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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

31. May 2005
Ref: LUNA 2005-20979-01/LPIL

Docket No. 2003N-0528
Draft Guidance for Industry on Manufacturing Biological Drug Substances, Intermediates, or Products Using Spore-Forming Microorganisms

Dear Sir/Madam

Novozymes is the biotech-based world leader in enzymes and microorganisms and has state-of-the-art expertise in microbiology, biotechnology and gene technology. Our biotechnology platform is based on the company's core competences. However, we are expanding our activities in the biopharmaceutical area and are currently developing several new projects based on Novozymes extensive experience with different spore-forming organisms e.g. *Aspergillus oryzae*.

The changes made to the requirements for spore-forming microorganisms to allow greater flexibility in manufacturing is fully supported by Novozymes. However, we would like to give the following comments:

The guidance focuses only on bacterial spore-formers and states that it does not apply to allergenic and fungi source material, or therapeutics.

We realise that the stated recommendations and precautions are only intended for manufacturing with the type of spore-formers that are currently used by the regulated industry. However, it is stated that any atypical or novel spore-formers may require specific controls that are unique for that

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particular organism. This would again not cover different fungal spore-formers.

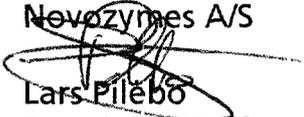
Novozymes is working on different sporulation deficient strains, however currently the most advanced projects are with different *Aspergillus* strains which are spore-formers. Furthermore, we are aware of other companies also working with different fungi spore-formers. Therefore, we do not understand the rationale to keep fungi source material out of the scope of this guideline.

In our opinion the justification provided in the Introduction and Background of the guidance is also applicable to different fungi e.g. *Aspergillus* and the exclusion of fungi from the scope may give the impression that none of the suggested modifications are feasible for fungi and all fungi source material still require permanently dedicated facilities.

Therefore we would like to suggest widening the scope of the guidance to include fungi source material giving manufacturers using fungi source material the opportunity to apply the modifications suggested and use the guidance together with specific controls unique for that particular fungus as justification.

On behalf of Novozymes, we appreciate the opportunity to comment on the Draft Guidance and hope that our comments will be taken into your consideration.

Sincerely,
Novozymes A/S



Lars Pilebo
Regulatory Affairs Manager