EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

11 September 2025
EMA/CVMP/VICH/250843/2021
Committee for Medicinal Products for Veterinary Use (CVMP)

VICH GL62 on target animal safety of veterinary monoclonal antibody products (VMAPs)

Draft

Draft agreed by VICH Steering Committee	August 2025
Adoption by CVMP for release for consultation	11 September 2025
Start of public consultation	15 September 2025
End of consultation (deadline for comments)	15 February 2026

Comments should be provided using this template. The completed comments form should be sent to vet-guidelines@ema.europa.eu

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000

International Cooperation on Harmonisation of Technical Requirements
for Registration of Veterinary Medicinal Products

VICH GL62 (BIOLOGICALS: TAS EVALUATION FOR VMAP)
August 2025
For consultation at Step 4

TARGET ANIMAL SAFETY EVALUATION FOR VETERINARY MONOCLONAL ANTIBODY PRODUCTS

Recommended for Consultation at Step 4 of the VICH Process
in August 2025
by the VICH Steering Committee

This Guideline has been developed by the appropriate VICH Expert Working Group and is subject to consultation by the parties, in accordance with the VICH Process. At Step 7 of the Process the final draft will be recommended for adoption to the regulatory bodies of the European Union, Japan and the USA.

Secretariat: c/o HealthforAnimals, Rue d'Idalie 9-13, Box 5, B - 1050 Brussels (Belgium)
e-mail: sec@vichsec.org – Website: www.vichsec.org

TABLE OF CONTENTS

1. INTRODUCTION

Submission of target animal safety (TAS) data is a regulatory requirement for the approval, registration, or licensure of veterinary medicines in the countries and regions participating in the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH).

The use of this VICH guideline (GL) is recommended for the TAS evaluation of a veterinary monoclonal antibody product (VMAP), a class of biological therapeutic products which contain a monoclonal antibody (mAb) or a mAb fragment.

This guideline contributes to the international harmonization of methods used for the TAS evaluation of VMAPs and aids in preparing and conducting VMAP TAS studies under laboratory and field conditions. A harmonized standard is intended to aid in development of mutually acceptable VMAP TAS programs. It is expected that harmonized guidance will accelerate the development and commercialization of novel VMAPs, leading to increased innovation and access to such products in veterinary medicine.

This guideline outlines general scientific principles for evaluating the safety of a VMAP and is intended to be used in conjunction with the required TAS study(ies). Not all recommendations in this document may be appropriate nor needed for all VMAPs and scientific advice should be sought from the relevant authority when needed. For some VMAPs, additional information not specified in this document may be needed to fully evaluate TAS.
The applicant should explain how the principles of this GL have been applied to their specific VMAP and scientifically justify any differences from the recommendations in this GL. The acceptability of the application of this GL is at the discretion of the relevant regulatory authority.

1.1 Objective

The purpose of this GL is to provide recommendations for determining the safety of a VMAP in the target animal. TAS evaluations should reflect the mode(s) of action of the target and the properties of the VMAP should be considered as they apply to a specific VMAP.
The purpose of this GL is to identify areas of specific importance for the TAS evaluation of a VMAP related to biological activity of the VMAP and target (pharmacodynamics), pharmacokinetics, immunogenicity, reproductive and developmental safety, mammary gland safety, local tolerance, field safety, and other considerations (e.g., general toxicity, and carcinogenicity).

1.2 Background

Currently, no VICH GL specifically supports marketing applications for VMAPs in the regions participating in the VICH. The VICH GLs available for TAS (i.e., VICH GL 43 for pharmaceutical products and VICH GL 44 for vaccines) do not fully address the TAS evaluation for a VMAP. Furthermore, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) GL S6 (R1) for the preclinical safety evaluation of biotechnology-derived pharmaceuticals is not fully applicable to VMAPs. Hence,

there is a need for specific guidance on the TAS evaluation of a VMAP.
Therefore, this guideline summarizes scientifically acceptable general principles for the TAS evaluation of a VMAP and should be used in conjunction with VICH GL 43.

1.3 Scope

This guideline is for VMAPs intended for use in companion animals and livestock animals.
The active ingredient of a VMAP is a mAb or a mAb fragment, which could be engineered to be specific for a target animal and target(s).
When needed, advice should be sought from the relevant regulatory authority for specific guidance on the design of the TAS study(ies) prior to their initiation or if the applicant determines an alternative approach to the TAS evaluation of a VMAP may be more appropriate.

This guideline does not fully address the TAS evaluation of an antibody-drug conjugate (ADC), in which a small molecule product is conjugated with an antibody or antibody fragment. However, the information in this guideline may be applicable for certain safety aspects of the antibody portion of an ADC.

This guideline does not include any recommendations for human food safety considerations.
Additionally, this guideline does not include any recommendations for human user safety evaluations, or for accidental human exposure while handling a VMAP.
This guideline does not apply to antibodies developed for diagnostic purposes.

1.4 General Principles of the TAS Evaluation for VMAPs

Safety information should be collected from the target species in a well-designed laboratory study(ies) in healthy animals and in field study(ies) in the intended target population.

A Comprehensive Risk Assessment (CRA) should be conducted by the applicant and used to determine the extent of data needed to support the overall TAS evaluation of the VMAP in the target animal. The laboratory and field studies should be designed to address the safety risks identified in the CRA. The CRA is expected to evolve over the course of development and should be provided to the regulatory authorities based on local submission requirements.

A CRA should include and take into account the following:

- Proposed therapeutic indication
- Proposed duration of treatment
- Proposed dose, route of administration, and product formulation
- Attributes of the VMAP (e.g., mAb immunoglobulin class, degree of speciation, directed or functional mutations)
- Target specificity of the VMAP, including potential cross-reactivity, cross-binding properties, or off-target specificity
- Pharmacokinetics (PK) of the VMAP
- Intended effect(s) and biological activity (i.e., pharmacodynamics (PD)) of the VMAP, including whether the effect is agonist or antagonist and the consequences thereof
- Risk and potential consequences of VMAP immunogenicity (e.g., anti-drug antibodies), immunotoxicity, and immunomodulation
- Risk and potential consequences for transplacental and transmammary passage or

transfer of the VMAP
- Characteristics and known biology of the intended target(s), including the mode of action or role of the target in physiological pathways (i.e., both the intended target pathways and unintended pathways)
- Location and expression of the target in healthy and diseased animals and potential body systems impacted
- Current scientific knowledge of the VMAP or similar mAbs (in both humans and animals)
- Current scientific knowledge of the effects of interference with the intended target by other products (e.g., a small molecule inhibitor)

The CRA may include reference(s) to scientific literature, explanation(s) of the molecular engineering of the VMAP, *ex vivo* or *in vitro* characterization data of binding properties, *in silico* exploration of homologues to the target, or *in vivo* exploratory studies in the target animal or relevant surrogate species. Any *in silico*, *in vitro,* or *ex vivo* method used to support the assessment of the safety risk should be justified in terms that support inference to the safety of *in vivo* usage of the VMAP in the intended target population.

Information obtained from all laboratory and field studies in the target species, including PK and PD studies, should be presented for the TAS evaluation of the VMAP. The entire body of information collected is intended to justify the details of the TAS evaluation and the overall safety of the VMAP.

The VMAP should be sufficiently safe for the intended target population, including potentially sensitive subpopulations if relevant. If a surrogate or non-target species is used to derive supportive safety information for the VMAP, the applicant should provide justification that the results obtained from the surrogate or non-target species are relevant to the target species. Consideration should be given to the relevance of studies in non-target species before they are conducted because these studies would not replace TAS studies in the target species.

VMAP studies should be conducted with the final formulation where possible and the VMAP should be administered by the intended route of administration. If a non-final VMAP formulation is used in any study (e.g., PK/PD study, pilot study, *ex vivo* analyses), then the applicant should provide justification that the results obtained are relevant for the final formulation in the target species.

Depending on the results of the safety evaluation, appropriate information should be included on the labeling.

2. STUDY DESIGN

TAS studies for VMAPs should be designed using the principles of VICH GL 43. This section covers and describes additional VMAP-specific considerations when conducting TAS studies to evaluate the safety of VMAPs in the target animals (e.g., Margin of Safety (MOS) studies, other laboratory safety studies, and field studies).

VICH GL 43 provides information on variables to be measured during a MOS study. The four

types of variables outlined in VICH GL 43 for a MOS study are physical examinations and observations, clinical pathology tests, necropsy (gross pathology), and histopathology examinations. The MOS study design, as described in VICH GL 43, may be adapted or extended to ensure evaluation of potentially significant safety risks specific to each VMAP. Deviations or adaptations to the above may be acceptable on provision that they are scientifically justified and that the complete data set allows for conclusions on the safety profile in the target species. In some cases, and at the discretion of the regulatory authority, a VICH GL 43 MOS study may not be necessary if an adequate TAS evaluation can be obtained from other studies, including field studies. In other cases, it may be necessary to conduct more than a MOS study to ensure proper evaluation of all significant TAS risks.

2.1. Study objectives and endpoints

The overall objectives, methods, and endpoints for VMAP TAS evaluations should be established based on conclusions from the comprehensive risk assessment (as described in Section 1.4).

TAS studies (e.g., MOS study, other laboratory study, field studies) should incorporate evaluations to assess for significant unintended pharmacological effects identified in the CRA. To understand the potential impact of these unintended pharmacological effects of the VMAP, the applicant should consider incorporating robust PK evaluations into the TAS studies.

TAS studies should include evaluation of the incidence and consequences of immunotoxicity or immunomodulation *(*i.e., the inadvertent effects on the immune system), the incidence and consequences of immunogenicity, and the incidence and description of idiosyncratic responses (e.g., anaphylactic reactions).

Infrequent adverse reactions, idiosyncratic responses, effects on the immune system, and immunogenicity may not be directly identified from *in vivo* laboratory studies due to the small numbers of animals and the limited duration of use. Therefore, in addition to the laboratory TAS studies, field studies with larger numbers of animals from the intended target population should also incorporate TAS evaluations based on conclusion from the CRA.

As a general principle, data should allow for the confirmation of margin of safety and the expected target organs or body systems affected, using the minimum number of animals appropriate for the studies.

2.2. Selection of study animals

TAS studies for a VMAP should be conducted in the target species.
Follow VICH GL43 for the selection of test animals and the number of animals per sex in the MOS study.

Generally, healthy animals are used in laboratory studies and animals in the intended target population (with comorbidities, concurrent treatments, individual genetic backgrounds, etc.) are used in the field studies.

2.3. Route of administration and dose

TAS studies should be designed using the intended route of administration and dosage, including repeat administrations and treatment duration, for the intended use of the VMAP. Specific dose, frequency, and duration combinations for use in TAS studies should be selected and justified based on the pharmacology and toxicology of the VMAP. When more guidance is needed, refer to VICH GL43.

The minimum (nominal) dose and dose intervals are typically established based on efficacy data. The minimum "1X" dose level used in laboratory TAS studies should be based on the highest dose exposure from the intended label dose (by body weight unless justified otherwise) of the VMAP.

As with pharmaceutical products, the same dose administration of VMAPs may lead to different exposure levels and safety risks in healthy, young laboratory animals compared to the intended target population. The dose multiples, 1X plus two appropriate overdose multiples used in MOS studies for VMAPs should reflect an understanding of the indication, a dose to response relationship, the pharmacology (unintended on- or off-target effects), general properties of mAbs, and specific properties of the VMAP. Even if target saturation is required to exert a pharmacological effect for the VMAP, and an increased dose is expected to provide little additional information related to the intended pharmacology, overdose testing should be performed to evaluate for increased tissue penetration, potential for binding to unexpected homologous epitopes, and other objectives related to evaluating the safety profile.

2.4. Product used in studies

As a general principle, in studies providing pivotal safety and PK data (including local tolerance evaluation and clinical field trials), the final formulation (drug substance, excipients) should be used. Appropriate justification for deviating from this approach should be provided and may be discussed with the relevant regulatory authority.

If non-final formulation is used for a TAS study, then relevance to the final formulation of the VMAP should be justified in all relevant aspects, to support that data can be reliably extrapolated to the final formulation.

The VMAP should be evaluated by comparison to an appropriate control.

3. TARGET ANIMAL SAFETY EVALUATION

3.1. Biological activity (Pharmacodynamics)

VMAPs are diverse in their biological activity and pharmacological actions, depending on the animal species, antibody characteristics, targets, mechanism of action, and targeted biology (including intended and unintended effects). Thus, the TAS evaluation of VMAPs should be based on a CRA that considers the direct effects of the VMAP and the potential for unintended on-target effects, off-target effects, and effects on the immune system.

An understanding of the biological activity of the VMAP should be established and the potential risks associated with the biological activity of the VMAP should be identified prior to

any pivotal target species studies. Biological activity of the VMAP can be evaluated using *in vitro* assays and *in silico* approaches. The pharmacological characterization of a VMAP's biological activity should include the specificity of binding to the intended target molecule or epitope, the potential for non-target binding, potential for complement fixation, and potential to induce cytotoxicity. Other factors may be relevant and should be addressed as appropriate for individual VMAPs. Biological activity of the VMAP may also be further examined *in vivo* in the target animals, using PK/PD tests.

3.1.1. Unintended effects

Potential unintended effects are an important safety aspect that should be considered and may occur due to the interaction of the VMAP with the target in target sites, with the target in off-target sites, or with off-target(s).

As noted in Section 1.4, a CRA should be conducted which includes identifying any potential unintended effects. Generally, those unintended effects can be categorized as either an unintended on-target effect or an off-target effect.

3.1.1.1. Unintended on-target effects

An unintended on-target effect may occur when a VMAP binds to the intended target and induces an unintended effect or induces an exaggerated pharmacological intended effect.

The CRA (see Section 1.4) and known biology of the intended target should be used to determine if additional study variables are needed to evaluate the clinical impact of potential unintended on-target effects by the VMAP in the laboratory and clinical field studies.

To evaluate for unintended on-target effects, the location (e.g., organs, tissues, cells) of the intended target should be identified and the potential biological activity of the VMAP at each target site evaluated.

The TAS studies should be designed to evaluate the incidence and consequence of unintended on-target effects and ideally determine a dose-response relationship and a dose level at which unintended on-target effects may occur.

Although the expression level of the intended target is an important factor in determining a potential impact of unintended on-target effects, the expression patterns of the intended target can be significantly different among animals and between animal species, and limited information may be available. Additionally, the expression patterns of the intended target can be significantly different between healthy laboratory target animals and the intended target animal population. Therefore, use or extrapolation (from laboratory animals or other species) of target expression data may not be appropriate or sufficient to evaluate the risk of unintended on-target effects in the intended target population.

3.1.1.2. Off-target effects

An off-target effect may occur when a VMAP binds to an unintended target molecule and induces an unintended effect.

To evaluate for unintended off-target effects, *in silico* tools to identify similar binding epitopes

between the intended target and off-target(s) may be used for the initial identification of potential cross-reactivity of the VMAP. The *in silico* analyses can be complemented with *in vitro* binding assays or functional cell-based assays to further describe the potential off-target effects of the VMAP.

The TAS studies should be designed to evaluate the incidence and consequence of off-target effects identified in the CRA and ideally determine a dose level at which off-target effects may occur.

3.1.2. Unintended effects on the immune system

Administration of a VMAP has the potential to unintentionally affect the immune system, through immunomodulation (modification of an immune response or function of the immune system), immunosuppression (dampening of an immune response or function of the immune system), or immunotoxicity (an adverse effect leading to immune system dysfunction). If any of these are suspected for the VMAP as unintended effects, ICH GL S8 “immunotoxicity studies for human pharmaceuticals” may be referred to for a discussion on the weight of evidence around potential risks.

For a VMAP with suspected or known unintended effect(s) on the immune system, the potential clinical impact of the effect(s) should be evaluated in the laboratory and field studies. The variables in the studies to evaluate for the effects on the immune system should be based on relevant aspects of the VMAP including, but not limited to, intended use, mode of action, class of antibody, route of administration and type of effect on the immune system induced (e.g., mechanism of modulation).

Additionally, as immunosuppressive effects may render the treated animals more susceptible to opportunistic or secondary infections and the development or worsening of neoplasia (due to impaired immune surveillance), the laboratory and field studies should assess the incidence and descriptions of these adverse reactions and correlate them with the study variables linked to effects on the immune system.

In addition to the safety data derived from laboratory and field studies, for some VMAPs the potential risks for unintended effects on the immune system may be evaluated through specialized assessments or additional studies. Depending on the potential risk to the immune system, additional assessment may include, but are not limited to, immunophenotyping, T-cell dependent antibody response, a pathogen challenge test, or an evaluation for a potential impact on the target animal’s ability to mount an adequate immune response to vaccination (a vaccine response safety study).

Depending on the immunoglobulin class or subclass and engineering of the VMAP, the effector activity of the Fc region of the VMAP may unintentionally affect the immune system and safety evaluation of the VMAP (e.g., antibody-dependent cell-mediated cytotoxicity, complement-dependent cytotoxicity, antibody-dependent cellular phagocytosis). Therefore, the effector activity of the Fc region of the VMAP should be determined, the potential clinical impact of any Fc effector activity described as appropriate, and, if needed, an assessment of the potential clinical impact incorporated into the TAS evaluation.

3.2. Pharmacokinetics

The PK data (e.g., exposure levels) of the VMAP following administration should support the establishment of a safety profile.

To evaluate the clinical impact of immunogenicity of the VMAP in an animal, PK data should be included as part of TAS studies and correlated with immunogenicity findings, when possible (see Section 3.3).

3.3. Immunogenicity

VMAPs may be recognized as foreign proteins by the immune system, and potentially induce the development of an immune response (immunogenicity). Hence, all VMAP applications should include an Immunogenicity Risk Assessment where appropriate.

The risk of immunogenicity for each VMAP should be assessed on an individual basis. An appropriate immunogenicity risk assessment should be included within the CRA. An immunogenicity risk assessment should include, but is not limited to, considerations for the intended target population and intended use, characteristics of the VMAP, and dosing duration. Conclusions from the immunogenicity risk assessment should be used to identify appropriate assays to evaluate relevant immunogenicity parameters and the need for additional safety evaluations in the laboratory and field studies. If a risk for immunogenicity is identified, treatment with the VMAP may result in an immune response which may cause the absence, reduction, or loss of effectiveness, or an increased risk for an adverse reaction or no apparent clinical impact.

Immunogenicity evaluations in the laboratory and field studies may include investigation of parameters for cellular (e.g., T-cell response assay) and humoral (e.g., detection of anti-drug antibodies) response before and after VMAP administration as appropriate. The safety of the VMAP related to immunogenicity is evaluated based on the clinical impact or consequences, which may be loss of effectiveness, an elicitation of adverse response(s), or no apparent clinical impact.

The assay methods used to evaluate immunogenicity should be appropriately designed and developed to be suitable for the intended purpose. If the assay methods are not suitable for the intended purpose, then the immunogenicity data generated may not accurately assess the clinical impact and the clinical relevance of the immunogenicity data collected may not be determined.

Samples to evaluate immunogenicity should be collected at justified intervals from animals receiving the VMAP in studies (e.g., PK, TAS, dose determination or confirmation, clinical studies) to allow for an overall immunogenicity evaluation.

When an immune response is detected, the clinical impact of that response (e.g., loss of effectiveness, elicitation of adverse responses, or no apparent clinical impact) should be evaluated by reviewing the immunogenicity data in combination with PD (e.g., biological activity, adverse responses) and PK (e.g., exposure, plasma concentrations) data.

3.4. Reproductive and developmental safety

Unless acceptable scientific justification for the absence of risk can be presented, reproductive safety and developmental safety studies should be conducted if the intended target population includes breeding, pregnant, or lactating animals. If such justification cannot be provided and if relevant data to allow an assessment of potential risks is not available, the product label should state that safety has not been determined in breeding, pregnant, or lactating animals, or their offspring.

The need for conducting specific reproductive or developmental safety studies in the target animal should be addressed in the CRA (see Section 1.4).

If the VMAP crosses the placenta or is excreted in milk, reproductive and developmental safety studies in the target species may be necessary when breeding animals are proposed to be treated during the reproductive period. The risk and potential consequences for the embryo, fetus, and newborn should be addressed.

The reproductive and developmental studies should be performed in the target species and adapted from Section 3.3 Reproductive Safety Studies in VICH GL43.

3.5. Mammary gland safety

Mammary gland safety studies should be conducted to evaluate the safety of VMAPs intended for intramammary use in lactating or non-lactating animals.

The mammary gland study should be performed in the target species and adapted from Section 3.4. Mammary Gland Safety Studies in VICH GL 43.

3.6. Local Tolerance

The final formulation of the product should be used to evaluate local tolerance, that is administration site or injection site safety. Evaluation of the administration site after VMAP administration (i.e., immediately after and throughout study) should be included in both laboratory and field studies following the endpoints listed in Section 3.1. Injection Site Safety Studies in the VICH GL 43.

3.7. Field Safety

Field studies also provide essential TAS data in addition to efficacy under conditions of intended use. The study design may be adapted from Section 4 (Target Animal Safety Data from Field Studies) in VICH GL 43 and include relevant TAS evaluations as established by the CRA (see Section 1.4).

3.8. Other Consideration

General toxicity and genotoxicity†:

As a VMAP is commonly designed to be species-specific and the safety of a VMAP in the target species can be directly evaluated in TAS studies using the intended target species, general toxicity laboratory studies using non-target species are not needed as preliminary data, including in regions or countries in which they are usually required as part of target animal safety assessment during drug product registration.

It is not expected that VMAPs would interact directly with DNA or other chromosomal material. However, if a genotoxicity concern for the VMAP is identified in the CRA, then any relevant studies should be conducted.

Carcinogenicity:

If a carcinogenicity concern for the VMAP is identified in the CRA, then the TAS studies should evaluate the risk of carcinogenicity (e.g., cytological or histological review of lymph node aspirates, growth biopsies, or aspirates of growths, or clinical pathology changes) with continued follow-up evaluations when appropriate.

---

† In regions except Japan, general toxicology and genotoxicity are not required for the assessment of target animal safety evaluation. This section addresses the unique circumstances in Japan where toxicity studies using rodents are required before evaluating safety in the target animals.

4. GLOSSARY

Antibody-Dependent Cell-mediated Cytotoxicity (ADCC): Cytotoxic activity exerted by immune cells such as natural killer cells and macrophages upon recognition of antibody-bound cells and pathogens via Fc receptors.

Antibody-Dependent Cellular Phagocytosis (ADCP): Phagocytic activity exerted by phagocytes (e.g., macrophages and neutrophils) upon recognition of antibody-bound cells and pathogens via Fc receptors and/or complement receptors.

Agonist: A molecule that binds to a receptor in an animal body and activates the receptor to produce a biological response.

Antagonist: A molecule that prevents an agonist from binding to its receptor in an animal body and prevents activation of the receptor to suppress a biological response.

Cellular immune response: An immune response that is mediated through activation and activity of cells such as macrophages, natural killer cells, and cytotoxic T cells.

Chimeric monoclonal antibody: Antibodies developed from more than one animal species, thus having domains from each.

Complement-Dependent Cytotoxicity (CDC): Cytotoxic activity exerted by the complement system upon binding of an antibody to the target cells and pathogens.

Comprehensive Risk Assessment (CRA): Comprehensive risk assessment involves a systematic process to identify, analyse, and evaluate potential risks of the VMAP to the target animal to determine the extent of safety data needed to support the overall TAS evaluation.

Epitope: The specific part of an antigen recognized by the antibody.

Fc receptors: Receptors for the Fc regions of antibodies.

Fc region: Fragment crystallizable (Fc) region or constant region of the antibody, which binds to Fc receptors on cells and fixates complement.

mAb Fragment: Manufactured antigen-binding fragment of a mAb, containing the variable region of an antibody. Examples of mAb fragments are single-chain variable fragment (scFv) and fragment antigen-binding (Fab, $F(ab')_2$) antibodies.

Humoral immune response: B-cell mediated immune response, which produces antibodies.

Idiosyncratic response: An adverse reaction that does not occur in most animals treated with a drug/VMAP and does not involve the therapeutic effect of the drug.
Excessive and abnormal reactions usually due to congenital predisposition to drugs and other substances to which animals with normal constitutions should not react (e.g., hypersensitivity

anaphylactic reaction).

Immunogenicity: The ability of a substance, such as an antigen, to provoke an immune response.

Immunomodulation: Modification of an immune response or function of the immune system.

Immunotoxicity: An adverse effect leading to immune system dysfunction.

ICH: International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use. The International Council brings together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of pharmaceuticals and develop guidelines regarding pharmaceutical regulation.

Margin of Safety Study: Well-controlled study designed to show if a VMAP is safe for the intended species. It is generally conducted by treating healthy target animals with two or three non-zero multiples of the proposed dosage followed by clinical evaluation, clinical pathology, necropsy, and histopathology of tissues to detect adverse effects.

Monoclonal antibody (mAb): Manufactured immunoglobulin derived from a single clone that are homogeneous in structure and binding specificity.

Off-target (for a monoclonal antibody) effects: An unintended pharmacological response caused by off-target binding (binding of a monoclonal antibody to a non-target(s)). It can affect the pharmacokinetics, tissue distribution, efficacy, and toxicity of the monoclonal antibody.

On-target (for a monoclonal antibody) effects: Refers to any consequences arising from binding of a mAb to the intended epitope. On-target effects include the effect on the target, associated effector functions if any, and secondary consequences at tissue, organ, and system levels.

Speciation (of a monoclonal antibody): The engineering of a mAb amino acid sequence to coincide with that of a specific antibody from the target species. Speciation can be partial (chimeric monoclonal antibodies) to complete (native monoclonal antibodies).

Target animal: The specific animal species, class and breed identified as the animal for which the VMAP is intended for use.

Target animal safety (TAS) study: In this guideline, TAS study refers to any study using the target animal species that supports the evaluation of safety in the intended target population, including but not limited to, a margin of safety (MOS) study, other laboratory studies and clinical field study(ies).

Target (for a monoclonal antibody): That to which the monoclonal antibody is intended to bind.

Target population: Intended group of patient animals that will be treated with the product.

Veterinary Monoclonal Antibody Product (VMAP): A class of therapeutic products for animal use, which contain whole monoclonal antibody or a fragment of a monoclonal antibody as active ingredients.

References

1. ICH, GL S6(R1): Preclinical safety evaluation of biotechnology-derived pharmaceuticals, 2011
2. ICH, GL S8: Immunotoxicity studies for human pharmaceuticals, 2005
3. VICH, GL43: Target animal safety for veterinary pharmaceutical products, 2008
4. VICH, GL44: Target animal safety for veterinary live and inactivated vaccines, 2008