BIOTECHNOLOGY INDUSTRY ORGANIZATION
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March 8, 2010

Dockets Management Branch (HFA-305)
Food and Drug Administration
5600 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2009-D-0568

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the draft guidance for industry entitled *"Planning for the Effects of High Absenteeism to Ensure Availability of Medically Necessary Drug Products*."

BIO represents more than 1,200 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products, thereby expanding the boundaries of science to benefit humanity by providing better healthcare, enhanced agriculture, and a cleaner and safer environment.

BIO agrees with FDA that ensuring a supply of medically necessary products (MNP) during events that may result in high absenteeism among pharmaceutical company employees is important to the protection of the public health. Indeed, most pharmaceutical companies have developed and tested disaster recovery and business continuity plans. This guidance provides important considerations that biopharmaceutical manufacturers, ingredient supplier, and contractors should incorporate into ongoing emergency preparedness planning. BIO is pleased to provide the following general and specific comments on the Draft Guidance.

GENERAL COMMENTS:

1. Consistent Terminology Should be Applied:

Throughout the Draft Guidance the terms "emergency plan", "contingency production plan" and "contingency plan" are employed, but these terms are not commonly used in the industry as part of risk management terminology and are considered unconventional. (Lines 22, 31, 32, 77, 84, 232, 261, and 310). For the sake of consistent terminology in accordance with current industry practices, we suggest that the Draft Guidance refer to these plans as "Business Continuity Plans" (BCP).

2. Business Continuity Plans Should be Consistent with, but not Subject to, cGMP Regulations

As previously noted, most biopharmaceuticals companies have already developed and are testing Business Continuity Plans. BIO appreciates FDA efforts to enhance the quality and availability of these plans, but we must note that these are business plans and requiring conformance to specified parts of 21 CFR 211, as called for in this document, is unnecessarily burdensome and provides no value to ensuring protection of the public health. For example, the Draft Guidance states that:

> *"The plan should be: developed, written, reviewed, and approved within the site's change control quality system in accordance with the requirements in 21 CFR 211.100(a) and 211.160(a); execution of the Plan should be documented in accordance with the requirements described in 21 CFR 211.100(b)." (lines 97-100)*

BIO does believe that a Business Continuity Plan should be approved and maintained consistent with a quality systems approach and should support operation consistent with GMP principles. However, given that emergency events will likely require prompt activation of the plan, there should be flexibility to maintain detailed plans in business documents because they will cover aspects of company operation other than GMP manufacture.

3. Manufacturers Cannot Directly Coordinate the Business Continuity Planning of Independent Business Partners

Additionally, the Draft Guidance makes a number of references to the expectation that manufacturers' work with ingredient suppliers, contractors, and other business partners associated with the manufacture of medically necessary drug products (lines 41, 61-64) to coordinate an emergency response plan. BIO fully supports robust communication and collaboration between manufacturers and their business partners to facilitate each company's respective business continuity planning. To the extent possible, manufacturers should be cognizant of their business partner's business continuity plans so that mutually beneficial actions may be initiated to mitigate the effects of potential

shortages. However, we note that it is not feasible for the manufacturer to "coordinate" the suppliers' and contractors' responses to personnel shortages. Those business decisions will ultimately rest with each individual company based on their respective staffing, contractual obligations, and unique circumstances.

4. Plan Testing Should Not Involve the Actual Manufacture of Pharmaceutical Product

Finally, we note that the Draft Guidance suggests that testing of the plan should include the manufacture of test batches of the drug or biologic (Lines 328-329, 344, 345). BIO agrees there should be some level of "testing" of the plan, but we do not believe that it is always necessary to actually manufacture a test batch of product as part of the plan testing. For many products including complex biologics, production of test batches will be expensive, could contribute to product shortages, and may inadvertently compromise GMP compliance. We believe that if the company employs prior experience, knowledge of the manufacturing process, and a risk assessment to develop the Plan, then that should provide a sufficient rationale to assure that product quality is not compromised when the product is manufactured under the Plan.

CONCLUSION:

BIO appreciates this opportunity to comment on *"Planning for the Effects of High Absenteeism to Ensure Availability of Medically Necessary Drug Products*." More detailed, specific comments can be found in following chart. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/

Andrew J. Emmett
Director for Science and Regulatory Affairs
Biotechnology Industry Organization (BIO)

SPECIFIC COMMENTS

SECTION	ISSUE	PROPOSED CHANGE	IMPORTANCE
I & II: BACKGROUND AND INTRODUCTION *(lines 19-76)*			
Lines 22, 31, 32, 77, 84, 232, 261, and 310:	Throughout the Draft Guidance the terms "emergency plan", "contingency production plan" and "contingency plan" are employed, but these terms are not commonly used in the industry as part of risk management terminology and are considered unconventional. For the sake of consistent terminology in accordance with current industry practices, we suggest that the Draft Guidance refer to these plans a "Business Continuity Plans" (BCP).	Please replace references to the plan with "Business Continuity Plan"	Medium
Lines 31-32:	The Draft Guidance "provides considerations for the development and implementation of a contingency production plan that will ensure the highest possible quality MNP under the circumstances, including specific elements that should be included in the plan." However, there are other ways to make sure you do not have a shortage besides contingency production plan, i.e. on-going inventory policy. With adequate inventory on hand, an absenteeism-specific business plan might not be needed.	Please change the wording to: "The guidance provides considerations for maintaining adequate inventory, and for the development and implementation of a business continuity plan ~~contingency production plan~~ that will ensure the appropriate ~~highest possible~~ quality MNP under the circumstances."	Medium

Lines 39-41:	The Draft Guidance later suggests that manufacturers coordinate with their suppliers, so it is important that the supplier receive a copy of the guidance.	Please change the wording to: "FDA strongly recommends that drug product manufacturers share this guidance with all suppliers and contractors associated with the manufacture of MNPs…"	Medium
Lines 59-61:	A pandemic is just one example of an emergency situation and the guidance is biased towards planning for pandemic emergencies. Adding other examples will ensure that the contingency plan is able to handle any type of absenteeism situation.	Please change wording to: "It is therefore vital for industry to prepare before an emergency situation occurs and to develop plans to ensure continuity of operations during emergencies such as natural disasters, an influenza pandemic, security issues, union strikes, etc.	Medium
Lines 61-64:	The Draft Guidance states that "It is especially important for manufacturers of finished drug products to coordinate their suppliers' and contractors' responses to personnel shortages to ensure the availability of high quality materials and services that contribute to the manufacture of MNPs." However, it is not feasible for the company to "coordinate" suppliers'/contractors' responses to personnel shortages.	Please change the wording to: "It is especially important for manufacturers of finished drug products to be cognizant of their suppliers' and contractors' responses to personnel shortages so that mutually beneficial actions may be initiated to mitigate the effects of such shortages."	High
Line 72:	The Draft Guidance suggests that manufacturers employ preventative measures including "ensuring that employees are immunized, as appropriate, if vaccine is available." However,	Please change the wording to: "Provide information on local vaccination services to employees. Offer employees	High

	immunization records are considered medical records and are not accessible. Further, employers cannot obligate employees to receive flu vaccination. Employees have the right to refuse or may not be medically able to take the vaccine. Of course, cGMPs should be followed in allowing access of staff to controlled areas.	immunization, if vaccine and medical staff are available."	
III. DEVELOPING AND EMERGENCY PLAN *(lines 77-322)*			
A. General Considerations (95-115)			
Lines 97-101:	As previously noted, most biopharmaceutical companies have already developed and are testing Business Continuity Plans. BIO appreciates FDA efforts to enhance the quality and availability of these plans, but we must note that these are business plans and requiring conformance to specified parts of 21 CFR 211, as called for in this document, is unnecessarily burdensome and provides no value to ensuring protection of the public health. For example, the Draft Guidance states that: *"The plan should be: developed, written, reviewed, and approved within the site's change control quality system in accordance with the requirements in 21 CFR 211.100(a) and 211.160(a); execution of the Plan should be documented in accordance with the*	Please include the following text and eliminate statements requiring that the plan must comply with specified parts of 21 CFR 211: "Companies should develop plans for addressing periods of high absenteeism that may impact manufacture, testing and distribution of medically necessary products. These plans should be developed and implemented in a way that supports conformance to the principles of GMP during its period of implementation."	High

	requirements described in 21 CFR 211.100(b).” BIO does believe that a Business Continuity Plan should be approved and maintained consistent with a quality systems approach and should support operation consistent with GMP principles. However given that emergency events will likely require prompt activation of the plan, there should be flexibility to maintain detailed plans in business documents because they will cover aspects of company operation other than GMP manufacture.		
Lines 100-101:	The Draft Guidance states that “As appropriate, standard operating procedures should be reviewed and revised or supplementary procedures developed and approved to enable execution of the Plan.” Supplementary procedures should not be necessary where effective and efficient processes or procedures are already in place. Rather, network level or site level risk management may be used to identify and prioritize which processes may require a supplemental or contingency plan.	Please replace the statement with: “Quality risk management may be used to help prioritize critical systems or processes used for manufacturing of MNPs, and determine where supplementary procedures ~~are~~ may be needed.”	Medium

Lines 103-108:	The Draft Guidance suggests that "A Plan should be specific enough to address unique considerations at each location where it is to be implemented. In the case of drug manufacturing, a company could consider developing a Plan for each individual manufacturing facility, as well as a broader Plan that addresses multiple sites within the organization. This approach provides for the specific and unique considerations of individual facilities and the flexibility to shift operations, resources, or personnel from one manufacturing facility to another." Developing both a broader plan and separate plans for each individual facility is burdensome and may not be necessary. BIO recommends that this paragraph should be made less prescriptive.	Please Change the wording to: "A Plan should be specific enough to address unique considerations at each location where it is to be implemented. ~~In the case of drug manufacturing, a company could consider developing a Plan for each individual manufacturing facility, as well as~~ A broader Plan may be developed to address multiple sites within the organization. This approach provides for the specific and unique considerations of individual facilities and the flexibility to shift operations, resources, or personnel from one manufacturing facility to another."	Medium
Line 114:	The Draft Guidance States that "In addition, each person or position identified in the Plan should have two designated alternates in the event the primary person is unavailable." We believe that this is too prescriptive and detailed for an FDA Guidance and would be handled by company internal delegation procedures.	Please delete the following text: ~~In addition, each person or position identified in the Plan should have two designated alternates in the event the primary person is unavailable.~~	High

C. Recommendations for Actions Prior to a Period of High Absenteeism (141-157)			
Line 143-145:	The Draft Guidance states that "When it is possible to anticipate an emergency that could result in a high rate of absenteeism affecting production of MNPs, CDER recommends that manufacturers take the following measures:" However, this implies that all actions would be prudent when a subset may mitigate the risks. Please revise the statement to not imply that all the measures listed should be taken.	Please revise the wording to: "When it is possible to anticipate an emergency that could result in a high rate of absenteeism affecting production of MNPs, CDER recommends that manufacturers consider one or more of the following measures:"	High
D. Considerations for Plan Implementation During a Period of High Absenteeism (158-229)			
Lines 187-190:	Though implied, it would be clearer if the risk assessment is stated as being completed prospectively.	Update the statement to: "CDER recommends that each manufacturer, in developing a Plan to address high rates of absenteeism, conduct a prospective risk assessment and ensure that appropriate risk control measures are identified, approved by relevant decision makers, and used in development of the Plan, with the objective of meeting the demand for MNPs while continuing to provide a high level of assurance that manufacturers comply with cGMPs and products meet specifications."	Medium

Lines 194-197:	Risk based decision making is an important element and should be emphasized in this section.	Please update the statement to: "CDER recommends that before taking such measures, a manufacturer have a well-supported conclusion, based upon its process and product knowledge and quality risk assessments to ensure that the actions planned to address absenteeism are not expected to unacceptably reduce assurance of product quality."	
Lines 212-214:	This provision emphasizes that activities that are being reduced do not unacceptably reduce assurance of product quality.	Revise the statement to: "If the demand for MNPs cannot be met by the measures described above, manufacturers can consider reducing activities that are more directly connected with batch manufacturing or a product accept/reject decision as long as they have a documented rationale or risk assessment to show that reduction in these activities does not unacceptably reduce assurance of product quality."	High
G. Documenting Emergency Activities (301-322)			
Line 303:	As long as the plan meets the expectations of the quality system for GMP activities, it does not need to be managed and executed through the quality system.	Revise the statement to: "CDER recommends that manufacturers manage the creation and execution of the Plan ~~per their quality system requirements to~~ ensure that	High

		manufacturing of MNPs during periods of absenteeism is in conformance with cGMPs ~~through their quality system in accordance with the CGMP requirements.~~"	
Lines 308-310:	Risk assessments are also supporting documentation for any decisions.	Please update the statement to: "~~Risk assessment,~~ Any supporting documentation for the Plan including risk assessments, management approval for any change to an approved procedure or activity, including delaying, substituting, or reducing the frequency of an approved procedure or activity as part of the Emergency Plan."	Medium
IV. TESTING THE EMERGENCY PLAN *(lines 323-349)*			
Lines 328-329, 344-345:	Finally, we note that the Draft Guidance suggests that testing of the plan should involve manufacture of test batches of the drug or biologic. BIO agrees there should be some level of "testing" of the plan, but we do not believe that it is always necessary to actually manufacture a test batch of product as part of the plan testing. For many products, production of test batches will be expensive, could actually contribute to product shortages, and may inadvertently compromise GMP compliance. We believe that if the company employs prior	Please remove the recommendations to manufacture product batches to test the Plan.	High

	experience, knowledge of the manufacturing process, and a risk assessment to develop the Plan, then that should provide sufficient rationale to assure that product quality is not compromised when it is manufactured under the Plan.		