Agência Nacional de Vigilância Sanitária, SIA
Trecho 5, Área Especial 57
Cidade: Brasília - DF CEP: 71.205-050

Dear Sir or Madam:

ISPE welcomes the opportunity to comment on the ANVISA document: **Brasil CP 03 09 - Boas Prática de Fabricação de Medicamentos**. Our specific comments are included in the attached table.

We also have some overarching conceptual comments as listed below.

1. ANVISA has made a significant step forward in revoking the RDC Resolution Nr. 210 dated August 4, 2003, which should now allow manufacturer's more flexibility in how they control the risk of cross contamination when dealing with high hazard compounds.
2. It is important to stress the difference between hazard and risk. The area of concern is high risk so risk should be assessed on a case-by-case basis. Risk should be reduced wherever it is determined to be above acceptable limits. ICH defines risk as the combination of the probability of occurrence of harm and the severity of that harm. All pharmaceutical compounds are hazardous, but when you factor in the manufacturing conditions, equipment, procedures, etc the risk could be quite low. ISPE's upcoming Baseline Guide, Risk Based Approaches for Manufacturing of Pharmaceutical Products (Risk-MaPP) suggests an approach to risk assessments for cross contamination.
3. The use of the term highly active or high hazard is preferred over categories or classes of compounds. The use of categories or classes of compounds tends to evoke an emotional response rather than a sound scientifically based response. Encouraging manufacturers to provide sound scientific justification to control the risk of cross contamination helps to ensure they are safely producing medicines for patients.

Thank you for the opportunity to comment. If you have any questions please do not hesitate to contact me.

Yours sincerely,

Robert P. Best
President/CEO

Attachments: ISPE Regulatory Comment Form; Brasil CP 03 09 - Boas Prática de Fabricação de Medicamentos (inglês)

ISPE Regulatory Comment Form
Proposed Regulation/Guidance Document: Brasil CP 03 09 - Boas Prática de Fabricação de Medicamentos (inglês)

No.	CURRENT WORDING	PROPOSED CHANGE	RATIONALE
1.	Section 12.24 So as to minimize the risk of serious health problems due to cross contamination, dedicated and separate installations must be used for the production of certain medications	So as to minimize the risk of serious health problems due to cross contamination, dedicated and separate installations **should be considered** as an option for the production of certain medications	Whilst dedicated or separated installations should be considered as an option to minimize risk when handling high hazard compounds alternative strategies should be possible and identified by means of a thorough risk assessment as suggested by ISPE Risk-MaPP
2.	Section 12.24 The production of certain highly active products, such as some antibiotics, certain hormones and cytotoxic substances must be carried out in separate areas.	For the production of certain highly active products, it may not be possible for cleaning to provide a sufficiently high degree of assurance that defined criteria can be met reproducibly. Under such circumstances production in separate areas should be considered.	Whilst dedicated or separated installations should be considered as an option to minimize risk when handling high hazard compounds alternative strategies should be possible and identified by means of a thorough risk assessment as suggested by ISPE Risk-MaPP
3.	Section 16.11 the most dangerous contaminants	the most severe hazards	The term hazard should be encouraged to reinforce the discussion of hazard and risk
4.	Section 16.11 Products whose contamination may cause greater damage to the users	Products whose contamination presents the greater risk of adverse effects to users	Reinforce the use of terms hazard and risk
5.	Section 16.12 The occurrence of cross contamination must be avoided by means of the appropriate techniques or organizational measures.....	A risk assessment should be undertaken to identify high risk processes and procedures. Options to reduce risk to an acceptable level may include, but are not restricted to.....	Reinforce the benefits of undertaking a risk analysis under all circumstances.
6.	Attachment II, Section 4.9 Crosscontamination must be prevented by adopting the following measures, when applicable:	A risk assessment should be undertaken to identify high risk processes and procedures. Options to reduce risk to an acceptable level may include, but are not restricted to.....	Reinforce the benefits of undertaking a risk analysis under all circumstances