to each procedure is known as its "risk evaluation score". (See Table 1) The following ranges of risk evaluation score is recommended to establish the ranking of the potential risks:

- 1–3 =Low
- 4–6 =Medium
- 7–9 =High

For instance, a Production procedure for the operation of a Jones Cartoner may have a risk evaluation score of 3 since the equipment is tasked with inserting leaflets containing dosing and product warning information, ensuring the integrity of the secondary package and imprinted the lot code and expiry on the carton, has direct product impact (High -3) yet the procedure for operating it is not subject to change unless the equipment undergoes modification and the fact that there are quality audits in place during operations to monitor the equipment's performance (Low -1).

Risk Assessment - Identification, Analyses and evaluation of potential risks.

There is no regulation that requires specific periods for review of SOPs. However, the required status for any SOP is to be current. The goals of any site are to assure it will continue to produce quality products and to meet the challenges of a regulatory inspection. Periodic review of SOPs to assure they are current is a critical component to meeting these goals. But this is a difficult task when SOPs may number in the hundreds or thousands at a given site. A risk management approach to periodic review/revision of SOPs is recommended to assure site resources are appropriately applied to meet this challenge.

The risk is the likelihood (PROBABILITY) of having non-compliant or deficient procedures which have the potential to impact product quality or regulatory compliance attributed to lack of timely document review and that could remain unchecked or undetected. In addition, the greater potential of an SOP to impact product quality and regulatory compliance directly corresponds to a greater likelihood of that SOP being reviewed during an inspection. The potential undesired consequence (OUTCOME) under such circumstances is a negative impact on product quality and a regulatory citation from having an SOP in a non-compliant status. Considering the number of SOPs that could be subject of periodic review at a site, a more practical approach is to categorize the SOPs on the basis of potential impact to product quality and regulatory compliance.

- Categorization of SOPs
  Site-level SOPs may be grouped into:
  - Quality
  - Validation and Qualification
  - Production
  - Packaging and Labeling
  - Materials
  - Laboratory
  - Facilities, Equipment, and Utilities

- Considerations for Risk Assessment – The following discussion is intended to give guidance for site SOP classification. General examples are provided in Table I.

would be deemed sufficient to assure compliance depending on the instrument complexity. Facilities, Equipment, and Utilities: These procedures are related to vital support systems in a plant such as the air handling systems, compressed air systems, electrical system, security systems, etc. While these procedures may seem routine in nature, they are impacted by equipment and structural changes that may accumulate over short time periods.

Adjustments in procedures may also be necessary to reflect changes in production equipment performance as process knowledge increases. A frequent review of equipment
specific SOPs may be needed while SOPs describing engineering systems may require moderate to low review frequency.

Risk Acceptance:
After agreement is reached on the risk associated with each procedure or type of procedure, a site should then define the level of risk it is willing to accept. This again, will depend on several factors such as the regulatory environment, type of products produced, etc. For the working example, four (4) separate frequencies of review have been proposed for implementation. Formal acceptance of these established risks occurs when the procedure defining the new risk-based approach is approved by the relevant site
management.

Recommended SOP Review Frequency:
The review frequency is calculated from the date the SOP is made initially effective or since its last revision. The frequency selected will depend on the maturity of the organization, the frequency of changes in the area, and the length of time the SOP is in operation. The following review frequency period is recommended:

- 3 years or less = frequent
- 3 -4 years = moderate
- 4-5 years = low
- As needed = depends on site needs, requirement, or urgency of situation

The above review frequencies should be treated as guidelines. Sites may adopt a more appropriate frequency based on SOP criticality and local operational needs.

Risk Control:
The results of the risk assessment (i.e. identification, analyses, and evaluation of potential risks) help identify the levels of risks confronting the sites with respect to potential issues encountered with SOP management and the pertinent requirements to keep them current.

The use of a risk management approach will allow sites to reach a balance between benefits, risks, and resources as they are now able to set priorities and effectively use available resources to address the review/revision of SOPs. After reaching a well-informed decision, a suitable SOP review period can be assigned for each SOP with a frequency that is reasonable and relevant to the site's own experiences. With a defined

SOP review period based on a risk assessment, sites can effectively reduce the risk identified through proper utilization of resources by focusing first on more critical ones and deferring on

Table I
General Examples

Typical Site Operations SOPs Risk Identifications (Examples)		Risk Analysis		Risk Evaluation	Recommended SOP Review Frequency
SOP Category	Subject	Probability	Outcome	Score	Maximum Period (in years)
Quality	Quality Management	3	3	9 (high)	frequent (3 or less)
	Training				
	Change Control				
	Investigation	3	3	9 (high)	frequent (3 or less)
	Material Disposition	3	3	9 (high)	frequent (3 or less)
	Inspection Services	3	2	6 (medium)	moderate (3 - 4)
Validation and Qualification	Systems (Equipment, Utilities, Facilities, Computers)	3	3	9 (high)	frequent (3 or less)
	Cleaning	3	3	9 (high)	frequent (3 or less or as needed)
	Analytical Method	2	3	6 (moderate)	Moderate (3 - 4)
	Process	3	3	9 (high)	frequent (3 or less)
Production	Basic operations such as Employee & Product protection	1	1	1 (low)	low (4 - 5)
	Equipment operations	1	2	2 (low)	low (4 - 5)
	Material Handling, weighing or lot reconciliation	2	3	6 (medium)	Moderate (3 - 4)
Packaging and Labeling	Basic operations such as Finished goods handling or Sublotting the Product	1	1	1 (low)	low (4 - 5)
	Equipment operations	1	2	2 (low)	low (4 - 5)
	Label Handling including labeling of API & INT containers	2	3	6 (medium)	Moderate (3 - 4)
Materials	Qualification of Supplier & Materials	3	3	9 (high)	frequent (3 or less)
	General procedures such as Receipt of materials, Sampling, etc.	3	3	9 (high)	frequent (3 or less)
	Storage	2	3	6 (medium)	Moderate (3 - 4)

