §820.30(a) that the plans shall be reviewed, updated, and approved as the design and development evolves. The details of updating are left to the manufacturer; however, design review meetings are a good time to discuss and review changes that may need to be made in the design development plan.

Interface. Design And Development Planning §820.30(b) states: the plans shall identify and describe the interfaces with different groups or activities that provide, or result in, input to the design and development process.

DESIGN CONTROL SYSTEM OUTLINE



If a specific design requires special raw materials, clinical trials, support by another company facility or support by contractors such as performing a special verification test, etc., then such activities should be included or referenced in the plan and implemented in order to meet the interface and general quality system requirements. Of course, the interface and general requirements also apply to needed interaction with manufacturing, marketing, quality assurance, or other internal functions.

Because the development and manufacture of gloves is manufacturing process dependent, the interface between the device development and process development staff is **extremely important** and should be addressed in all of the general design control procedures.

Design Input

Design input means the physical and performance requirements of a device that are used as a basis for device design per §820.3(f).

Design input, requires that each manufacturer shall establish and maintain procedures to make certain that the design requirements relating to a device are appropriate and address the intended use of the device, including the needs of the user. FDA considers shelf life or expiration dating to be a significant factor in meeting the needs of the user. Thus, shelf life should be considered under design input as part of the activities to meet user/patient needs. Also, FDA has published a proposed rule proposing that labeling contain an expiration date. FDA is further proposing that patient examination gloves be reclassified as class II after which they would be subject to design controls. Also, a design requirement in §820.130 requires that each manufacturer shall make certain that device packaging and shipping containers are designed and constructed to protect the device from alteration or damage during the customary conditions of processing, storage, handling, and distribution.

The design input requirements shall be documented and shall be reviewed and approved by a designated individual(s). The approval date and signature shall be documented.

Design input includes determining customer needs, expectations and requirements plus determining regulatory, standards, and other appropriate requirements. These requirements are documented by the manufacturer in a set of device requirements. The design input stage usually is a continuum because input requirements activities usually occur near the beginning of the design feasibility stage and continue to the early physical design activities. After the initial design input stage there are also activities to reduce the input requirements to engineering specifications. A set of design input requirements, when converted to engineering terminology, finalized and accepted as part of the device master record is called a device or product specification, or, in this case, a glove specification.

As the concept of the new or modified glove design is established, various user, patient and/or intended use questions should be answered. The questions and answers will vary for different types of gloves and accessories. Some typical broad and basic design input questions are:

1. Where will the new glove be used?
2. Who will use the new glove?
3. How will the new glove be used?

4. With what devices will the new glove be used?
5. The glove needs to be resistant to what chemicals?
6. How long will the new glove be used?
7. What is the appropriate labeling and packaging? and
8. Other questions related to the specific glove to be developed.

Glove and process requirements and specifications should be reviewed and approved before physical design and process development begins to help control and direct all activities and increase the probability of achieving desired safety and performance characteristics. As the design evolves, the glove design, packaging, labeling, etc., shall be verified per §820.30(f) and reviewed per §820.30(e) against their specifications to verify that design input requirements have been met.

Glove requirements should identify all of the desired performance, physical, safety and compatibility characteristics of the proposed glove and, ultimately, the finished glove. Design input also includes requirements for labeling, packaging, and manufacturing. The final glove specifications should cover ALL of the glove characteristics. The glove specifications may incorporate other specifications by reference such as the manufacturer's generic list of specifications for a type of glove, or specific paragraphs or all of a standard, etc. It should be very clear exactly what is going to be met. A failure to properly address characteristics or factors such as biocompatibility (chemicals and proteins), barrier integrity, aging, packaging protection, shipping stability, reliability (expiration date), etc., can have disastrous consequences for barrier devices.

Input Checklists. It is possible to diligently develop glove requirements and still forget elements in the final specification. To reduce the probability of a requirement or characteristic being left out, a specification checklist(s) or general design list may be used during the design input stage. A checklist should be developed that is broad based but germane to the product line of the manufacturer. If used, a checklist should be part of a standard operating procedure such as a Design Input Procedure. A sample two-page general design and process control checklist is located at the end of this chapter.

The input requirements should cover applicable standards such as the glove standards by the:

American Society for Materials and Testing (ASTM).
100 Barr Harbor Drive
West Conshohocken, Pennsylvania 19428 USA
Phone: 610-832-9500 FAX: 610-832-9555

Information about most national and international standards may be obtained from the American National Standards Association (ANSI), 11 West 42nd Street, New York, New York, 10036, phone 212-642-4900.

The design input procedures must address incomplete, ambiguous, or conflicting requirements. Thus, every reasonable effort should be made to collect all of the requirements. Then the designers can review them and generate detailed design specifications that are clear, correct and complete. The design input requirements shall be documented, reviewed and approved by a designated individual(s). The approval date and signature shall be documented.

To the extent feasible, glove specifications should be derived from the input requirements and be documented before beginning the design of the actual glove. The glove and other related specifications **should** be kept **current** as the design of the glove, packaging, labeling and manufacturing processes evolve during the development program. As the physical design evolves, the specifications usually become more specific and detailed. The specifications will undergo changes and reviews as the design evolves. However, one goal of market research and design reviews is to establish complete glove requirements and specifications that will **minimize** subsequent changes.

Old versions of the input requirements and subsequent input specifications are put in the design history file (DHF) or indexed in the computer as part of the DHF to help show that the design plan was followed. The final specifications are part of the device master record.

Design Review

Design review [§820.30(e)] is one of the key design control elements in a quality system. As the design and production processes evolve, design reviews reduce errors, help avoid problems, find existing problems, propose solutions, increase producibility and reduce production transfer problems. The relentless inquiry during design reviews will expose needed design input requirements and/or design corrections that otherwise may have been overlooked. Design reviews help assure that the final design of the glove, labeling, packaging and processes meets the current design requirements and specifications. Please see Chapter 3 of the *Medical Device Quality Systems Manual: A Small Entity Compliance Guide.*

Design Output

Design output per §820.3(g) means the results of a design effort at each design stage and at the end of the total design effort. The finished design output is the basis for the device master record. The total finished design output consists of the glove, its packaging and labeling, and the device master record. The device master record (DMR) as defined in §820.3(j) means a compilation of records containing the procedures and specifications for a finished device.

The output at each stage is the documents and physical design elements that are either complete or are used to move the design into the next stage. For example, the first design output will usually be the design requirements documents from which the designers will derive the preliminary design specifications. Then the physical design begins including the selection of known components and raw materials and begin documenting their purchasing and acceptance requirements. Section 820.50(b), Purchasing Data, requires that each manufacturer shall establish and maintain data that clearly describe or reference the specified requirements (i.e., a specification), including quality requirements, for purchased or otherwise received product and services. Other components and raw materials will be selected as the design evolves. The design output for some special or new components, or components in unusual applications, will include verification protocols and data; and also include subsequent purchasing and acceptance requirements.

Many of the design output documents are directly part of the DMR. The remaining DMR documents are created by quality assurance, production or process engineering, technical writing, etc., using design output data and information. For example, the finished glove final-test methods

and data forms may be derived from the design verification protocol(s). When these design and documentation activities are completed, the DMR is complete. When the DMR is complete and initial production units, including packaging, meet all specifications, the complete finished design output exists. The requirements in §820.30(d) contain three parts (numbers added) as follows:

1. Each manufacturer shall establish and maintain procedures for defining and documenting design output in terms that allow an adequate evaluation of conformance to design input requirements.

2. Design output procedures shall contain or make reference to acceptance criteria and ensure that those design outputs that are essential for the proper functioning of the device are identified.

3. Design output shall be documented, reviewed, and approved before release. The approval, including the date and signature of the individual(s) approving the output, shall be documented.

Documenting Design Output (1) Documenting design output in terms that allow an adequate evaluation of conformance to design input requirements (or the requirements converted to specifications) is a significant design activity. A matrix or index of input specifications may be compared with the outputs to assist in assuring conformance. Another common technique for achieving conformance is listed below.

- Convert the general input requirements to a list of specific design engineering specifications and give each item a paragraph number.
- Develop the design to meet the parameters and characteristics in the engineering specification.
- Generate a verification requirement document(s) and test method(s) for the design and give each parameter and characteristic the same paragraph number that it has in engineering specification.
- Generate a verification data form that lists each parameter or characteristic and give each parameter or characteristic the same paragraph number that it has in the engineering specification.

Each document has a different drawing number but the paragraph numbers are the same for each parameter. The first document generated may be copied and used as the format for the next one. Therefore, it is almost impossible to leave out a design parameter. When verification is performed and documented, conformance or lack of conformance from input specification to output documents and to output specification data is obvious.

Acceptance Criteria (2) The verification (discussed below) documents and data contain more information than is typically needed for production evaluation and acceptance of components such as latex, in-process items and finished gloves. Therefore, it is easy to copy and modify verification documents to meet the quality system requirement that:

- design output procedures shall contain or make reference to acceptance criteria and

- ensure that those design outputs that are essential for the proper functioning of the device are identified.

Deriving production test procedures from the verification protocols also yields the DMR test methods and data forms needed to meet the QA procedures and acceptance criteria in §820.181(c). Some test methods such as for protein and powder exist as ASTM or other national or international standards. These may be used where appropriate.

Design Output Approval (3) The third output requirement is that design output shall be documented, reviewed, and approved before release. The approval, including the date and signature of the individual(s) approving the output, shall be documented. This means that:

- Manufacturers may have a group or an individual review documents.

- Output documents that are part of the DMR are reviewed, dated and signed by the author; and reviewed, dated and approved by individual(s) designated by the manufacturer. As appropriate, these reviews should cover technical issues as well as adequacy for use in production, purchasing, etc. DMR documents that are generated and approved under §820.30, Design Controls automatically meet the requirements of §820.40, Document Controls and these DMR documents do not have to be re-approved under §820.40.

- Design output reports, data and any other document that will be used to create additional documents in the DMR are reviewed, dated and signed by the author which is current practice; and reviewed, dated and approved by individual(s) designated by the manufacturer.

Design Verification and Validation

Each manufacturer shall establish and maintain procedures for verifying the device design. Design verification shall confirm that the design output meets the design input requirements and associated specifications. The results of the design verification, including identification of the design, method(s), the date, and the individual(s) performing the verification, shall be documented in the DHF.

Verification means confirmation by examination and provision of objective evidence that specified requirements have been fulfilled. The design of gloves, and packaging and any subsequent changes should be verified by testing. Verification test data covers parameters such as shelflife (expiration date), tensile strength, elongation, pinhole AQL, protein residues, chemical residues, biocompatibility, correct labeling, etc. Because a major part of the glove specifications are usually derived from final or draft consensus standards, this means that the manufacturer determines by standard test methods that the gloves meet appropriate standards, guidance and any other claim established by the manufacturer for the gloves.

Design verification is done before final design validation [some validation may be done throughout the development program.] Design verification is always done against input specifications and validation is done against input requirements.

Verification and validation should be done by skilled personnel using test equipment calibrated and controlled according to quality system requirements. Verification and validation should be done per written protocol(s) that includes defined conditions for the testing. Protocol(s) may not be perfect, particularly a new design. Therefore, verification and validation personnel (with authority to made changes) should carefully annotate any changes to a protocol. Likewise, comments about any deviations or other events that occurred during the testing, use or simulated use should be recorded. The **slightest** problem should not be ignored. During design reviews, the comments and any deviations may be as important as verification test data

Design validation means establishing by objective evidence that device specifications conform with user needs and intended use(s). Validation follows successful verification testing and analysis. Each manufacturer shall establish and maintain procedures for validating the device design. Design validation shall be performed under defined operating conditions on initial production units, lots, or batches, or their equivalents. Design validation shall ensure that devices conform to defined user needs and intended uses and shall include testing of production units under actual or simulated use conditions… The results of the design validation, including identification of the design, method(s), the date, and the individual(s) performing the validation, shall be documented in the DHF. Validation may include use under real or simulated conditions to assure that the users are satisfied with the donning ability, feel, size, shape, texture, holding ability, tactile sensitivity, lack of fatigue, lack of irritation, color, odor, etc., of the gloves.

Appropriate laboratory and animal verification (performance, reliability, biocompatibility, etc.) testing followed by analysis of the results should be carefully performed before clinical testing (a validation test) or commercial distribution of the gloves. The manufacturer should be assured that the design is safe and effective to the extent that can be determined by scientific tests and analysis before clinical testing by humans or routine use by humans. Clinical testing is not needed for gloves substantially equivalent to gloves legally marketed in the United States.

Gloves manufactured for use in clinical studies under an IDE are exempt ONLY from the production section of the GMP/QS regulation. They are not exempt from design controls listed in §820.30. In addition, the IDE regulation has labeling requirements in §812.5 and quality assurance requirements in §812.20(b)(3) that shall be met. Further, manufacturers should remember that human subjects are protected via informed consent requirements and product liability laws.

Labeling Verification

Labeling should be checked to see if it is directed to the user and not to the glove designers, which is a common fault found in labeling. Text should be short and to the point yet transfer the maximum information to the user. Data, identifications, or other key information should be current, complete, unambiguous, and accurate. Note that much of the labeling text for gloves is specified by regulations and guidance. During verification, labeling is checked against the labeling requirements of the manufacturer, standards and FDA. Any instructions should be followed **exactly** by the verification test operators and such action should result in correct use of the glove. A checklist may be used to aid in the review of labeling.

Design Transfer

The design controls require that each manufacturer shall establish and maintain procedures to ensure that the device design is correctly translated into production specifications [§820.30(h)].

A significant part of the transfer requirement is met when the design output is properly created. That is, many of the design output documents are part of the DMR. The remaining DMR documents are based on design output information. A procedure may be needed to cover the generation of the remaining DMR documents. Employee training, as needed, should be covered by the design transfer procedure. Design transfer should assure that the design being transferred:

- meets input requirements and subsequent specifications;
- contains acceptance criteria, where needed;
- contains design parameters which have been appropriately verified;
- is complete and approved for use;
- is fully documented in the DMR or contains sufficient design output information to support the generation of remaining DMR documents; and
- is placed under change control if not already done.

The design output is transferred for initial production and validation. If problems occur, changes are made per change control procedures including design controls for Class II gloves. The transfer is complete when the finished gloves are validated, and all requirements are met.

Design Changes

Changes to a design element are controlled per §820.30(i) *Design Changes* which states that: each manufacturer shall establish and maintain procedures for the identification, documentation, validation or where appropriate verification, review, and approval of design changes before their implementation. However, the original design activities and subsequent change control activities for the design are **both** done under the full set of quality system design controls. For example, a major problem may result in additional design inputs, design planning, etc. An easy method for design change control is to use a change request procedure in conjunction with the regular design control procedures. This method reduces the number of procedures, amount of learning, and errors because the change control work is done using the regular design control procedures.

As the design activity progresses toward the final stage and as more items are approved, it is expected that the degree of change control will increase. Those elements of the design that have been verified and accepted should be under change control. Elements that have been released need to be under change control in order to develop production processes. A design that has been submitted to FDA for marketing clearance should be under change control. A design that is released for production must be under design control §820.30 and general document change control §820.40.

After the physical design evolves into an approved and accepted glove, subsequent changes to the glove specification(s) are to be proposed, evaluated, reviewed, approved, and documented per §820.30 [not just 820.30(I)]. The revised specification(s) becomes the current design goal in accordance with the manufacturer's procedures for design control, design change control, and

document control. An overall design change control procedure should cover:

- under what conditions change control is required;
- notifying parties affected by the proposed change;
- documenting the reason for the change;
- any differences in the change control process when a distant facility or outside parties are involved;
- procedures for the control of changes to gloves, labels, packaging and processes or use the regular design control procedures;
- analysis of the design to identify other elements that are impacted by the change; and
- placing the reason for significant changes in the design history file along with the required design verification, validation and review documentation.

Design History File

Design history file (DHF) means a compilation of records which describes the design history of a finished device [§820.3(e)]. The DHF covers the design plan, procedures and activities used to develop the device, accessories, major components, labeling, packaging and production processes. The design controls in §820.30(j) require that each manufacturer shall establish and maintain a DHF for each type of device. Each type of device means a family of gloves that are manufactured according to one DMR. Documents are never created just to go into the DHF.

The QS regulation requires that the DHF shall contain or reference the records necessary to demonstrate that the design was developed in accordance with the approved design plan and the requirements of this part. This requirement cannot be met unless the manufacturer develops and maintains plans that meet the design control requirements. The plans and updates should be part of the DHF. In addition, the QS regulation specifically requires that the results:

- design review, including identification of the design, the date, and the individual(s) performing the review, shall be documented in the DHF. For distant or outside parties, this may include electronic or written records of review correspondence, annotated draft design output drawings or procedures.
- design verification, including identification of the design, method(s), the date, and the individual(s) performing the verification, shall be documented in the DHF.
- design validation, including identification of the design, method(s), the date, and the individual(s) performing the validation, shall be documented in the DHF.
- design plans (not specifically mentioned but you cannot show that plans are met without a copy in the DHF);

The DHF is not required to contain all design documents or to contain the DMR, however, it will contain historical versions of key DMR documents that show, to some extent, how the design of the glove, labeling, packaging, and processes evolved. Typical documents that may be in, or referenced in, a DHF are listed below:

- design plans;

- input requirements and preliminary input specifications;
- design review meeting information such as notes, minutes, attendees, etc.;
- sketches, drawings, procedures, photos;
- engineering notebooks;
- component qualification information;
- biocompatibility (verification) protocols and data;
- annotated versions of key preliminary DMR documents;
- verification protocols for, and data from, evaluating prototypes and/or finished gloves;
- validation protocols and resulting data for initial finished gloves; and
- contractor and consultant information.

Sample Design Input Requirements Procedure

A sample Design Input Requirements procedure is presented below which covers basic activities for obtaining requirements that are needed to develop glove specifications. This procedure uses the multiple specification approach; however, a single combined specification would use a similar procedure. This procedure should be modified to meet specific needs before being adopted.

Sample procedure. Do not use without modifying to meet your specific needs

C O M P A N Y L O G O		Sheet 1 of 2
Title: **Design Input Requirements Procedure**	SOP Number	
Prepared by:	Date Prepared	
Approved by:	Date	Rev
ECN notes		

POLICY - Design specifications covering all design requirements shall be established for all proposed glove designs before any significant physical design activities are started.

SCOPE - This policy applies to all gloves and accessories developed by our company or developed by a contractor for us. For purchase of completed designs, refer to SOP ####. The glove specification(s) **must** exist or be generated regardless of the source of the initial design.

CONFIDENTIALITY - Development plans and activities are confidential. Market research reports and documents such as specifications with parameter data shall be marked confidential.

Design control procedures, standard SOPs, and required design review and design verification/validation records may be shown to, and copied by, FDA investigators as required by the QS regulation. Design parameters are not covered by the QS regulation. Therefore, confidential specification characteristics and parameters in the copies of documents shall be blacked out unless the document is being collected during an inspection related to a marketing submission.

RESPONSIBILITY

Marketing and Engineering have the primary responsibility for determining safety and performance requirements and developing input specifications; however, all departments are expected to support the development of input requirements and subsequent specifications.

MARKETING - Marketing shall plan and conduct all customer contacts to obtain information on customer desires, needs, expected pricing, opinions about existing gloves, etc.

To the maximum extent feasible, market research shall be conducted in a manner to reduce leaking of manufacturer confidential information and plans.

Design review meetings shall normally precede and follow all significant outside market research activities. Initial market research activities shall be previewed with top management.

Market research results are to be documented and marked confidential.

PRODUCTION - Production engineering has primary responsibility for assuring producibility and establishing manufacturing requirements. Some of these requirements may be general during the early design stages. (Process development is also done under design controls.)

R&D ENGINEERING - R&D Engineering is expected to supply design input information on most requirements. Such inputs may parallel data obtained by market research.

R&D has primary responsibility for specifying what technology to use.

R&D shall analyze input data on requirements and reduce it to preliminary specifications.

R&D has primary responsibility for addressing incomplete, ambiguous, or conflicting requirements and shall see that such issues are appropriately discussed at design reviews.

RA & QA - RA and QA managers or their designees shall attend all design input or specification review meetings to provide input on, and to assure that, regulatory, company, quality, safety,

performance, etc., procedures are followed and that requirements are met.

SPECIFICATIONS

STRUCTURE - Multiple specifications shall be used. A separate specification shall be developed for accessories, labeling, packaging, etc. An overall glove specification shall be developed and shall include an index that points to supporting specifications. The specifications, among other factors, shall address:

1. Performance and efficacy;
2. Human factors, fatigue, donning, color, and odor;
3. Length, cuff, size, and thickness;
4. Chemical safety;
5. Allergenicity (protein levels);
6. Pinhole AQL;
7. Biocompatibility;
8. Glove compatibility, with blood, saline and any intended chemical contact;
9. Environmental compatibility;
10. Packaging (in a separate specification document);
11. Any FDA design requirements in part 801; and
12. Labeling in a separate document and, as appropriate, in the glove primary specification.

CHECKLISTS - Checklists of requirements germane to our product line may be used to develop and support specifications. If used, such checklists become part of this procedure and part of the design documentation.

DESIGN REVIEW - Each glove specification shall undergo design review before it is approved for physical design activities or is used as a background document to support further market research. Such reviews shall be documented.

APPROVAL - The Marketing manager and R&D Engineering manager shall approve all input specifications after these have been subjected to design review.

DOCUMENTATION - The approved specifications shall be given document numbers and become part of the device master record for the new glove.

CHANGE CONTROL - The Engineering manager shall decide when design activities have progressed to the stage that the various specifications shall be subject to our Design Change Control Procedure. Approved items that have been released for use shall be under change control. Design change control can start ***no*** later than the submission of a 510(k).

*****End of Procedure*****

DEVICE MASTER RECORD

A device master record (DMR), required by §820.181, is a term used in the QS regulation for all of the design output and related documentation required to manufacture a glove. A DMR contains documents for typical manufacturing activities such as procurement, processing, labeling, test and inspection, and packaging. The device master record contains the design, formulation, specifications, complete manufacturing procedures, quality assurance requirements or acceptance criteria, packaging and labeling of a finished glove. Almost all sections of the QS regulation have requirements related to the DMR. The device master record is described in Chapter 8 of the *Medical Device Quality Systems Manual: A Small Entity Compliance Guide*.

A device master record for medical gloves manufactured by complex processes such as latex dipping usually contain many documents. For convenience, many manufacturers generate an index or table of contents which lists all of the documents in a device master record. An index is a valuable list which increases a manufacturer's state-of-control, reduces costs by reducing the effort and time required to locate a document, and helps manufacturers meet the QS accessibility requirement for records. Also, a matrix, table or diagrammed DMR index may be used to help show that design outputs fulfill design input requirements per §820.30(d). The DMR should contain a glove (device) specification. Generally a medical glove specification will include the:

- product trade and common name(s);
- intended use(s);
- performance characteristics such as tensile strength and elongation;
- regulatory classification;
- physical characteristics such as cuffs, thickness, length, size, etc.;
- environmental limitations and product shelflife or expiration date;
- user safety characteristics such as a pinhole and chemical residue limits;
- water-extractable protein limit;
- powder/particulate/debris limit;
- packaging and labeling specifications;
- etc.

Written Procedures

Many sections of the QS regulation require written procedures for guidance in performing various design, QA and manufacturing tasks. Written procedures are used to:

- improve communications and guidance;
- assure consistent and complete performance of assigned tasks; and
- promote management of operations.

Medical gloves tend to require a relatively large number of written procedures because of the lack of visual clues and complex nature of the manufacturing processes. Written procedures and history records are needed, for example, for mixing of latex, coagulant, dipping, leaching, cleaning, and other solutions. A written procedure is needed for the collection, storage, accelerated testing and real-time evaluation of finished gloves to establish shelf life or expiration dating.

***** SAMPLE RECORD ***** This is an example of an examination glove specification including some typical parameters. You may modify this form and use it to meet your needs. Do **not** use this example as is.

C O M P A N Y L O G O		Sheet 1 of 1
Title: **Glove Specification**	SOP Number	
Prepared by: Crystal Thompson	Date Prepared 8-1-95	
Approved by: Althea Barcome	Date 8-8-97	Rev C
ECN notes: ECN 429 Protein limit added 8-1-96; no label claim -- no new 510k required; ECN 436 Rev B powder level changed to 120 mg per glove		
ECN 438 Rev C protein reduced to 1200 µg per glove by process improvement		

COMPANY PRODUCT NAME: Crystal Touch

Trade Name:	Patient examination gloves, **non**-sterile		
Intended Use:	Medical activities except surgery		
U.S. FDA Status:	Class I, Classification Number 80LYY; 510(k) marketing clearance required. Must be manufactured under quality system program.		
Material:	Natural rubber latex		
Donning Lubricant:	U.S.P. Absorbable corn starch		
Catalog Numbers:	Crystal Touch 100S	Crystal Touch 100M	Crystal Touch 100L
Sizes:	Small	Medium	Large
Overall Length:	240 mm minimum	240 mm minimum	240 mm minimum
Width:	80 +/- 10 mm	95 +/- 10 mm	111 +/- 10 mm
Palm Thickness:	0.10 mm minimum		
Finger Thickness:	0.10 mm minimum		

	BEFORE AGING	**AFTER AGING**
Tensile Strength:	22 Mpa minimum	17 Mpa minimum
Ultimate Elongation:	750% minimum	550% minimum

Orientation:	Ambidextrous
Cuffs:	Yes
Color:	Natural
Residual Powders	120 mg max. per glove
Protein Max.	1200 µg per glove max.
Packaging:	100 units in dispenser box by weight
Disp. Carton Labeling:	Per Packaging specification P-192 Rev. C
Ship. Case Labeling:	Per Packaging specification P-193 Rev. B
Product Coding:	

Record Retention

The QS regulation in section 820.180 requires that all records pertaining to a device be retained at least two years from the date of release for commercial distribution or for a period of time equivalent to the design and expected life of the device. For most medical gloves the longer of two years or the labeled expiration/shelflife date, is an adequate period for retaining records.

COMPONENTS AND MANUFACTURING MATERIALS

The QS regulation requires that both components and manufacturing materials be addressed by the manufacturer's quality assurance program. More information is described in Chapter 10 of the *Medical Device Quality Systems Manual: A Small Entity Compliance Guide.*

Components, raw materials, manufacturing materials, etc., are called products in the QS regulation. Components and materials are products used during manufacturing which are intended to be part of the finished gloves. Examples of such products are: the latex concentrate; the various chemicals which will be mixed with the latex or polymer during compounding; and the donning lubricant. Labeling and packaging are specified and procured the same as components. Manufacturing materials are substances used to help in the manufacturing process but are not intended to become part of the finished gloves. Examples include: most of the ingredients in the coagulant dipping solution, any detergents that are used to clean the formers, and starch if the starch is added and then removed to make "powder-free" gloves.

Components, labeling, packaging, and manufacturing materials must:

- have specifications as required by §§820.30, 820.181 and 820.50;
- either be tested or received under a certificate of analysis or otherwise verified per §820.80;
- be formally approved or rejected per §820.80;
- be identified so that only approved components are used in production per §§820.60 and 820.86; and
- be stored and handled to prevent contamination and mixup per §§820.140 and 820.150.

The quality program should assure that the incoming product is:

- acceptable for the intended use,
- of satisfactory quality upon receipt, and
- handled to prevent mixups and contamination while in the manufacturer's control.

Component Qualification

Qualification consists of verifying through documented testing, evaluation, and review that a product will reliably perform its function in the intended application per §820.30(f) (that is, a component or material meets the specifications derived from the glove input requirements).

Components and other materials should be selected using the requirements of the finished glove as a guide. Standard products that are used in their normal application will need only

minor testing unless some characteristic such as chemical allergenicity was not adequately covered in past studies. New products such as donning lubricants, protein modified latex or new accelerators usually need testing. A design history file of any qualification (verification) testing of components, raw materials and manufacturing materials must be maintained for surgical gloves. This record should include the product identity, testing methods that were used, who performed the testing, date, and the actual test data and results.

Specifications

Component and material specifications are required to be part of the device master record. The specifications should adequately describe the characteristics, dimensions, design, materials, viscosity, performance, and any other feature or parameter necessary to assure receipt of the product desired. For standard products that have a known performance history, a catalog designation may be adequate to describe a component or material and assure purchase of the desired product. For unusual, new, or very important components or materials, the specification data is derived primarily from the qualification data plus minor details from catalog data. Specifications should reflect design requirements, quality and reliability needs. For some components, such as donning powder, the specifications should include a limit on micro-organism contamination.

Supplier Evaluation

To the extent feasible, the selection of suppliers of services and product and the evaluation of them by audits, performance analysis, etc., should be part of a quality program per §820.50. If the manufacturer does not have the capability to test certain product for conformance to specifications, then supplier test data or outside lab results are acceptable per §820.80. Any outside test results should be for the specific lot received and should be accompanied by relevant raw data so that a judgment of authenticity may be made by the finished glove manufacturer.

Acceptance Procedures

Section 820.80 requires a written procedure for accepting components, raw materials, manufacturing materials or other product. Before being accepted, all incoming products should be either physically separated (quarantined) or clearly identified as not yet accepted per §820.86. The decision to separate or tag not-yet-accepted products should be made based on the characteristics of the components, materials, manufacturing materials and gloves; the potential for mixups; plant conditions; manufacturing practices; etc.

Acceptance Criteria

To the extent technically feasible, manufacturers should have specific acceptance criteria for components, materials, manufacturing materials, etc., to meet §§820.30, 820.181, and 820.50. Acceptance criteria are the attributes of a product that determine its acceptability, such as appearance, color, dimensions, MST, percent solids, preservative levels, protein levels, viscosity, purity, pH, or performance characteristics. Typically, acceptance criteria are part of the inspection and test procedure or may be in a separate document.

Testing and Inspection

All incoming components, materials, or other product should receive at least a visual inspection for contamination and/or damage and be identified as the product specified on the purchase order. Product must be tested if deviations from specifications could result in medical gloves being unfit for the intended use. Any testing and inspection must be performed according to written procedures in order to meet the documented QA or QS program requirements and written acceptance test requirements.

Manufacturers who decide not to sample or test selected product should be able to justify that decision based on such factors as knowledge of the supplier's previous performance in providing quality product, the product performance history, and application of the component, material or other product. If product is tested by the supplier, acceptance of incoming product can be based on certification and review of test data submitted by the supplier for the specific components, materials, etc., supplied. Certification should accompany each lot of product. When certification is used, the manufacturer should periodically verify the validity of the certification through an audit of the supplier, testing of the received product or other means.

If a contract laboratory is used to test components, materials, manufacturing materials, etc., the laboratory becomes an extension of the glove manufacturer's quality system. The glove manufacturer is responsible for assuring that the contractor's test and inspection procedures and quality system are acceptable. Typically, this assurance is obtained by documented audits.

Acceptance and Rejection Records

The QS regulation specifies that a record of product acceptance and rejection be maintained per §820.80. These records are a part of the device history record (DHR) and should be maintained in a format that will help in the review of the history record. The records are not required to be maintained in a single file with other records, and are typically filed in the receiving or quality control area. Typically, acceptance and rejection records should contain:

- the identity of the component, material or other product;
- acceptance activities performed and the date performed;
- quantities approved and rejected;
- results;
- where appropriate, the equipment used (equipment may be listed in the procedures); and
- signature of the individual conducting the acceptance.

Obsolete, Deteriorated, and Rejected Product

Occasionally a lot of gloves or product will not meet specifications. Typically, defects in chemicals, polymers, and finished gloves are not visible. Therefore, it is very important that containers of rejected gloves and product and obsolete and deteriorated product be identified per §820.86; and, these should be placed in a separate quarantine area or specially identified area to prevent mixups. To assure that unacceptable products are not used, §820.90 requires that records of their disposition be maintained. These records should state whether the gloves, components, materials, or other products were returned or scrapped.

Product Storage

When components, raw materials, manufacturing materials, etc., are not immediately processed, such product should be held in a quarantine area or identified upon receipt as not yet accepted per §§820.86 and 820.150. Components, raw materials, manufacturing materials, etc., must be identified or stored so that their status is obvious; that is, the material has been accepted, rejected, or is awaiting a disposition decision. A quarantine area can be either a physically secure area or simply a limited access area identified as a quarantine area.

Components should be stored such that they are protected from moisture, dirt, and insects. Components or materials such as latex and starch must be stored so as to retard the growth of micro-organisms §820.70(e). Where components and materials degrade, the components must be stored in a manner to facilitate stock rotation such as first-in, first-out use per §820.150. Ceramic formers and other items not affected by the environment may be stored in sheds or outside.

If you use any sample procedures or forms in this manual, you should modify them to meet your specific needs.

***** SAMPLE RECORD***** **sheet __ of __**

RECEIVING HISTORY RECORD

Description of Product:								Test/Inspection* Procedure #:
Purchase Order #	Lot #	Date Rec'd	Supplier	Lot Size	Quantity Accepted	Quantity Rejected	Inspect Date	Signature

* The acceptance activities and test equipment are listed in the test and inspection procedures for each product.

***** SAMPLE RECORD ***** **sheet ___ of___**

Do not use without modifying to meet your specific glove and operations.

RECEIVING LATEX TEST DATA		
SUPPLIER:		Date Received
SOURCE:		Date Tested
LATEX GRADE:		Lot
PARAMETER	PROCEDURE NO.*	RESULTS
% TOTAL SOLID CONTENT		
MST (sec)		
% DRY RUBBER CONTENT		
% NON-RUBBER CONTENT		
% ALKALINITY (NH_3%)		
VFA NUMBER		
KOH NUMBER		
VISCOSITY		
pH VALUE		
OTHER:		
Remarks: *Acceptance activities and test equipment to be used are stated in the respective test procedures		
Tested by (signature):		Time

*** SAMPLE RECORD Status labels or decals (next page) to help meet §§820.80 and 820.86 in the QS regulation. Note that these sample records are **different** from those previously published for the 1978 GMP regulation.***

COMPONENT AND MATERIAL STATUS DECALS (Samples)

(RIR = receiving inspection report)

QUARANTINED	**RIR**

APPROVED			**RIR**
Product or Material			
Part or Spec #	**Quantity**	**Signature**	**Date**
Remarks			

REJECTED **By Quality Control**			
Product or Material			
Part or Spec #	**Quantity**	**Signature**	**Date**
Remarks			

BUILDINGS AND ENVIRONMENT

Buildings in which components, raw materials, manufacturing materials and finished gloves are handled, processed, and stored should have sufficient space and be designed to allow proper cleaning, maintenance, and other operations. There should be adequate space for receiving, manufacturing, packaging, labeling, and storage to minimize contaminates, assure orderly handling procedures and prevent mix-ups. Buildings should be designed and arranged so that operations can be performed in an orderly manner and thus reduce confusion that can lead to unsatisfactory job performance and mix-ups. Different operations or processes should be separated either by walls or partitions or by providing enough space between operations to preclude mix-ups and assure that no activity will emit spray or dust, or otherwise have an adverse effect on adjacent activities. Some raw materials and gloves with different sizes, formulations, characteristics are not readily identifiable by sight. Therefore, orderly operations, product status, identification, etc., are very important to prevent product mix-ups. Buildings and environment are also described in Chapter 6 of the *Medical Device Quality Systems Manual: A Small Entity Compliance Guide.*

Contamination Control

The need for contamination and environmental control during the collection, compounding and processing of latex is well known. Studies by FDA of micro-photographs have shown that particulates are often associated with pinholes and weak spots in gloves. Thus, for each area in the building where components and gloves are processed, any element such as dust, paint chips, rust, starch residues, protein residues, microorganisms, humidity, temperature, static electricity, etc., which a manufacturer has determined might cause contamination should be controlled. Buildings should be appropriately constructed to prevent, reduce, and control these conditions and support the manufacturer's environmental control program. For example, the control of dust may require that driveways and parking lots be paved. Floor sweeping and floor polishing scatter dust which can contaminate wet formers, coagulant dipping tanks, latex/polymer dipping tanks, finished gloves, etc. Therefore, floors must be cleaned by washing or other dust reducing methods. Floor polishers should not be allowed in glove factories. Likewise, equipment should be cleaned as needed by methods that will reduce or prevent contamination of tanks, formers and gloves with dust and other debris.

Environmental Control

The lack of environmental control will result in the contamination of materials, formers, dipping tanks, wet product, etc. Some environmental factors to be considered are lighting, ventilation, temperature, humidity, static electricity, insect and pest control, and particulates such as dust, rust, paint chips, grease drips and starch. If rodenticides, insecticides, etc., are used, written procedures to limit their use and for their removal from work surfaces should be established to prevent any adverse affect on the manufacturing process or the device per §820.70(c) and (e). For example, finished gloves, solution tanks, etc. should be covered during application of pesticides to the room.

Each manufacturer should make prudent decisions as to what environmental controls are necessary to assure the quality of gloves made by their particular process. When determining the control needed, the manufacturer should identify exactly what needs to be controlled, such as:

- the in-processs or finished glove itself,
- the area for one task such as a cover over a tank, and/or
- a large production or packaging area.

Packaging and starch should be stored in a clean, dry, insect-free area. Latex should be preserved to prevent bacterial growth. Components such as starch that support bacterial growth should be stored in a controlled environment such as sealed containers or bags. Unfiltered air should not be used to dry washed formers or coagulant-coated formers as the resulting contamination may cause pinholes. Unfiltered factory air should not be used to cool or dry finished surgeon's gloves. Open windows and doors should be screened to control insects.

Monitoring

An appropriate system for regular monitoring should be established and maintained for the environmental factors to be controlled. This will assure that equipment is performing properly and filters, floors, equipment, etc. are clean, and other aspects of the environment are within specifications. Periodic inspections of environmental controls and documentation and review of the inspections are required by §820.70(c). The inspection record should be kept simple.

Personnel Practices

Adequate bathroom, dressing, storage and waste facilities should be provided, as appropriate, for personnel to maintain cleanliness per §820.70(d). Such facilities should be maintained on a scheduled basis. Where necessary, such as in a controlled room for inspecting and packaging surgeon's gloves, special clothing and an area to don and store these garments may be needed. Clean area clothing should **not** be worn into uncontrolled rooms or outside per §820.70(e) because the clothing will become contaminated.

Eating and smoking create particulates that may cause pinholes in medical gloves. Smokers exhale particles up to 15 minutes after they finish smoking. These activities should be confined to designated areas. Also, containers or equipment should be provided for timely and safe disposal of trash, by-products, effluents and other refuse per §820.70(e).

EQUIPMENT AND MANUFACTURING MATERIALS

The QS regulation requires that all equipment used to manufacture a device be designed, constructed, placed and installed to facilitate maintenance, adjustment, cleaning, and use. The degree of maintenance of equipment and frequency of calibration of measuring equipment will depend on the type of equipment, frequency of use, and importance in manufacturing processes.

Manufacturing materials such as mold release compounds, cleaning agents, lubricating oils, and other substances used to facilitate manufacturing are procured and received the same as components. If any of these materials has an adverse effect on the finished glove, then the adverse material must be removed to an amount that does not adversely the quality of the glove

using an approved written procedure per §820.70(h). Equipment, manufacturing materials and calibration are described in Chapter 7 of the *Medical Device Quality Systems Manual: A Small Entity Compliance Guide*.

Maintenance, Inspection, and Adjustment

Glove formers should be automatically cleaned each cycle by a validated process. Formers should be inspected as gloves are stripped or as appropriate. Defective formers should be lifted, or removed and repaired, or replaced. Because dust, grease, charred starch, paint chips, etc., can cause pinholes and other defects in medical gloves, manufacturers must maintain formers and maintain, clean, protect and adjust processing equipment. Therefore, manufacturers should:

- have a written schedule for performing these activities per §820.70(g)(i);
- post the schedule or make it readily available to employees per §820.180;
- document the activities, date and individuals conducting the activities per §820.70(g);
- where adjustment is necessary to maintain proper operation, post the inherent limitations and allowable tolerances of the equipment or make these readily available to personnel responsible for making adjustments per §820.70(g)(3);
- audit the activities and document the audit per §820.22; and
- keep maintenance records for each piece of equipment.

Manufacturing Materials

The proper or optimum operation of manufacturing equipment and the operation of a dipping processes usually require the use of manufacturing materials. The QS regulation in §820.3(p) defines “manufacturing material” as any material or substance used in or used to facilitate the manufacturing process, a concomitant constituent, or a byproduct constituent produced during the manufacturing process, which is present in or on the finished device as a residue or impurity not by design or intent of the manufacturer. “Concomitant constituent” means naturally occurring material and for natural rubber latex includes latex proteins. Manufacturing materials also include latex or polymer processing chemicals that are not intended or desired to be in the finished gloves. Manufacturing materials are included in the definition of product in §820.3(p) and are specified, procured, inspected and/or tested, etc., the same as other products such as components per appropriate requirements in §§820.30, 820.50, 820.181 and 820.80. The Quality System regulation in §820.70(h), *Manufacturing material* states:

Where a manufacturing material could reasonably be expected to have an adverse effect on product quality, the manufacturer shall establish and maintain procedures for the use and removal of such manufacturing material to ensure that it is removed or limited to an amount that does not adversely affect the device’s quality. The removal or reduction of such manufacturing material shall be documented.

Control Use

The use of manufacturing materials that may adversely affect the finished glove should be carefully analyzed. Each process should be designed to use a minimum amount of adverse chemicals so as to reduce costs, reduce removal efforts, and increase the safety of the glove.

The QS regulation in §820.70(h) requires a written procedure for the use and removal of manufacturing materials that can have an adverse effect on devices. For medical gloves, processing of raw latex and leaching and washing processes are commonly used to remove or denature natural water-soluble proteins and remove adverse materials such as processing chemical residues. Manufacturers should develop, validate, document and control latex processing and leaching and post-cure washing or treating processes to assure that the finished medical gloves meet their (the manufacturer's) specification for residual or trace powder level, chemical residues, and water-soluble proteins or specific allergens, as appropriate. When residues from sterilization agents such as ethylene oxide need to be removed, instructions for aeration are necessary.

Where starch is added to medical gloves to expedite handling and is then removed during further processing, for example, during the production of some "powder-free" gloves, the starch becomes a manufacturing material. A written processing and test/inspection procedure should be used to assure that powder residues on the finished gloves meet finished device specifications.

LABELING AND PACKAGING

Glove manufacturers must include labeling and packaging in their QS program per §§820.120 and 820.130. Labeling includes dispenser box labels, case labels, package labels, and directions for use such as caution statements about the removal of starch from gloves after donning. The QA program should assure that labeling meets the device master record requirements with respect to readability and content and assure that labeling operations are controlled so that the correct labeling is always issued and used. Labeling and packaging are also described in Chapters 11 and 13 of Medical Device Quality Systems Manual: A Small Entity Compliance Guide.

Specifications are required in the device master record for the content and design of labeling. Specifications are the engineering drawing and/or artwork for each item of labeling, and the appropriate inspection and control procedures. The drawings or purchase specifications should specify, as appropriate, the label dimensions, ink, finish, and content so that the purchased label and/or printed packaging will remain legible during the customary conditions of processing, storage, handling, distribution, and use; and contain the correct and intended claims. Labeling claims must match glove characteristics and contain required labeling in order for the gloves not to be misbranded (see chapter 6 on labeling.) All procedures, drawings, and artwork must have the name of the author, an approval signature, and a date. The approval signature and date may be on the back of artwork or on a labeling approval form. Labels and printed packaging are specified and purchased as components.

Before transfer for initial use, labeling should be reviewed and approved by marketing, quality assurance, and other appropriate managers. Manufacturers should have a design control procedure which covers the drafting, review, and approval of labeling. Approval forms are generally used in conjunction with such a procedure. This procedure helps prevent misbranding.

Labeling is part of the device master record; therefore, all changes to labeling must be made under a change control system. Changes must be formally reviewed and authorized before use according to §820.30 for surgeon's gloves and per §820.40 for patient examination gloves. [If gloves become Class II as proposed, then patient examination gloves must also be subject to §820.30].

Receipt and Release

Upon receipt, packaging and labeling materials must be examined and, if deemed necessary by the manufacturer, tested to assure conformance with specifications per §§820.80 and 820.120. A designated individual(s) shall examine the labeling for accuracy, where applicable, the correct expiration date, control number, storage instructions, and any additional processing instructions. After being accepted, these labels and packaging materials may be placed into inventory or into production. This release, including the date and signature of the individual performing the examination, must be recorded in the device history record. These activities should be repeated when labeling is removed from storage and released for use in production.

Area Separation and Inspection

All labeling and packaging operations being performed at the same time should be separated as necessary to assure there are no mixups between similar labels or various sizes of gloves. Gloves with different protein levels should have a high degree of separation. Separation may be either a physical separation or by performing the labeling and packaging at different times for different types or sizes of gloves. Before beginning any packaging and labeling operation in which mixup could occur, the production area and equipment should be examined to make certain that any gloves and labeling materials from previous operations have been removed. Unused labeling that contains a pre-coded manufacturing date, expiration date, or lot number, should be destroyed and not returned to the label storage area.

Storage

Preprinted packaging and labeling materials should be stored in a suitable area and manner to prevent mixups. Labeling or prelabeled glove dispenser boxes should be identified and segregated as necessary to prevent mixing of similar labeling. Access to labeling should be limited to authorized personnel.

Packaging

An effective primary package for a medical glove should be designed and developed along with the product by considering glove characteristics, contamination control, sterilization process, sealing, labeling, secondary packaging, shipping, environment, shelf life (expiration date), end use, and FDA regulations per the design controls in §§820.30 and 820.140. The primary package and the shipping container should adequately protect gloves under all reasonable conditions from original packaging to final use. Complete storage and stability data should be compiled for packaging for sterile gloves or obtained from the supplier of the packaging.

The process capability of packaging and sealing equipment for sterile gloves should be determined and documented. Then a sealing cycle should be selected. Because every package is not tested or inspected, the cycle must be validated, and then documented in a setup and operations procedure to be used for routine packaging and sealing of the glove with the selected packaging materials. Finally, manufacturers should perform quality assurance tests and inspection on samples of the **finished packages** to further assure that company specifications are met.

Procurement, Acceptance and Storage

The device master record should contain appropriate specifications so that the desired packaging, labels and components may be purchased, properly stored, and properly used. Primary packaging for gloves to be sterilized should be kept clean before sterilization. A manufacturer should have adequate procedures for approval or rejection of all incoming adhesives, packages, cartons, etc. Suppliers may test and inspect these components and provide the manufacturer with the results for **each** batch (i.e., certificate of conformance). The manufacturer could accept this specific data as sufficient certification or order his own testing and inspection.

Packaging Process

The packaging operation is a manufacturing process. Therefore, the QS sections for processing controls (§§820.70 and 820.75) and finished device inspection (§820.80) apply to packaging operations. Controls should be adequate to assure that labeling is correct for the package contents and that only gloves approved for release are packaged and released. Released gloves should meet the manufacturer's specification for dryness (moisture content). It is very important that starch-coated gloves be dry because starch supports microbiological growth.

Section 820.181(d) requires that the device master record include packaging and labeling specifications, methods and processes. Written instructions should be provided to assure that the necessary controls are understood and consistently used. Manufacturers should have a written procedure for test and/or inspection of finished packages. The packaging of sterile gloves should be tested and/or inspected before and after sterilization for integrity; and such testing and inspection is usually done on a sampling basis. The results of test and/or inspection should be recorded in the device history record along with lot numbers, if any, because §820.184(d) requires records which demonstrate that the device was manufactured in accordance with the DMR requirements.

***** SAMPLE ***** For training purposes only. Do not copy. Always check labeling requirements in 21 CFR 801.

MANUFACTURER'S LOGO	**Drawing Number** 301-443-6597	**Rev** C
USE: Exam Gloves	**Title:** Dispenser Box	**Sheet** 1 of 1
Drawn By JF DSMA **Date** Jan 14, 1989	**Approved** Larry Andrews	**Date** 2/5/89

Size: See drawing below. **Material:** Fiberboard weight ____ gms/m^2

Closure: Suitable for Acme No. 123 Hot Melt or equivalent.

Style: Rectangular box with round end dispenser top slot 1" wide x 5" long.

Application: For convenient dispensing of examination gloves.

Folding: Scored for folding. **Shipping:** Ship flat.

Printing: Lettering - Carolina Blue Type Font - Bold
Background - Arctic White

Size: Minimum ¼" for "LATEX EXAMINATION GLOVES" Minimum 3/16" for other printing

.6

10"

3" [*Note: Sample drawing does not contain all labeling or drawing details. Not to scale.*]

3"

5" Powdered With Absorbable Cornstarch U.S.P

CRYSTAL

POWDERED LATEX EXAMINATION GLOVES

Quantity: 100 Pieces by Weight

Size: Medium

"Caution: This product contains natural rubber latex which may cause allergic reactions. FDA recommends that this product contain no more than 120 mg powder and 1200 µg extractable protein per glove. This product contains no more than 120 mg powder and no more than 1200 µg extractable protein per glove."

3" Expiration Date:

LATEX EXAMINATION GLOVES

Distributed by: CRYSTAL GLOVES INC.
200 RUBBER MEETS THE RD
LOS ANGELES CA 01234

Product of China Lot #:

5"

"Caution: Users should consider the circumstances of use in deciding whether to remove residual powder from gloves after donning. Powder can be removed by thoroughly wiping gloves with a sterile wet sponge, sterile wet towel, or other effective method"

0.6"

Shipping for Processing

Either a quarantine area or a label control system must be used to prevent distribution of gloves marked "sterile", but not yet sterilized. **The required level of control is high**.

If the labeled gloves are to be shipped to a contract sterilizer, the shipping, handling, and processing must be controlled as required by the QS regulation **and** §801.150(e) of the labeling regulation. Section 801.150(e) is reprinted below.

(e) As it is a common industry practice to manufacture and/or assemble, package, and fully label a device as sterile at one establishment and then ship such device in interstate commerce to another establishment or to a contract sterilizer for sterilization, the Food and Drug Administration will initiate no regulatory action against the device as misbranded or adulterated when the non-sterile device is labeled sterile, provided all the following conditions are met:

(1) There is in effect a written agreement which:

(i) Contains the names and post office addresses of the firms involved and is signed by the person authorizing such shipment and the operator or person in charge of the establishment receiving the devices for sterilization.
(ii) Provides instructions for maintaining proper records or otherwise accounting for the number of units in each shipment to insure that the number of units shipped is the same as the number received and sterilized.
(iii) Acknowledges that the device is non-sterile and is being shipped for further processing, and
(iv) States in detail the sterilization process, the gaseous mixture or other media, the equipment, and the testing method or quality controls to be used by the contract sterilizer to assure that the device will be brought into full compliance with the Federal Food, Drug, and Cosmetic Act.

(2) Each pallet, carton, or other designated unit is conspicuously marked to show its non-sterile nature when it is introduced into and is moving in interstate commerce, and while it is being held prior to sterilization. Following sterilization, and until such time as it is established that the device is sterile and can be released from quarantine, each pallet, carton, or other designated unit is conspicuously marked to show that it has not been released from quarantine, e.g., "sterilized—awaiting test results" or an equivalent designation.

Compliance with §801.150(e) may require **two** written agreements when importing pre-labeled "sterile" but not-yet-sterilized surgeon's gloves. The two agreements are:

- one between the importer and the glove manufacturer, and
- a second between the importer and the contract sterilizer.

Where the contract sterilizer and manufacturer or importer are located in the same state, a written agreement such as described by §801.150(e) will also satisfy the QS status requirements in §820.86 and some of the handling requirements in §820.140 for shipments between the person authorizing shipment and the contract sterilizer.

Gloves that have been sterilized and shipped to the manufacturer's warehouse before final release must be properly labeled. Pallets, or other designated units, must be marked to indicate the status of the gloves, such as "sterilized awaiting test results". The manufacturer should be able to show that it has control of the gloves until final release and, if necessary, could have them destroyed or returned for reprocessing.

A 510(k) for surgeon's gloves should be submitted by the person having direct or contractual control over the sterilization. If the manufacturer does the sterilization or contracts for the sterilization, the manufacturer submits the 510(k).

For imported prelabeled "sterile" but not-yet-sterilized surgeon's gloves, the importer that contracts for the sterilization should submit the 510(k) to the FDA. However, the manufacturer of the gloves should be identified in the submission.

PRODUCTION CHANGE CONTROL

Change control is of the utmost importance and is described in detail in Chapter 9 of the *Medical Device Quality Systems Manual: A Small Entity Compliance Guide*. Inadequate change control:

- exposes a manufacturer to product liability actions,
- results in product recalls,
- causes internal confusion,
- may lead a manufacturer into violating the Premarket Notification regulation, and
- is a serious violation of the Quality System regulation.

Change control applies to all QS elements. For example, change control applies to:

- glove design;
- processes;
- components, coagulants, dewebbers, donning lubricants, etc.;
- labeling and packaging;
- colorants, flavors, odorants, antimicrobials, antiozonants, antioxidants, etc.;
- environmental control, facilities, employees practices, etc.;
- production and measuring equipment;
- manufacturing materials; and
- standard operating procedures, quality assurance procedures, data forms, and product-specific documentation.

Design change control requirements for gloves are covered at the beginning of this chapter under Design Controls. The production documentation and document change control requirements are in §820.70(b) and §820.40 Document Controls and require that each manufacturer shall establish and maintain procedures to control all documents that are required by this part. The procedures shall provide for the following:

(a) Document approval and distribution. Each manufacturer shall designate an individual(s) to review for adequacy and approve prior to issuance all documents established to meet the requirements of this part. The approval, including the date and signature of the individual(s) approving the document, shall be documented. Documents established to meet the requirements of this part shall be available at all locations for which they are designated, used, or otherwise necessary, and all obsolete documents shall be promptly removed from all points of use or otherwise prevented from unintended use.

(b) Document changes. Changes to documents shall be reviewed and approved by an individual(s) in the same function or organization that performed the original review and approval, unless specifically designated otherwise. Approved changes shall be communicated to the appropriate personnel in a timely manner. Each manufacturer shall maintain records of changes to documents. Change records shall include a description of the change, identification of the affected documents, the signature of the approving individual(s), the approval date, and when the change becomes effective.

Change Control Procedure

A change control procedure and associated forms is one of a family of SOP's used to produce, number, select drawing size, change, and control documentation. The production change procedure must describe the manufacturer's approved procedures to be followed **from** the time the device master record is first released for production of a glove, or a change is requested for a glove design or manufacturing processes, **through** review of the change in relation to other appropriate documents, activities, **and** use. [Design change control before transfer to production is also required for surgeon's gloves. See §820.30 and the beginning of this chapter.] The change procedure should be flexible because all changes do not need the same degree of evaluation and approval. However, all changes **MUST** be made according to the manufacturer's procedure. Making uncontrolled changes is a very serious violation of several sections of the QS regulation.

Evaluation

Each changed glove; component such as colorants, flavors, odorants, antimicrobials, stabilizers, antioxidants, lubricants, etc.; and labeling, packaging, or process must be thoroughly evaluated and reviewed by appropriate personnel to verify that manufacturing specifications are met. Specifications include allergenicity parameters such as residue levels for adverse manufacturing materials, primary skin irritation and dermal sensitization. Thus, the need for allergenic studies should be considered when raw materials, manufacturing materials and processes are changed. Then the test results and all information related to the change should be reviewed by the change-control board (review group). [This procedure covers the same activities as needed for introducing a new product or process into production.] The change control procedure should state the details of the evaluation and review process. The procedure should define the responsibilities of the various departments and members of the change-control board.

***** SAMPLE PROCEDURE *****

C O M P A N Y L O G O

Title *Change Control Procedure* SOP Number _____

Prepared by _____ Date Prepared _____

Approved by _____ Date _____ Rev _____

ECN Notes _____

PURPOSE AND SCOPE: To establish a procedure and form for requesting, evaluating and approving changes. This policy and procedure covers all of our gloves intended for distribution.

POLICY: It is our policy that any change to the glove design/formulation, manufacturing, labeling and packaging must be evaluated, reviewed and approved before the change is made. This procedure is used in conjunction with our design control and process validation procedures.

FORMS: Engineering Request **(ECR)** Form and Change Order **(ECO)** Form**.** The form is a request form until the proposed changed is approved.

REVIEW BOARD: Proposed changes and accepted changes shall be reviewed by a group composed of at least the Engineering, QA, and Production Managers. (Manufacturer Type A approval) If a glove, labeling or packaging change is proposed, Sales and marketing shall participate in the ECR review. (Manufacturer Type B Approval)

If the proposed change is estimated to have a significant cost impact, the Plant and Finance Managers shall be informed. (Manufacturer Type C Approval)

The Engineering Manager shall be the chairperson of the Review Board.

RESPONSIBILITY: Engineering has the major responsibility for managing the change control and review process.

CHANGE CONTROL PROCEDURE

Identification: The person proposing the change must complete the top of the ECR form and check the ECR block. State the item to be changed, date, drawings, and other appropriate information. Give the ECR to Engineering for an initial review.

ECR Review: The Review Board shall review ECR's and decide if a requested change will be accepted, and developed into a change order (ECO).

Effective Date: The Review Board shall set the processing date and/or shipping date for the first lot of gloves processed under a specific change order.

Responsibility: The Engineering Manager, with guidance from the Review Board, shall decide which department or designee is responsible for each task to be performed in order to develop the change, evaluate it, and implement it.

Evaluation: Glove performance, barrier properties, allergenicity and biocompatibility must be considered after each change. After the changed glove, label, process, etc., is developed and tested, the results must be thoroughly verified and evaluated by appropriate departments. Process validation must be considered and performed if needed. Then the test results and all information related to the change shall be reviewed by the change-control Review Board. The meeting notes plus the change-control forms, drawings, or other appropriate documents shall record the details of the change. The revision level letter on each changed drawing or procedure shall be increased by one letter. For example, from Rev. A to Rev. B. (During initial production, the revision codes will be numbers; the example changes from Rev. 1 to Rev 2.)

Documentation Distribution: Engineering shall distribute the revised device master records to the persons responsible for the operations affected by the change and shall remove old documents and file or discard them, as appropriate. **Supervisors are responsible** for overseeing the use of new device master record documents, especially if a change is being phased in and the old and revised documentation are being used in their department at the same time.

Disposition of In-Process Items: The Change Review Board is responsible for any special instructions for the disposition of old products. The Manager affected by the change shall be responsible for the disposition of in-process items such as labeling and packaging that cannot be used after the change.

Premarket Notification: The Change Review Board shall determine if a 510(k) needs to be submitted for, and cleared before, the change may be implemented. “YES” or “NO” decisions shall be documented. (Some manufacturers may have a Regulatory Affairs person to assist with these decisions.)

Remedial Actions: The Change Review Board and complaint handling personnel, if appropriate, shall be responsible for advising the Plant Manager if a recall is proposed.

Quality Assurance Review: After the change is implemented, QA personnel must make certain that finished gloves meet the specifications in the revised Device Master Record by:

- reviewing production records;
- approval of packaging, labels, components, materials, etc.;
- assuring that QA checks are appropriate, adequate and performed correctly;
- by finished glove evaluation; and collection and review of history record data; and
- other appropriate activities.

MANUFACTURER LOGO	**Engineering Change Order (ECO)**	**ECO #**

Signatures	**Date**	**Approvals**	**Date**	**Reason for Change**
Originator		Type A		[ ] Improve process **[ ]** Biocompatibility
				[ ] Design improvement
Project Engr.		Type B		[ ] Correct error **[ ]** Cost reduction
				[ ] Customer request
TYPE		Type C		[ ] Labeling or packaging
A[ ] B[ ] C[ ]				[ ] Regulatory

DESCRIPTION OF CHANGE	**Action Code**	**Drawings Affected**	**REVISED From**	**To**

CHANGE ACTION REQUIRED		**CODES**	**CHANGE ACTION REQUIRED**		**CODES**
Purchasing and Production	Scrap in-process products	1		Bioburden control	8
	Rework finished gloves	2		Labeling	9
	Repackage finished gloves	3		Packaging	10
	Re-sterilize finished gloves	4	Other Action	For reference only	11
	Notify supplier	5		Employee training	12
	Allergen control	6		10(k) required for Change	13
	future	7		510(k) not required	14

PRODUCTION AND PROCESS CONTROL

During production, all of the factors covered by the QS regulations should be considered in order to control the manufacturing process and produce safe and effective medical gloves. The objective of production and process control is to assure that:

- the design is accurately transferred into written specifications for the glove and manufacturing processes; and
- production processes are adequate and controlled to the extent necessary to assure that finished gloves are manufactured according to these specifications.

Specifications describe the intent of the design, and processes are planned so that gloves produced by them meet these specifications. For a given design, note that these specifications are the glove-specific documents in the device master record. Of course, general documents in the device master record are also used to manufacture gloves.

Specifications

The QS regulation requires manufacturers to establish procedures to ensure that the DMR is prepared and approved in accordance with §820.40. Because surgeon's gloves are listed in 820.30(a), the DMR is prepared per §§820.30 and 820.40. The DMR is adequate if the design configuration and performance requirements can be consistently met when the gloves are manufactured and packaged according to the DMR specifications for raw materials, compounding, processing, quality tests and inspections, packaging and labeling, etc.

Processing Controls

Manufacturers must establish process controls to insure that the gloves are not adversely affected by the process and that the process will achieve its intended purpose. Process controls include process validation, standards, drawings, written procedures and instructions, monitoring, in-process glove evaluation, operator certification, finished glove inspection and test, etc. The number of written procedures to assure process control depends on the nature and complexity of the process and the training of the operator(s).

Manufacturers should assure that all processes are conducted properly by controls such as training, supervision, audits, inspection, testing, documentation, automated processes, etc. All changes to processes must be properly reviewed, validated, documented, and communicated to appropriate employees in a timely manner.

The physical examination and testing of all in-process and all finished gloves for all parameters is impractical with present technology. For example, only a small statistical sample of gloves is usually tested for pinholes; and allergen tests are usually done on a design basis with infrequent follow-up tests. Therefore, gloves need indirect control by process validation, sample testing, and subsequent monitoring of the processing methods, equipment, and personnel. A sample two-page general design and process control checklist is located at the end of this chapter. Such processes must be developed, validated, documented, and controlled such that the finished gloves consistently meet the manufacturer's glove specifications. Guidance on process validation is on the web at: http://www.fda.gov/cdrh/comp/ghtfproc.html

Pinholes. Studies by FDA of micro-photographs of defective latex gloves have shown that dust, dirt, rust, paint chips, charred starch, insect parts, and other debris are often associated with pinholes. Therefore, appropriate environmental and processing controls are needed to reduce debris on wet formers and in compounding and dipping tanks. Unfiltered air should **not** be used to dry wet formers where the resulting dusty/dirty former will go into a coagulant or latex/polymer dipping tank. Floors and equipment must be cleaned by methods that minimize the amount of debris released into the environment. As feasible, dipping tanks should be protected from environmental debris. Equipment components, construction materials, rollers, paint, etc., should be selected to reduce initial and long-term production of debris. Likewise, rollers, bumpers, parts, etc., that could shed debris into dipping tanks should be replaced before they become heavily oxidized or degraded. (See the *Appendix* for a list of labs that perform water-leak testing.)

Excessive grease may fall on formers or into tanks and cause defective gloves. Also, only the very thin film of grease at the contact surface lubricates. Therefore, the amount of grease should be limited on chains and equipment moving over formers and processing tanks.

Starch and charred starch in the environment are debris and need to be controlled. Obviously, the amount of starch released into the environment needs to be minimized. Cleaning methods such as washing should be used that will remove starch without further scattering it into the environment. (Also see the section on *Environmental Control* in this chapter.)

Manufacturers should control other causes of pinholes such as vibration, air bubbles in the dipping tanks, dirty formers, defective formers, incorrect formulation, exessive curing temperatures, too little dewebber, wet coagulant, etc. These controls are necessary because manufacturers should use controls and processes that, to the maximum extent feasible, produce finished gloves that meet the manufacturer's specifications and regulatory requirements. Inspection and testing of finished gloves to separate good gloves from defective gloves is not acceptable to FDA as the primary means of process control.

Processing Chemicals. Coagulating and other processing chemicals that are **not** intended to be on the finished gloves are manufacturing materials. These must be reduced on the finished device below the adverse level per §820.70(h). For gloves, the level is set such that the gloves will meet the manufacturer's quality claims and regulatory requirements. Leaching, washing, surface treatment or other processes for removing adverse manufacturing materials should be developed, validated, documented and continuously controlled in order to meet the established device master record specifications. Suitable test methods should be developed and validated for routine testing of samples of finished gloves to assure that manufacturing material residue levels are met. If used, any secondary test method should be validated versus appropriate chemical or other standard primary test method. Also see http://www.fda.gov/cdrh/ode/944.html.

Water-Soluble Proteins. Water-soluble proteins and manufacturing materials on latex gloves have been implicated in the literature and in adverse incidents as the cause of allergic reactions. Processing controls include the reduction of adverse manufacturing materials and water-soluble proteins. Of course, the control would be the reduction of specific allergens if all of such allergens are known. If standard or regulatory recommendations or limits exist, they should be met. (See *Labeling* in Chapter 6.)

Current investigations and conventional manufacturing techniques indicate that one way of minimizing such reactions is to remove as much of the water-soluble proteins and adverse manufacturing chemicals as is feasible from latex gloves. This removal is primarily done by:

- removing or denaturing the proteins in the raw latex,
- using and controlling pre-cure leaching and post-cure washing processes,
- assuring that the leaching tanks and spray or washing tanks use water that is flow-controlled and continually refreshed to avoid chemical (manufacturing material) and protein saturation, and
- leaching and washing for an appropriate time.

Washing after curing is important because proteins become more water-soluble and/or move to the surface of latex gloves during heat curing. Thus, washing should be done before the final donning powder or lubricant, if any, is applied. Otherwise, the starch slurry tank is saturated with water-soluble proteins. Chemical residues, protein on the surface of the gloves, and protein in the slurry tank become attached to, or coat, the starch and other particulates. Later, some of the particulates with residues and protein could become airborne during handling and use of the gloves.

The temperature of the leaching and washing water should be established by each manufacturer as the temperature needed varies based on the parameters of the overall compounding, dipping and curing methods. Preliminary studies by the Malaysian Rubber Research Institute and others indicate that the purity (flow rate) and agitation of the leach water and total leaching time are more important than water temperature.

Surface treatment of the cured latex glove with chlorine or similar agents denatures surface constituents such as water-soluble proteins. These treatment processes also wash and rinse away proteins and manufacturing residues. Chlorine is an adverse manufacturing material and must be removed per §820.70(h) from the gloves after chlorination by washing, neutralization, etc

Synthetic polymer gloves, polymer-coated latex gloves, or any gloves with a labeled or controlled protein level should not be dipped in any tank (particularly starch slurry tanks) or tumbled in dryers where regular protein coated latex gloves have been produced unless the tanks are cleaned before the production of the low- or non-protein gloves. Otherwise, such low- or non-protein containing gloves may become contaminated with protein.

The processes used to control water-soluble proteins and manufacturing materials must be developed per §820.30, validated per §820.75, documented per §820.181, thereafter controlled per §§820.70 and 820.75 and operated by trained personnel. Validation guidance is available on the web at www.fda.gov/cdrh/comp/ghtfproc.html.

A suitable method should be used for sample testing for water-soluble proteins and adverse chemical residues or specific allergens during routine production. Such methods should be validated versus standard laboratory methods. Data from validation of the testing methods for proteins and manufacturing materials or specific allergens should assure that the test methods are adequate. Use of these test methods in production should show that leaching, cleaning or treating processes being used adequately reduce water-soluble proteins, adverse manufacturing materials or specific allergens to, or below, the level set in the manufacturer's specifications. (ASTM or

other standards organization may establish protein, chemical, total extractables, and/or specific allergen levels in the future. Meanwhile, manufacturers should set their own levels which should be consistent with current practice and medical needs. Please see the FDA proposed recommendations for protein and powder in Chapter 6, *Labeling*.)

Bioburden Control. Medical gloves, particularly those powdered with starch, can support the growth of micro-organisms. Therefore, processing controls, as appropriate, should include:

- purchasing starch with a low bioburden,
- properly storing the starch until it is used,
- applying starch per established procedures,
- cooling the starch slurry and/or using an antimicrobial in the starch slurry tanks,
- sampling finished gloves to assure that excessive starch is not applied,
- keeping the finished gloves clean,
- establishing and meeting a dryness specification for finished gloves, and
- protecting finished gloves from the environment.

An example which stresses the need to exercise controls over conditions related to microbial growth is demonstrated by a recall of examination gloves. It was the manufacturer's practice to reduce the temperature of the glove drying oven when serious mechanical problems occurred. After experiencing a problem and restarting the operation, a lot of insufficiently dried gloves containing cornstarch was packaged in a moist state. After distribution, a hospital called FDA and complained that they had noted a visible black film on the surface of the lot of gloves, and that their analysis revealed cultures of Aspergillus and Fusarium. Fortunately the manufacturer had lot numbers on the product which were traceable to the date the moisture problem occurred, and thus were able to restrict the recall to specific lots of examination gloves.

Finished Glove Evaluation

Finished gloves must be evaluated according to written procedures to show that the lot of meet all of the manufacturer's specifications (acceptance criteria) per §§820.80 and 820.181. The finished device evaluation must include inspection and testing of samples of completely finished gloves. Because of different flow/bleeding/leaking characteristics from pinholes, leak test procedures for synthetic polymer gloves may have to be different than for natural rubber latex. The gloves selected for testing, as appropriate, are powdered, powder-free, cured, post-washed, chlorinated, lubricated, packaged, sterilized, etc., such that they are the same as the gloves delivered to the user. Glove evaluation, as appropriate, covers parameters such as:

- width;
- length;
- weight;
- thickness;
- pin holes;
- elongation;
- cuffs/beads
- rips or tears;
- tensile strength;

- powder and/or lubricant level;
- color discoloration and/or embedded debris;
- measurement or indication of manufacturing material residues;
- measurement or indication of proteins or allergens;
- moisture content or dryness level;
- fisheyes, webbing, or folds;
- package integrity;
- bioburden count; and
- labeling.

Evaluation of finished gloves is usually done on a sampling basis. The sampling level and sampling frequency for each parameter are not necessarily the same. Device evaluation also usually includes appropriate in-process inspection and testing. The evaluation data for a lot of gloves, etc., must be recorded in the device history per §820.80(e) and §820.184, and reviewed per §820.80(d) before the lot is released for distribution. Historical data may be used to tighten or loosen sampling plans. There is some concern that the number of pinholes increase as gloves age. Thus, glove aging during shipment and storage before use should be considered before any sampling plans are modified [§§820.250, 820.100, and 820.40].

Powder Measurement. The American Society for Testing and Materials (ASTM) D-6124 Standard Test Method for Residual Powder on Medical Gloves was published September 1997. FDA has accepted this standard as the method for measuring total residues (trace powder) on "powder-free" gloves. (ASTM is developing a method for measuring donning powder on powdered gloves and FDA is considering accepting this method when it is published. Currently, it is expected to be a second part of D-6124.)

Reworking

If medical gloves fail to meet specifications for parameters that can be tested and/or inspected, the gloves may be 100 per cent tested and/or inspected to separate those that meet specifications. The QS requirements for reworking nonconforming product in §820.90 and finished device evaluation in §820.80 apply to these activities.

Specifications for reworking should document the specific tests and processes to be performed. These specifications should be based on studies that measure the effects of reprocessing operations. For process type industries, manufacturers should evaluate reprocessing to assure that gloves will not be adversely affected. The results of the evaluation should be documented. For example, following re-sterilization, gloves should be inspected on a sampling basis for characteristics which may have been altered. Some examples of effects that may need consideration are:

- temperature and moisture effects on steam-sterilized devices and packages,
- vacuum and pressure effects and by-product residue levels for gas-sterilized devices, and
- package and device material degradation for radiation-sterilized devices.

Gloves and components to be reprocessed must be identified to distinguish them from acceptable gloves and components per §820.86. Identification of these may be done, preferably by marking their containers, or by identifying the area in which they are held.

Retesting

Manufacturers should implement appropriate QA checks (acceptance criteria) to assure reworked gloves meet specifications. When gloves are reworked, the gloves must be subjected to reinspection, and/or testing, as necessary to assure that the reprocessing was adequate and did not have an adverse effect on the performance of the gloves per §820.90(b)(2). In most cases the procedure(s) used to inspect and test the original gloves are adequate for reworking.

***** SAMPLE OF AN IN-PROCESS RECORD *****

LAB ANALYSIS OF LATEX COMPOUNDING		
DATE		**SHIFT**
Batch Number		**RESULTS**
Compounding Tank No.		
Date & Time Compounded		
Date and Time of Test		
	PROCEDURE* NUMBER	**BEFORE COMPOUNDING**
1. pH		
2. TSC		
3. CCl_4		
4. NH_3		
5. VISCOSITY		
6. OTHER		
	PROCEDURE* NUMBER	**AFTER MATURATION**
1. pH		
2. TSC		
3. CCl_4		
4. NH_3		
5. VISCOSITY		
6. OTHER		
Remarks: *The test & acceptance activities performed & equipment used are described in the procedures		
Tested by: Signature:		

*** SAMPLE OF AN IN PROCESS RECORD ***Do not use without modifying to meet your specific needs.

MACHINE DIP LINE PARAMETERS PER DAY

LINE: _____ SHIFT: _____ DATE: _____

OPERATOR: _____ SUPERVISOR: _____

ITEM OR PROCESS	TIME & PARAMETER			ACTION TAKEN
1. Acid tank 55-60^0 C.				
Level				
2. Rinse 45-50^0 C.				
Level				
3. Water 55-60^0 C.				
Level				
4. Wash oven 80-85^0 C.				
5. Coagulant 50-55^0 C.				
Level				
6 Coagulant oven 80-85^0 C				
7. Latex dip 27-29^0 C.				
Level				
8. Tack oven 85-90^0 C.				
9. Beading				
10. Leaching 55-65^0 C.				
(1) Level				
11. Leaching 55-65^0 C.				
(2) Level				
12. Cure oven #1 temp.				
13. Cure oven #2 temp.				
14. Cure oven #3 temp.				
15. Protein Rinse operating				
Chain speed				
Line start time				
Line stop time				
~ items produced / hour				
Length of glove (23-24 cm)				
Weight of glove (gm)				
Reject weight (kg)				
Remarks				

STERILIZATION

For gloves imported into and **sterilized** in the U.S., the 510(k) must be submitted by the importer, U.S. subsidiary of the foreign manufacturer, or other U.S. party having control over the handling, shipping and sterilization. The sterilization information required in a 510(k) for gloves that are labeled "sterile" should include the following:

- the sterilization method;
- the method used to validate the sterilization cycle, but not the validation data itself;
- the sterility assurance level (SAL) for the device that the manufacturer intends to meet;
- the packaging to maintain the device sterility (do not include packaging integrity test data in the 510(k) submission);
- the maximum levels of residues of ethylene oxide, ethylene chlorohydrin, and ethylene glycol on the device when EO is used to sterilize; and
- the radiation dose, if radiation sterilization will be used.

Guidance on sterility is in ODE Bluebook Memo K90-1 510(k) “Sterility Review Guidance 2/12/90” which may be obtained from DSMA by phoning Facts-On-Demand 301-827-0111 or 800-899-0381 and requesting document number 361 or obtained from our web site at:
http://www.fda.gov/cdrh/k90-1.html

The physical parameter and biocompatibility data in a 510(k) submission should be data obtained from test and inspection of packaged and sterilized gloves or it will **not** be accepted by FDA. The original document (not a copy) of biocompatibility study results should identify the test laboratory and should be kept on file by the organization submitting the 510(k).

If the inner package of surgeon’s gloves is labeled “sterile” before sterilization, the shipping containers of gloves must be handled, labeled, shipped and sterilized as required by U.S. 21 CFR 801.150(e). These factors must also be controlled in order to meet Quality System requirements in 21 CFR Part 820.

Packaging, package seals, labeling (i.e., ink) and bioburden for gloves must be compatible with the intended sterilization process. Please see *Bioburden Control* in the preceding section on Production and Process Control.

The U.S. FDA seeks a sterility assurance level (SAL) of 10^{-6} for surgeon's gloves. That is, the sterilization process should be designed so that the probability of a glove being non-sterile is 1 in 1,000,000 even if the gloves originally contained highly resistant microorganisms.

Medical gloves must be sterilized with a validated sterilization process. Gloves sterilized during the validation runs may be distributed if all sterilization and performance specifications are met. A sample from each sterilization load of the packaged and sterilized gloves should be inspected for physical parameters and package integrity after sterilization. Gloves may be re-sterilized if the manufacturer has process validation data to demonstrate that re-sterilization will not degrade the product or packaging below the finished device specifications.

Ethylene Oxide (EtO)

The lethality of EtO sterilization is usually monitored with certified biological indicators (BI's) and by measuring process parameters. These BI's usually consist of 10^6 (i.e., 1,000,000) **Bacillus subtilis var. niger** spores on a prepackaged strip or self contained spore strip and growth media. Before cycle validation, the load configuration for cartons of gloves to be placed in the sterilizer should be established and documented. Likewise, the location of BI's should be specified. Usually BI's are located in a geometric pattern that covers the entire chamber load with at least one BI located in the coldest location. The coldest location is determined by a heat distribution study after the sterilizer is calibrated and determined to be working correctly.

During process development, the packaged gloves in the shipping cartons with BI's are placed in the chamber. The chamber is evacuated to remove air and steam is injected to heat and humidify. The EtO gas is then injected to expose the product load per the proposed process parameters for one-half of the proposed cycle. Then the BI's and gloves are tested for sterility per the consensus requirements of the United States Pharmacopoeia (U.S.P., a private company) to determine if all organisms are killed or the time for total kill may be extrapolated from the fractional kill data. Usually three half-cycle runs are done during process development to make sure the time for total kill of the 10^6 BI spores and glove bioburden is correctly determined. The half-cycle is doubled for production on the basis that an additional 10^6 spores would be killed to yield a SAL of 10^{-6} (commonly called a SAL of 6). The three half-cycle lots may be re-run for a full cycle and distributed if all parameters including EtO residues are met.

Usually the first three production runs are considered to be validation runs and require sterility testing of the sterilized gloves, and extra operator attention, extra temperature monitoring, and BI monitoring to make certain that the production cycle yields consistent results. (See guidelines by Association for the Advancement of Medical Instrumentation (AAMI), 3330 Washington Blvd., Suite 400, Arlington, Virginia, 22201-4598, United States.) For routine production using the validated full cycle, exposure and testing of BI's and process parameter measurements are sufficient for sterility assurance -- sterility testing of samples of the sterilized gloves is **not** required.

EtO sterilization leaves residues of EtO, Ethylene Chlorohydrin, and Ethylene glycol. Natural rubber has a relatively high absorption rate for EtO when compared to common plastics. The recommended residue limits are those for "devices contacting skin" as stated in the June 23, 1978, pg. 27482, U.S. *Federal Register*. Residue dissipation curves are generated during the development and validation runs. Aeration cycles are established such that the finished gloves will always have residues below the limit set by the manufacturer. Residue levels do not need to be measured for each production run.

Primary packaging for gloves to be sterilized with EtO must allow the rapid passage of air and EtO through the package to prevent blowouts and allow degassing while preventing the passage of microorganisms.

Radiation Sterilization

The primary packaging, adhesive, gloves, and sterilization dose must be designed or selected and verified per §820.30 so that the packaged product will not immediately or later be degraded

below specifications by the radiation. [For sterile examination gloves the manufacturer performs these per their company requirements in order to meet their label claims in §820.181, Device master record.] Degradation studies should be conducted. Exposure to high temperature may be used for accelerated life testing but should be followed by real-time testing. The test plan and results must be documented per §§820.30 and 820.70.

If AAMI methods are used, the radiation dose to achieve sterility should be based on the bioburden of the **packaged** gloves. The gloves used for bioburden testing and establishing the dose should represent routine manufacturing conditions. To assure that the bioburden for routine production is as low as the levels used to establish the radiation sterilization dose, packaging materials and gloves should be kept clean throughout storage, handling, processing and post-processing handling, and storage until the packaged gloves are sterilized.

If a manufacturer decides to use a dose of 2.5 mega-rads (25KGy), AAMI method 3 may be used provided the bioburden of the packaged gloves does not exceed 100 colony forming units. When samples of packaged gloves are exposed to a verification dose of 4.4KGy, statistical verification is accepted if there is zero or one positive sterility sample observed. A glove sterilized by the over-kill method should meet an SAL of 10^{-6}.

The packing density and load configuration should be established and documented. Then the load is dose mapped by the sterilizer. Previous dose mapping results may be used to reduce but not eliminate dose mapping for the specific product now being considered. Packing density and load configuration affect the radiation penetration of the product. If packaging density, glove thickness, or load configuration are significantly changed, the manufacturer or contract sterilizer should decide if revalidation of the product sterilization process is needed.

Gamma sterilization is usually monitored by dosimeters. Beta (electron-beam) sterilization is usually monitored by recording the beam current and other accelerator equipment parameters. The electron-beam dose is verified by dosimetry.

Contract Sterilization

Production and contract sterilization of gloves must be performed such that the glove manufacturer and the contract sterilizer meet the applicable parts of the QS regulation and the labeling requirements in §801.150(e). (Please see the section on Shipping for Processing for details.)

COMPLAINT INVESTIGATIONS

Complaint processing is described in Chapter 15 of Medical Device Quality Systems Manual: A Small Entity Compliance Guide. Information that tends to be specific for gloves manufactured by dipping processes is presented in this section.

Complaint Handling System

Complaints from all sources should be processed per the manufacturer's complaint handling procedure. The manufacturer should assure that personnel in marketing, sales, engineering, manufacturing, etc., report complaints. These employees must be made aware of this QS requirement and this should be noted in their training records. Complaints may be received from:

- customers by letter, phone, credit memo, or returned goods form;
- a manufacturer's salespersons, representatives, or other employees;
- importers and distributors;
- test laboratories; or
- the FDA including failure of a port of entry inspection.

Because gloves are a low cost device, user reporting for tears and leaks is estimated to be low. Thus, a small increase in the rate of complaints may be significant.

Complaint Responsibility

Employees that maintain complaint files and conduct complaint investigations should have a thorough knowledge of latex gloves in order to make an informed, reasonable decision as to the severity of a complaint and to decide if an investigation is necessary. If it is decided that an investigation is not necessary, a record must be made of the reason for, and the individual responsible for, this decision. For example, the complaint may be about another manufacturer's product or the same as another **recent** complaint that has already been investigated and resolved.

Complaint Records

Each manufacturer should establish a method for maintaining records of complaints and investigations that is easy to use, meets their needs and meets the requirements of the QS regulation. A form, usually two-sided, is commonly used to help process complaints. A computerized system may be used. One side or page is typically used to record incoming complaint information and the other side or page is typically used to record the investigation of the complaint. An example procedure and forms are shown below. These forms list typical data that may be received and information that may need to be sought in order to adequately document complaints and investigations for gloves.

Investigation Records and Location

An investigation may be triggered by individual defects or failure of a lot depending on the nature of the failure, the manufacturers acceptable quality level (AQL), claims about incorrect labeling, regulatory requirements or customer criteria.

In some cases the failed gloves may be available for an investigation of the mode of failure. Failure analysis should be conducted by appropriately trained and experienced personnel and may require the services of a test laboratories. Investigators should use written procedures to assure that handling and analysis of returned defective gloves will **not** destroy the evidence that may show the cause of failure. For example, washing contaminated gloves will destroy evidence about chemical and protein residues. The failure investigation and analysis should determine the actual problem or actual failure mechanism to the level necessary to correct the problem. When the same failure, contaminant, or other problem has been diagnosed several times, a manufacturer need not analyze all additional gloves that are returned with the same complaint.

When an investigation is made under §820.198(e), a record of the investigation shall be maintained by the manufacturers formally designated unit identified in §820.198(a). The record of investigation shall include:

1. The name of the glove;
2. The date the complaint was received;
3. Any glove identification(s) and control number(s) used;
4. The name, address, and phone number of the complainant;
5. The nature and details of the complaint;
6. The dates and results of the investigation;
7. Any corrective action taken; and
8. Any reply to the complainant.

When the manufacturer's formally designated complaint unit is located at a site separate from the manufacturing establishment, the investigated complaint(s) and the record(s) of investigation shall be reasonably accessible to the manufacturing establishment per §820.198(f). Complaints are required to be accessible to the actual manufacturing site so that quality problems can be identified and corrective action implemented as required by §820.100. If a manufacturer's formally designated complaint unit is located outside of the United States, records required by this section shall be reasonably accessible in the U.S. at either:

1. A location in the U.S. where the manufacturer's records are regularly kept; or
2. The location of the initial distributor.

Records of non-valid complaints need not be sent to the actual manufacturing site. Relabelers, importers, and others who distribute under their own name should forward complaints to the actual manufacturer. The forwarding of complaints should be considered when developing contracts or other business arrangements with importers.

Medical Device Reporting

Per §820.198(d) any complaint that represents an event which must be reported to FDA under 21 CFR parts 803 or 804 shall be promptly reviewed, evaluated, and investigated by a designated individual(s) and shall be maintained in a separate portion of the complaint files or otherwise clearly identified. In addition to the information required by §820.198(e) [the list numbered 1-8 above], records of investigation for MDR events shall include a determination of:

1. Whether the device failed to meet specifications;
2. Whether the device was being used for treatment or diagnosis; and
3. The relationship, if any, of the device to the reported incident or adverse event.

***** SAMPLE PROCEDURE *** Do not use without modifying to meet your needs. In this example, management with executive responsibility is stating what shall be done by their company personnel.**

C O M P A N Y L O G O		Sheet 1 of 5
Title: **Complaint Processing Procedure**	SOP Number	
Prepared by:	Date Prepared	
Approved by:	Date	Rev
ECN notes		

PURPOSE: To establish and implement a procedure and forms for recording customer complaints, analysis, response, and corrective action.

POLICY: It is the policy of our company that all complaints regarding safety, performance, labeling, or quality of our gloves will be subject to management review and/or investigation and will result in prompt response and corrective action where indicated.

SCOPE / DEFINITION: This policy is applicable to and must be complied with by all personnel who receive a customer complaint, including personnel in Sales and other departments.
We define "complaint" as a written or oral expression of dissatisfaction relative to the identity, labeling, packaging, quality, durability, reliability, safety, biocompatibility, effectiveness, or performance of any glove or other device manufactured by us.

Types of complaints intended to be covered by this policy are as follows:

1. PRODUCT PERFORMANCE: the product in some way does not perform to user's expectation or to any level of performance conveyed to the customer by printed labeling or verbally by company employees.

2. INTERFACE: the product in some way is difficult or awkward to open or use.

3. PRODUCT SAFETY: all safety complaints are covered by this procedure.

4. PRODUCT APPEARANCE: visual defects inconsistent with the user's expectations for gloves manufactured by our company.

5. GENERAL COMPLAINTS: order or shipping error delayed or unacceptable response to problems, unfulfilled promises, etc.

FORMS USED: Customer Complaint / Analysis (two-sided) and Complaint Log

PROCEDURE: Upon receipt of a customer complaint, the recipient completes side one of a CUSTOMER COMPLAINT form and if the complaint is written, attaches the complaint letter to the form. The recipient then gives the form, with any attachments, by the next day to the Manager of Quality Assurance.

Quality Assurance:

1. Assigns a sequential complaint number and enters the complaint into the Complaint Log.

2. Determines and notes on the complaint form the person to whom the complaint is to be assigned for investigation and/or corrective action and the date a response is required from the assignee.

3. Notes any specific instructions to the assignee.

4. Distributes a copy to appropriate Department(s) as checked on side 1 of the complaint form.

5. Makes 2 copies of both sides of the in-process form and attachments, and distributes:

   Original to the Assignee.
   One copy to the "UNDER INVESTIGATION" complaint folder.

The Assignee:

1. Performs the investigation and/or corrective actions and records the results on the form; and attaches any investigation records.

2. Returns the original of the in-process form to QA.

Quality Assurance:

1. Records on the Analysis side:

   If no action is taken, the reason for inaction should be recorded on the analysis form.
   Any additional corrective action taken or directed by QA.

   The nature and date of any response made to the originator or the customer. If this response is written, a copy of the letter or FAX is attached to the analysis form.

   The final disposition of the complaint.
   QA signature and date.

2. Records the final disposition of the complaint on the complaint log.

3. Files the completed form in the appropriate complaint file for the type of product involved; and discards the copy previously filed in the "UNDER INVESTIGATION" complaint folder.

4. Distributes the complaint log monthly to Staff and specifically involved departments. This log should include a trend of complaints for the month correlated with trends noted in previous months.

***** SAMPLE RECORD *****

COMPLAINT LOG			Sheet 3 of 5	**MONTH YEAR**
Seq. No.	Date Rec'd	Type Glove	COMPLAINT	DISPOSITION

*** SAMPLE RECORD *** Sheet 4 of 5 of Complaint Proced. No. _____

CUSTOMER COMPLAINT (Side 1) SEQUENTIAL COMPLAINT NO. _____

Glove Type _____

Catalog Number _____ Lot Number _____

Distributor _____

Complainant _____

Account Name _____

Account Address _____

Complaint Received by _____

Title _____ Date Received _____

By: [ ] Visit [ ] Phone [ ] Letter [ ] Sales [ ] Credit Memo [ ] Other

Association With User/Patient _____

COMPLAINT ABOUT:

[ ] Pinholes, Tears, Fisheyes, Degradation _____

[ ] Expiration Date / Shelf Life _____

[ ] Pinholes, Tears, Fisheyes, Degradation _____

[ ] Powder, Lubricant, Tacky _____

[ ] Particulates: Type _____ Location _____

[ ] Packaging _____

[ ] Sterility _____

[ ] Labeling _____

[ ] Thickness, Mold, Appearance, Attributes _____

[ ] Dermatitis _____

[ ] Hypersensitivity _____

[ ] Describe Other Defects _____

Comments _____

_____

_____

ATTACHMENTS: [ ] Implicated Sample [ ] Associated Sample [ ] Letter

Received By QA Mgr. _____ Date _____

Assigned To _____ Response Due _____

Instructions _____

Distribution: [ ] Quality Control [ ] Engineering [ ] Production [ ] QA

***** SAMPLE RECORD ***** Sheet 5 of 5 of Complaint Proced. Number _____

COMPLAINT ANALYSIS (side 2) Sequential Complaint Number _____

Glove Type _____ Cat. Number _____

Date of Complaint Report _____ Lot Number _____

Name of Complainant _____

Nature of Complaint _____

ASSIGNEE EVALUATION & CONCLUSIONS: _____

_____

_____

_____

_____

_____

[ ] Pinholes, Tears, Fisheyes, Degradation _____

[ ] Powder, Lubricant, Tacky _____

[ ] Particulates _____

[ ] Labeling/Packaging _____

[ ] Non-Sterile _____

Thickness, Appearance, Color Attributes of:

[ ] Fingers_____ [ ] Palm_____

[ ] Crotch _____ [ ] Cuff/bead _____

[ ] Elongation _____ [ ] Tensile _____

[ ] Chemical Residues Above Spec. _____

[ ] Protein Level Above Spec. _____

[ ] Improper Use _____

[ ] Shipping Damage _____

[ ] Describe Other Defects/Problems _____

_____

_____

_____

ACTION: [ ] Recalled [ ] Replaced [ ] Credited [ ] Sales Follow Up

[ ] Letter _____

[ ] Referred To _____ for Further Investigation or Correction

[ ] NONE. Reason for no action _____

_____

_____

NOTES: _____

_____

FINAL DISPOSITION _____

_____

_____

Reviewed by: Quality Assurance _____ Date _____

If requested: Engineering _____ Date _____

Production _____ Date _____

QUALITY SYSTEM AUDITS

A quality audit is an independent inspection and review of **all aspects** of a quality system. This audit covers all of the manufacturers operations that could affect the safety and effectiveness of the device and thus, as appropriate, should also include suppliers, calibration laboratories, and contractors. Audits are described in detail in chapter 17 of the Medical Device Quality Systems Manual: A Small Entity Compliance Guide.

Because the definition of manufacturer includes initial distributors (importers), initial distributors of gloves are subject to the audit requirements for their operations that are covered by the QS regulation. These operations include such activities as environmental control for, and handling and storage of, finished gloves and forwarding complaints to the actual manufacturer.

Gloves are presently made by causing a polymer solution, on a macro and microscopic basis, to completely coat formers. Among several other reasons, this process will consistently produce quality gloves only if the:

- formulation of coagulants (or other destabilizer) is correct, and is clean and controlled;
- formulation of polymer dipping solution is correct, and is clean and controlled;
- formers have no interfering defects or debris; and
- polymer solution contains no air bubbles and no lumps.

Therefore, contamination and environmental control are very important and should receive specific attention during audits. These and a few other specific items to audit are listed below in short trigger sentence/phrase form. These questions should be expanded into multiple questions, as appropriate, and should be asked in addition to typical or basic audit questions.

Audit Checklist. Are there written procedures, and related records for:

- Cleaning tanks and equipment per schedule?
- Prevention/reduction of air bubbles during compounding?
- Allowing the release of air bubbles?
- Ball milling chemicals to yield proper size and prevent contamination?
- Filtering compounded polymer solutions?
- Inspecting formers on and off line for defects and debris?
- Washing formers each (or as designated) line cycle?
- Protecting wet formers from dust and other debris?
- Controlling the environment by screening or closing doors and windows?
- Protecting dipping tanks from dust and other debris?
- Maintaining covers, shields, ledges, etc., to reduce debris falling into processing tanks?
- Controlling the use of grease and oil to eliminate drips into the processing tanks?
- Inspecting lines, tumblers, etc., to assure there are no protrusions, vibrations, etc., that could cause product defects?
- Cleaning equipment by debris reducing methods?
- Cleaning floors by dust reducing methods such as washing?
- Maintaining floor or other waste material drains?

- Controlling & assuring that leach tanks are functioning (i.e., manufacturing material is being removed, e.g., test data in the device history record)?
- Controlling and assuring that protein wash/rinse tanks are functioning (i.e., manufacturing material is being removed)?
- Controlling and assuring that chlorination tanks are functioning (i.e., specifications met, gloves not degraded)?
- Controlling and assuring that neutralizer wash/rinse tanks are functioning (i.e., manufacturing material is being neutralized per specifications)?
- Identifying and controlling finished gloves to prevent mix-ups?
- Analyzing defective gloves when acceptance criteria are not met to determine the cause of the problems?

CORRECTIVE AND PREVENTIVE ACTION

Analyzing problems, negative and/or exceptional information to solve product or quality system problems is a very important and vital part of a quality system. Without feedback and corrective and preventive action (CAPA) a quality system degenerates into disjointed activities which is not self correcting; and it will, to various extents, be out-of-control. Unfortunately, the manufacturer will not know the extent that the system is out-of-control until a significant problem occurs. (Please see the system diagrams at the beginning of this chapter.)

Corrective and preventive action is required by §820.100. Feedback information for CAPA comes from observations and data derived from routine activities such as design verification, manufacturing data, customer complaints, etc. For example, cut gloves observed during stripping may indicate a protrusion has fallen into the line processing area. Feedback data also comes from directed activities such as audits to search for any deficiencies in the quality system.

To ensure that CAPA is performed, §820.100 lists a series of required activities. Section 820.100 also requires that CAPA activities be documented and that management be informed about quality problems and CAPA. Therefore, management has the information on which to base quality-related decisions.

A first CAPA action should be to make certain that adequate system and product data are being collected and an adequate audit procedure and checklist or other suitable method is being used to assure complete coverage of the audit requirements and the company quality system. Without adequate data, and analysis of the data to find non-conformances, a CAPA program cannot function.

During an inspection, FDA investigators will, on a priority basis, look at management of the quality system and CAPA activities because of their vital importance in maintaining a quality system.

Checklist for the design of gloves and associated processes. It does not cover all possible parameters. It is in keyword form; therefore, it should be used by appropriately trained persons. Do **not** use this checklist without modifying it to meet your specific approach to glove and process design.

CHECKLIST FOR DESIGN OF NATURAL RUBBER LATEX GLOVES AND PROCESSES

REACTIONS / PHYSICAL PROPERTIES AND SURFACE CHARACTERISTICS

	a	b	c	d	e	f	g	h	i	j	k	l	m	n	o	p	q	r	s	t	u	v	w	x
COMPONENTS, PARAMETERS AND PROCESSES	**Irritation**	**Type IV Allergy**	**Type I Allergy**	**Barrier**	**Shelf Life**		**Tack / Grip**	**Bricking**	**Blocking**	**Particles**	**Discoloration [1/]**	**Extractables**	**Donning Ease**	**Comfort**	**Roll Down**	**Hand Fatigue**	**Thickness**	**Uniformity**	**Bioburden**	**Endotoxins**	**Spoilage**	**Modulus**		
1. RAW LATEX Non Rubber Solids; Ammonia; Copper & other metals; Centrifugation; Maturation			✓	✓	✓							✓					✓	✓						
2. FORMULATION Selection; Amount Added; Amount processed out (removed)	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓		✓		✓	✓					✓		
3. CHEMICALS Chemical purity; Microbial purity; Particle size; Supplier Change control	✓	✓		✓	✓							✓												
4. PRE-PROCESSING Ball milling or grinding efficiency; Premixing	✓	✓	✓	✓	✓					✓	✓	✓							✓	✓				
5. COMPOUNDING Correct ingredients; Correct order; Cleanliness; Homogeneity; Maturation; Stir / Fill bubbles	✓	✓	✓	✓	✓			✓	✓	✓	✓	✓												
6. FORMERS Dimensions; Orientation; Length**;** Composition; Surface texture; Embossing; Cuff Width; Rotation; Dynamics; Age/wear				✓			✓			✓				✓	✓	✓			✓	✓				
7. COAGULANT Composition; Agitation; Former temperature / dry; Agitation	✓	✓	✓	✓		✓		✓	✓	✓		✓					✓	✓						
8. LATEX DIP Temperature; Agitation; Level; Dwell; Foam; Drip; Fallout				✓						✓							✓							
9. SET - BEAD 1				✓									✓		✓	✓								
10. LEACH Temperature; Water direction; Water speed; Dwell time; Depth; Fresh Water ratio; Water purity	✓	✓	✓	✓	✓		✓	✓	✓		✓				✓ [2/]									
11. OVENS Temperature Profile; Dwell; Air circulation; Humidity **2**	✓	✓	✓	✓	✓			✓	✓	✓	✓	✓	✓						✓	✓				
12. POST-CURE RINSE POWDERED GLOVES Purity; Volume; Duration; Exposure	✓	✓	✓	✓	✓			✓	✓											✓				

	a	b	c	d	e	f	g	h	i	j	k	l	m	n	o	p	q	r	s	t	u	v	w	x
COMPONENTS, PARAMETERS AND PROCESSES	**Irritation**	**Type IV Allergy**	**Type I Allergy**	**Barrier**	**Shelf Life**		**Tack / Grip**	**Bricking**	**Blocking**	**Particles**	**Discoloration** [1/]	**Extractables**	**Donning Ease**	**Comfort**	**Roll Down**	**Hand Fatigue**	**Thickness**	**Uniformity**	**Bioburden**	**Endotoxins**	**Spoilage**	**Modulus**		
13. POWDERED GLOVE SLURRY antimicrobial; Surfactants; Ingredients; Temperature; Amount used; Agitation; Microbial growth; Clean out frequency **3**	✓	✓	✓					✓	✓		✓								✓	✓	✓			
14. CHLORINATION POWDER FREE GLOVES Concentration; Filtration; Duration; Load; Reversals; pH; Agitation; Drain efficacy and speed; Neutralization; Rinse Quality	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓	✓			✓	✓		✓		
15. LUBRICANT Type; Concentration; Distribution; Microbial Growth	✓	✓					✓	✓	✓				✓						✓	✓	✓			
16. DRYERS Delay; Temperature; Duration; Cross Contamination; Humidity; Filtration; Load / Space; Airflow	✓			✓	✓			✓	✓	✓	✓	✓							✓	✓	✓	✓		
17. PACKAGING Line Clear; Clean up; Label control; Packaging material; Stack method; Sun / light exposure **4, 5**			✓	✓	✓					✓	✓	✓							✓	✓	✓			
18. TRANSPORT / STORAGE Temperature; Moisture; Protection; Insulation	✓			✓	✓			✓	✓	✓	✓	✓							✓	✓	✓			
19. CLEANING HOW? WHEN? Formers; Filters / Screens; Tanks; Mop (no sweeping); Air / Surface; Line Change; Personnel; Chain guards	✓	✓	✓	✓	✓					✓		✓							✓	✓	✓			
20. COATINGS Laminates, Bound polymers **6**	✓	✓					✓			✓		✓	✓	✓		✓	✓	✓				✓		
21. EXTRACT TREATMENTS Enzymes, Protein binders	✓	✓	✓	✓	✓					✓		✓												
22. Other (Add for your glove and processes)																								

GENERAL: Line speed alters the dynamics of every step and process. Environmental conditions impact barrier, quality, appearance, etc.
Parameters in general are interdependent. Standing water or wet glove on hold is a potential problem: microbial endotoxin, oxidation.
Sterilization must be closely monitored with routine checks on glove and packaging bioburden.

Notes: 1. Also affects drying inside the bead 2. Can cause gloves to be brittle 3. Slurry also affects powder distribution
4. Sidedness 5. Mixes 6. Delamination potential

1/ Refers to yellow in latex affected by carotenes 2/ Rolldown of hand or glove material.

A way to remember the outline of the CAPA requirements is to note that an avid approach to CAPA should be used. This memory association yields:

A	Analyze
I	Investigate
I	Identify
V	Verify and validate
I	Implement
D	Disseminate

And, of course, quality system activities are documented and management is kept informed