OVERVIEW OF COMMENTS RECEIVED ON
VICH GUIDELINE ON STATISTICAL EVALUATION OF STABILITY DATA (VICH GL 51)

	Name of VICH delegation that commented on Draft VICH GL on Statistical Evaluation of Stability Data
1	SwissMedic, Swiss Agency for Therapeutic Products, Dept. of Veterinary Medicines
2	Canadian Animal Health Institute (forwarded by Health Canada's Veterinary Drugs Division)
3	Canadian Food Inspection Agency, Veterinary Biologics (forwarded by Health Canada's Veterinary Drugs Division)
4	Republic of Senegal, Ministry of Livestock, Directorate for Veterinary Services
5	Nigeria, Federal Department of Livestock

Discussion of comments

GENERAL COMMENTS - OVERVIEW		
1.	SwissMedic The content of the guideline is identical to the ICH GL Q1E from February 2003 except for the lines 54-55, where it is mentioned that the application for veterinary drug products entirely optional (see below), and except for the references made towards veterinary guidelines. We support this statement as well as the guideline itself.	Noted. (No changes needed.)
2.	Canadian Animal Health Institute We have no issues with the draft Guidance as written. We are more concerned with how the statistically derived storage conditions and shelf life will be related to the labeled storage conditions as this has been an area of difficulty. ICH defines Canada as a zone 1 country and therefore 25°C/60% RH is the long term condition and according to ICH is sufficient to justify the shelf life at Canadian temperatures and humidities including excursions. With Health Canada's "crackdown" on storage conditions the issue has become confused. The labeled storage conditions must cover a sufficient range that a distributor/customer is not out of compliance so the labeled conditions are now "Store at or below 30°C" to cover excursions that may occur in the field. But since the labeled conditions must be supported we are starting to see scope creep where 30°C/65% RH is now the baseline. However according to ICH a shelf life calculated at 30°C/65% RH is suitable for zone 2 countries like Venezuela and Brazil so these conditions are actually far too harsh for Canadian conditions.	Noted. However, these climatic zones have been established for many years for both ICH and VICH purposes and are enshrined in many (V)ICH Quality guidelines. It would therefore not be possible to resolve this concern by amendment of this one guideline. It would need to be addressed within (V)ICH at a higher level. No changes are therefore to be made.

3.	Canadian Food Inspection Agency, Veterinary Biologics Although it is mostly applicable to veterinary drugs, the wording of the guideline did suggest that it may be considered for veterinary biologics (since it applies to veterinary medicinal products which does include veterinary biologics). This guideline (section 2.4.1) proposes that extrapolation from 'long-term' (real-time) stability data could be used to request even longer shelf lives than the existing data supports. We would not consider extrapolation of stability data to extend the expiry date due to the inherent batch to batch variability of veterinary biologics.	This VICH guideline GL51 on Evaluation of Stability Data is an extension to the parent VICH guideline GL3 (Stability Testing of New Veterinary Drug Substances and Medicinal Products). For specific requirements regarding biotechnological/biological veterinary medicinal products, the parent guidance VICH GL3 refers to VICH GL17 (Stability Testing of New Biotechnological / Biological Veterinary Medicinal Products) and even this is not applicable to conventional vaccines. Furthermore, the Scope (section 1.3) of VICH GL51 does state "*This guideline addresses the evaluation of stability data that should be submitted in registration applications for new molecular entities and associated veterinary medicinal products.*" It would not be usual for immunological or biological products to be considered as a "new molecular entity". This would normally be interpreted as meaning a new chemical/pharmaceutical active substance. Considering the above, and in order to keep this guideline similar to the corresponding ICH GL Q1E, it is considered not necessary to make any further specific references to the exclusion of vaccines from the scope of VICH GL51.

4.	Republic of Senegal, Ministry of Livestock, Directorate for Veterinary Services Manufacturers are free to use statistical analysis to justify a retest period or shelf life estimation for products. Regression analysis is an appropriate approach to analysing quantitative stability data for retest period or shelf life estimation and the guideline recommends that a statistical test for batch poolability be performed using a level of significance of 0.25. However, for a regulatory authority, the fewer the variants and extrapolation there are, the easier and more justifiable its decisions are. Until now, we have relied on original studies submitted to us, which are based on stability tests conducted under highly specific temperature and humidity conditions. In exceptional cases, for certain substances and dosage forms, extrapolation and statistical analysis may be essential for performing product stability studies and retesting. In conclusion, draft guideline GL51 needs to be improved and discussed further to minimise the possibilities of extrapolation. Indeed, not all regulatory authorities are proficient in quantitative or even descriptive statistics, especially in countries not yet members of VICH.	The parent VICH GL 3 (R) on Stabiltiy Testing of New Veterinary Drug Substances and Medicinal Products already allows limited extrapolation of the real time data from the long term storage condition beyond the observed range. This guideline describes when and how extrapolation can be considered. It is not the intention of this GL to minimise the possibility of extrapolation but to lay down acceptable criteria in case that extrapolation is proposed (no changes in guideline).
5.	Nigeria, Federal Department of Livestock The GL is suitable and can be followed by the institute.	Noted (no changes in guideline).

SPECIFIC COMMENTS ON TEXT

SECTION ….

Paragraph no.	Comment and Rationale	Proposal for consideration
Section 1.1, paragraph 1, last sentence	SwissMedic Comments: We support this statement. Proposed change (if any): None.	Noted. (No changes needed.)
Section 2.1, paragraph 6, last sentence	Nigeria, Federal Department of Livestock There is need to spell out the type of data evaluation that can be used for qualitative attribute if they are important for setting retest period or shelf life of veterinary medicinal products.	Qualitative attributes (e.g., identity) are not amenable to statistical data analysis and extrapolation. Therefore there is basically no data evaluation of qualitative attributes in the context of the generation of stability data (no changes in GL).