AUT-F0476	FORM
VERSION 1	EFFECTIVE DATE 25 NOVEMBER 2014

EVALATUION RECORD FOR REVIEW OF RETROSPECTIVE ASSESSMENT

PROJECT AUTHORISATION NUMBER	[redacted]
PROJECT TITLE	**THE DETERMINATION OF POTENCY VALUE FOR BOTULINUM TOXIN PRODUCTS INCLUDING POTENCY TESTING ASSOCIATED WITH THE MANUFACTURE OF BOTULINUM TOXIN PRODUCTS**
PROJECT MANAGER	[redacted]

A. ANIMAL NUMBERS AND SEVERITY

1. Comment on whether the animal numbers differed from the original project authorisation and the reasons for this.

720,000 mice are authorised for use, however only 196,698 mice have been used to date under this project authorisation. Fewer animals have been used to date than anticipated as the number of animals required is determined by the number of samples that are submitted by the Client for testing, which is difficult to predict accurately.

2. What was the actual overall severity of the project and was this as predicted in the original project evaluation? If so, can you identify any reasons for this difference?

The actual severity to date has been:
- Severe for 85,519 animals
- Moderate for 26,190 animals
- Mild for 84,989 animals

It was expected that a large proportion of the animals would experience severe suffering, therefore this is as predicted in the original project evaluation.

B. IMPLEMENTATION OF THE 3RS

Detail any elements identified that may contribute to the further implementation of the 3Rs should similar work be conducted in future.

Although [redacted] have an alternative in vitro test to replace the LD50 testing in certain circumstances, the remaining Clients [redacted] do not. These Clients are currently working on developing and validating an alternative but it is not available as of yet.

[redacted]

[redacted]

C. WELFARE CONCERNS, UNEXPECTED ADVERSE EVENTS AND DEVIATIONS

Comment on any welfare concerns, unexpected adverse events and deviations which may have arisen during the course of the project, and describe how these were dealt with.

There were no unexpected adverse events; it was expected that death would be the endpoint.

D. ACCURACY OF ORIGINAL HARM-BENEFIT ANALYSIS AND ACHIEVEMENT OF OBJECTIVES

Were the proposed objectives of the project actually achieved? If not, outline the reasons for this.

Yes. The objective of the project is to obtain critical information regarding toxin potency (LD50 potency) for every new batch produced by the manufacturers. This objective is being obtained to allow final release of the Botulinum products onto the market for human use.

In retrospect, was the original harm-benefit analysis accurate and in line with the actual harms that occurred and the benefits that were achieved? If not, outline the key areas in which this differed and any possible reasons for this.

Yes, the original harm-benefit analysis was accurate. The benefits are being achieved as predicted. Although the project remains severe, [redacted] are dedicated to the implementing more refined humane end-points, however this will take time to implement fully.

E. FEEDBACK PROVIDED TO PROJECT MANAGER

Enter the feedback to be given to the project manager

Thank you for providing the completed retrospective assessment report for the above project authorisation. We have reviewed your assessment and are satisfied with the outcome of this project.

In particular, we are satisfied that a commitment has been made to replace the use of live animals where possible and refine the humane end-points.

[redacted]

Please do not hesitate to contact us if you need any clarification on the content of this e-mail or the retrospective assessment process

F. FEEDBACK FOR SCIENTIFIC ANIMAL PROTECTION ASSESSORS

Outline the key points of the feedback for scientific animal protection project assessors below.

This is a severe project, which includes death as an endpoint for LD50 testing of Botulinum toxin products. Although [redacted] have an alternative in vitro test to replace the LD50 testing in certain circumstances, the remaining [redacted] do not. These Clients are currently working on developing and validating an alternative but it is not available as of yet.

This project authorisation was renewed in [redacted] and at the time the assessor [redacted] included the following specific conditions:
1. Death as the end-point of the procedures in this authorisation shall be avoided and replaced by early and humane end-points.
2. The project manager must [redacted] detailing the progress made in applying humane end-points on this project, including information on success rates with regards the identification of moribund animals for culling.

The project manager has recently submitted an update in relation to the implementation of humane endpoints (see correspondence from [redacted] uploaded to [redacted] [redacted] have informed their Clients of their plan to conduct pilot studies to allow the implementation of humane endpoints. The pilot studies will provide information on the time points at which the onset of the moribund status will be detected, allowing humane intervention to prevent further pain and suffering, without impacting on the performance of the assay. All Clients have agreed to this approach. It is planned to conduct the first study by [redacted]

G. KEY FINDINGS FOR THE NATIONAL COMMITTEE

Outline the key findings from this retrospective assessment which can be provided in the future to the National Committee if required.

This is a regulatory project involving Botulinum toxins and LD50 testing. Humane endpoints are being introduced for a procedure that to date has required death as an endpoint. This will involve increasing the monitoring of the animals to humanely euthanise the animals prior to death. In addition, one client has developed an alternative in vitro test to replace the LD50 testing in certain circumstances. However the remaining clients have not yet been able to replace LD50 testing with an alternative.

ASSESSOR SIGNATURE: [redacted]

DATE: **09/03/16**