Veterinary Medicines Directorate

Technical guidance for completion of Standard and Urgent Signal Notifications

This guidance applies only to signal notification submissions. For Benefit-Risk Submission Reports, refer to the guidance document 'Technical guidance for completion of the Benefit-Risk Submission Reports' and for sales submissions, refer to the guidance document 'Technical guidance for completion of the Pharmacovigilance Sales Submission (PSS)' which can be found at Benefit-risk report (BRR) and signal notification submissions.

Related guidance can be found at Pharmacovigilance of Veterinary Medicinal Products in Great Britain.

Submission queries should be sent to psur.queries@vmd.gov.uk or via VMDS secure messaging to the PSUR Queries group.

1. General guidelines

1.1 Submissions

Signal notifications should be submitted as a single completed Excel document using the BRSR template at Benefit-risk report (BRR) and signal notification submissions per Marketing Authorisation (MA) number or Product Group Code (PGC). See section 1.6 of this guidance for further details on PGCs.

They should be used to inform the VMD of all validated signals which following assessment, suggest a new risk, change to the benefit-risk balance, or require further investigation.

One signal notification (one Excel document) should be submitted per signal (per Preferred Term (PT)) or set of related signals.

Validated signals that are deemed to not require any further action should be submitted within the BRSR.

Signal notifications should be submitted using the Veterinary Medicines Digital Service (VMDS), a secure messaging service. Any Marketing Authorisation Holder (MAH) not signed up to VMDS can register.

Once signed in to the VMDS account, the MAH should select the relevant group. This is PHV Signals for Standard (30-day) Signals and PHV Urgent Safety Signals for Urgent Safety Signals.

Urgent safety signals notifications should be used for signals containing new information affecting the benefit-risk balance of a product which require *rapid* implementation of risk minimisation/safety measures.

Enter either the file name as per the naming convention guidance below or the PGC/MA number as applicable within the subject line of the VMDS message.

Further information on the types of signal notification can be found in sections 2 and 3 of Guideline IV of Pharmacovigilance of Veterinary Medicinal Products in Great Britain.

Further information on signal submissions can be found in section 3.1.3 of Guideline IV of the Pharmacovigilance of Veterinary Medicinal Products in Great Britain, including specific details on the reporting of signals during the transition period.

Follow-up signal notification submissions

A follow-up signal notification should be submitted if further significant information related to that signal is identified or the MAH wishes to alter/add to a previously reported action, unless the VMD has already agreed with the MAH that the information should be received via a different method. Follow-up signal notifications can be submitted at any time, including across reporting periods. Further details on when a follow-up signal notification should be submitted can be found in section 3.1.3 of Guideline IV of the Pharmacovigilance of Veterinary Medicinal Products in Great Britain.

1.2 Language and scope

All signal notifications must be completed in English.

All signal notifications must take into account all adverse events occurring in the UK and in third countries.

1.3 Document type and formatting

The template must be submitted in the Excel format type .xlsx

The layout of the template must remain the same to allow mapping into VMD systems. Do not delete any sheets even if no data needs to be entered into that sheet. The document will fail validation if there is incorrect data entry or data added to cells where data is not required, and the MAH may be requested to amend and resubmit.

Note that for accessibility reasons, the template found on Gov.uk at Benefit-risk report (BRR) and signal notification submissions is in ODS (OpenDocument) format.

If copying and pasting data from another source, only paste the values, not format or other parameters.

Template tab names must not be changed (underscore separators must remain e.g. Benefit-risk_statement).

1.4 Naming convention for signal notifications

The Excel document should be named using the applicable MA number or PGC, the year of submission, type of signal (Signal for standard signals and Urgent for urgent signals) and number describing the order of signals submitted, separated by underscores:

MAnumber_YYYY_Signal_x or MAnumber_YYYY_Urgent_x

PGC_YYYY_Signal_x or PGC_YYYY_Urgent_x

Number 1 should be used for the first signal for that product of that type submitted in that year, and 2, 3, 4 etc used for subsequent signals. For example, the first standard signal document for a product with an MA number 09285/8019 being submitted in the year 2024, would be named 09285_8019_2024_Signal_1. The second would be 09285_8019_2024_Signal_2. And if subsequently the first urgent signal was submitted for the same product within the same year, the document would be named 09285_8019_2024_Urgent_1.

No special characters should be used within file names, except the underscore (_) character that should be used as a separator between individual components of the file name e.g. VMDDEFRA-BENEFITAS_2024_Signal_1 and instead of the '/' in MA numbers e.g. MA number 09285/8019 becomes 09285_8019. Spaces should not be used. The total number of characters should not exceed 40 characters (if the PGC is too long, and the total number of characters will exceed 40 characters, use only the overarching group name rather than the entire PGC e.g. BENEFITAS_2024_Signal_1, where the PGC is VMDDEFRA-BENEFITAS).

1.5 Naming convention for additional and follow-up documents

It is not anticipated that additional documents other than the Excel signal document will be submitted. If further documentation is considered necessary, use the same naming convention as described above, followed by underscore A1, 2, 3 for subsequent additional documents. For example, an additional document submitted for the above-described urgent signal should be named 09285_8019_2024_Urgent_1_A1. A further additional document should be named 09285_8019_2024_Urgent_1_A2. Each additional document must have a unique number identifier.

Multiple documents can be submitted per VMDS submission using any of the following file types: .pdf, .doc, .docx, .xls, .xlsx.

The document name of a follow-up signal notification should mirror that of the initial signal notification with the addition of an 'a', 'b', 'c' at the end. The year that was used for the initial signal notification should be retained. If the first signal notification was named 09285_8019_2024_Signal_1, the first follow-up to this notification would be named

09285_8019_2024_Signal_1a. If another follow-up was required, it would be named 09285_8019_2024_Signal_1b, and so on.

No special characters should be used within file names, except the underscore (_) character that should be used as a separator between individual components of the file name e.g. VMDDEFRA-BENEFITAS_2024_Signal_1a and instead of the '/' in MA numbers e.g. MA number 09285/8019 becomes 09285_8019. Spaces should not be used. The total number of characters should not exceed 40 characters (if the PGC is too long, and the total number of characters will exceed 40 characters, use only the overarching group name rather than the entire PGC e.g. BENEFITAS_2024_Signal_1a, where the PGC is VMDDEFRA-BENEFITAS).

1.6 Product Group Codes (PGCs)

A PGC links a set of individual MAs together into a single group. It should be used to link both UK MAs and, at minimum, their EEA equivalent products if the product is authorised in EEA.

If one or more PGCs are to be used, they must be agreed at least one month prior to the first BRSR or PSS submission using these PGCs. PGCs can be either proposed by the MAH and accepted by the VMD or requested by the MAH from the VMD.

Note that if a signal notification (Standard or Urgent) needs to be submitted and no PGC has been pre-agreed, the VMD should be contacted at the earliest opportunity.

Any future changes to products grouped within the PGC should also be agreed at least one month prior to the next submission.

Further details on PGCs can be found in section 4.3 of Guideline IV of Pharmacovigilance of Veterinary Medicinal Products in Great Britain.

Queries related to PGCs should be directed either via VMDS to the PSUR Queries group or via e-mail to psur.queries@vmd.gov.uk.

2. Signal notification template completion

2.1 Benefit-risk statement sheet

The table below explains the required content of each cell on the first sheet of the template.

Validation rules **must** be followed for data entered within the cell. The 'Validation type' determines whether the field is mandatory or not (whether data must be provided or not) and which character and number types are allowed.

If data is not entered into a cell, leave the cell blank. Do not enter N/A or any other text unless requested to do so by the following guidance.

Ensure the cell format is correct as per the 'Required cell format' before submission. If data is copied from another source into the Excel template, ensure only values, not formats are copied.

If the dropdown menus provided within the template are not used, ensure the content of the cell matches one of the options in the dropdown menu exactly.

All mandatory data required must be completed for every row.

For signal notification submissions, no cells need to be completed below cell B4 (Submission type)

Cell	Type	Required content	Validation rules	Validation type	Required cell format
B1	Product Name	For signals involving a single MA number, enter the name of the product as stated in the national MA and associated documentation. For signals involving split GB/NI MA numbers, enter the product name as stated in the national MA and associated documentation if it is the same for GB and NI, or a partial product name if it is not. For example, for a product named Benefitas chewable tablets for dogs in GB and Benefitas chewable tablets in NI, enter Benefitas chewable tablets. For signals involving multiple strengths of the same product, enter partial product name (product name as stated in the national MA and associated documentation without the strength information). For example, for a product named Benefitas chewable tablets, if 10 mg, 20 mg and 30 mg strengths were all applicable to the signal, enter Benefitas chewable tablets.	Not applicable	Mandatory for signal notifications involving a single MA number Non-mandatory for signal notifications involving a Product Group Code *Numbers, special characters, text*	General
B2	Marketing Authorisation Holder	Enter the business name of the MAH as stated in the national MA and associated documentation.	Name(s) must be identical to the business name of the MAH as stated	Mandatory *Numbers, special*	General

		If multiple MAH names apply, both can be entered into this cell, separated by a comma or forward slash.	in the national MA and associated documentation	*characters, text*	
B3	Marketing Authorisation Number/Product Group Code	For signals involving a single MA, enter the MA number as stated in the national MA and associated documentation, unless the MA number has been updated since initial authorisation, in which case the *current* MA number must be used. If a national authorisation number is used enter only the authorisation number **without Vm or Vh** preceding it. Where a PGC has been agreed, enter the PGC.	MA number must be identical to that stated in the national MA and associated documentation, unless the MA number has been updated since initial authorisation, in which case the **current** MA number must be used PGC must be identical to that agreed with the VMD	Mandatory **Must be entered correctly to allow mapping** *Numbers, special characters*	General
B4	Submission type	Enter the applicable option from the pre-defined list: Signal notification Urgent signal notification	Contents of cell must be identical to one of the pre-defined options	Mandatory **Must be entered correctly to allow mapping** *Text*	General

2.2 Signals and regulatory actions

Note that all validated signals which following assessment are not deemed to suggest a new risk or change to the benefit-risk balance, must be submitted annually via the BRSR template and not via a signal notification.

The table below explains the required content of each cell on the final sheet of the template.

Cell	Type	Required content	Validation rules	Validation type	Required cell format
Column A (cell A2 onwards)	Signal VeDDRA Preferred Term (or non-VeDDRA term if no suitable preferred term)	Enter the applicable VeDDRA PT. If there is no suitable PT, enter 'Non-VeDDRA term' and add a description of the signal within the Evaluation and summary of findings cell along with your evaluation of the signal. PTs should be used wherever possible. Each individual PT should be entered on a different row. If the same PT affects multiple species, it should be entered multiple times on different rows (one row per species). Only related PTs should be submitted within the same signal notification (one signal per notification). All cells for each row must be completed as per these guidelines.	As selected from the Combined VeDDRA list of clinical terms which can be found on the EMA website (unless no PT is suitable)	Mandatory *Text*	General
Column B (cell B2 onwards)	VICH Species Code	The species of the animal(s) affected by the signal PT. Enter 'HUM' for human exposure reports. If the same PT affects multiple species, it should be entered multiple times on different rows (one row per species). All cells for each row must be completed as per these guidelines.	Select the most relevant species code from Guidelines | vichsec	Mandatory *Text*	General
	Date first detected	Date the signal was first noted within a MAHs signal		Mandatory	Date

Column C (C2 onwards)		management process or highlighted by a regulatory authority, whichever occurred first. This date will not be used by the VMD to determine whether a signal notification has been submitted within the appropriate timeline but will be used to guide assessment of adverse events in relation to the signal submitted. If the exact date is unknown or only an approximation can be provided, enter at minimum the month and year and enter '01' for DD i.e. for APR-2024, enter 01/04/2024. If applicable, clarifying details can be added to the 'Evaluation and summary of findings cell'.	Enter in format DD/MM/YYYY	*Numbers, special characters*	
Column D (D2 onwards)	Current status	This is the current status of the signal's action (action taken). Select Ongoing or Closed. Closed should only be selected for any signal where the final action has been completed e.g. signals for which a variation has been completed, or follow-ups to signals where there is now 'No further action required'.	Select Ongoing or Closed only	Mandatory *Text*	General
Column E (E2 onwards)	Date closed (for closed signals)	The date the action was finalised. Only applicable for signals with closed actions ('closed signals'). For variations, this would be the date the MAH receives final confirmation of completion from the VMD.	Enter in format DD/MM/YYYY	Non-mandatory *Numbers, special characters*	Date

		For batch/product recalls, this would be the date the recall was fully completed. If applicable to the signal, clarifying details can be added to the 'Evaluation and summary of findings' cell.			
Column F (F2 onwards)	Source of Signal	Examples of sources include MAH database, regulatory authority database, literature review or regulatory authority. Where a regulatory authority is the source, the name of the regulatory authority should be entered. For EMA, enter EMA, for FDA, enter FDA, and so on. For literature review, enter Literature. For signals based on spontaneous reports received by the MAH, enter MAH database. If multiple sources apply, either: 1. List the sources, separated by commas. 2. If one or more of the sources is a regulatory authority, enter the name(s) of the regulatory authority/authorities. If multiple sources apply, none of which are a regulatory authority, enter 'Multiple'. Further clarification can be provided within the 'Evaluation and summary of findings' cell.	Not applicable	Mandatory *Text, special characters*	General

Column G (G2 onwards)	Country (2-character country codes ISO 3166)	For GB or UK-wide signals enter GB. If the signal is not country-specific, leave blank. Further location-related information should be entered within the 'Evaluation and summary of findings' cell if applicable to the case e.g. region or county.	Enter in ISO 3166 format Do not enter more than one country code into this cell. If the signal is not specific to one country, leave blank and provide details within the 'Evaluation and summary of findings' cell	Non-mandatory *Text*	General
Column H (H2 onwards)	Evaluation and summary of findings	This should provide adequate evidence of how the signal was validated and assessed, and an action determined. Information that should be considered for inclusion within this section may include: • signalment and clinical details • brief description of event outcome • location related data if non-country specific • observed patterns of event development • details of other products • reversibility • supporting lab data • assessment of the causal relationship • details of regulatory procedures ongoing at the time of submission e.g. variations or signal processes, including those involving other regulatory authorities	Not applicable	Mandatory *Text, numbers, special characters*	General

		• details of the source • event incidence • an evaluation of the potential impact Incidence should be calculated for signals submitted as per section 4.4 of Guideline IV of the Pharmacovigilance of Veterinary Medicinal Products in Great Britain. No incidence calculations are required when no signals are submitted. Incidence calculations may be included within this cell or provided within a separate document submitted alongside the BRSR. Overall incidences can be added to cell H2 only, with a note that these apply to all events/species. Any other extended supporting information may be submitted within a separate document submitted alongside the BRSR but at least a brief summary should be provided within this cell (at minimum number of animals affected, signalment if relevant, outcome, causality assessment and other regulatory authority actions). For follow-up signal notifications, this section should clearly detail the additional information received or reason for a change to the 'Proposed Action', as applicable.			
Column I (I2 onwards)	Proposed Action	The action that was initially proposed by the MAH or regulatory authority. To be entered for all 'Ongoing signal actions'.	Contents of cell must be identical to one of the pre-defined	Non-mandatory unless Ongoing has been entered	General

		Select one of the options from the dropdown menu: • Product/batch recall • No further action required • Post-marketing surveillance study • Risk management plan • Suspension • Withdrawal • Variation, including change to the product literature • Other • Close monitoring Only select 'Other' if no other option applies. If more than one option applies, select the most applicable, and provide further information within the related 'Proposed Action Details' cell.	options or left blank	into cell D of the same row. *Text, special characters*	
Column J (J2 onwards)	Proposed Action Details	Provide further details of the proposed action. If a product/batch recall is proposed, details such as of the batches affected and whether they have been distributed should be provided. If a post-marketing surveillance study is proposed then details regarding the scope, objectives and timelines should be provided. If a risk management plan is proposed, details should be provided e.g. details of communications disseminated	Not applicable	Non-mandatory unless cell I of the same row has been completed *Text, special characters, numbers*	General

		to specified stakeholder groups and a proposed timescale, or details of a restriction. If a suspension or withdrawal is proposed, details should be provided including dates if applicable. If a variation is proposed, details of this should be provided. If the variation proposed involves a change to the product literature, then details of the section of the product literature affected and proposed wording should be provided. If close monitoring is proposed, the period over which the product will be closely monitored should be specified, alongside any details of additional monitoring processes that may be put in place. Extended details/images/graphs can be provided within a separate document submitted alongside the BRSR if required but at least a brief summary should be provided within this cell. Do not submit documents unless this is deemed to be a necessity.			
Column K (K2 onwards)	Final Action (for closed signals)	The action that was finally taken by the MAH or regulatory authority. Select one of the options from the dropdown menu: • Product/batch recall • No further action required • Suspension	Contents of cell must be identical to one of the pre-defined options	Non-mandatory unless 'Closed' has been entered into cell D of the same row.	General

		• Withdrawal • Variation completed • Other Only select Other if no other option applies. Leave blank for ongoing actions, such as a post-surveillance study, risk management plan or close monitoring. If these actions were both carried out as proposed and a resulting final action was also completed within the reporting period (such as a variation or a new decision made that no further action is required as a result of the proposed action), this resulting final action should be entered. If more than one option applies, select the most applicable, and provide further information within the related 'Final Action Details' cell.		*Numbers, text, special characters*	
Column L (L2 onwards)	Details of Final Action (for closed signals)	Provide further details of the final action if there are any changes to the 'Proposed Action Details' previously submitted. If a product/batch recall has been carried out, further details should be provided if applicable. If 'No further action required' is selected, an explanation should be provided, unless this matches the initial proposed action and therefore an explanation has already been provided within the proposed action details section.	Not applicable	Non-mandatory unless there are changes to the 'Proposed Action Details' previously submitted *Text, special characters, numbers*	General

		If a variation, such as a change to the product literature, was initially proposed, and a variation has since been completed which differs from the proposed variation (e.g. the final wording has altered), details should be provided. The VMD will contact the MAH for further information if required.			

Signal actions overview (completion of columns I-L)