Title:	**HOVON Template for Quality Risk Management Plan**	
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Also see HOVON policy Risk Based Quality Management of Clinical Trials

Trial name: HOVON xxx yyy

Sponsor: HOVON

Version history		
Version number	**Version date**	**Effective date**
01	dd-mon-yyyy	dd-mon-yyyy
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QRMP authors	
Name	**Role**
	Principal Investigator
	Trial Manager
	Statistician
	Central Data Manager
	Monitor

Completion guideline

Risk assessment

The table contains a pre-defined list of trial aspects to consider during risk assessment. Trial specific items may be added to the list, but pre-defined aspects should not be removed from the list.

Risk identification

Describe the perceived risks for each aspect listed in the template. See **appendix 1** for examples of questions to ask. **Focus on the aspects of the trial that are unusual, different from what is common practice in HOVON trials.**

Use a new line for each separate risk. If there are no risks for a pre-defined trial aspect, record this as "no risk". If the pre-defined aspect does not exist in the trial, record this as "not applicable".

Probability

Score the probability that this risk will occur in this trial:
1=low 2=medium 3=high

Impact

Score the severity of the impact on patient safety and/or data validity if this risk occurs in this trial:
1=low 2=medium 3=high

Risk score

Add the score of Probability + Impact
2-3=mild 4=moderate 5-6=severe

Risk mitigation level

Choose one of three options how you will handle this risk.

Accept: You choose to accept this risk and will not take any measures to reduce the probability and/or impact. Suitable for mild risks.

Limit: You choose to take measures to reduce the probability and/or impact of this risk to an acceptable level. The amount of risk reduction and the effort and cost you will spend on it, depends on the risk score. Suitable for any risk score.

Avoid: This risk is unacceptable and you will take measures to reduce the probability of this occurring to (almost) zero. This may include changing the intended design or procedures, and it may involve a substantial effort or cost. Suitable for severe risks.

Risk mitigation

Risk mitigation strategy

For each risk that you choose to "limit" or "avoid", describe the measure you will take to limit or avoid the risk. See **appendix 2** for examples.

Please note that substantial changes to the trial design or trial procedures may introduce new risks or change the scores of risks, and may therefore require a revision of the risk assessment.

Risk assessment

Trial aspect	Risk identification	Probability	Impact	Risk score	Risk mitigation level
	Risk mitigation strategy				
Patient rights					
Safety					
Protocol compliance					
Data validity					
GCP compliance					
Other					

Appendix 1 – Guidance for risk assessment

Please note that this is only a guidance to help you think through the potential risks in a trial. Not all examples will be applicable for a specific trial, and a trial may have risks that are not mentioned here.

Trial aspect	***Risk identification – questions to ask***
Patient rights	
Informed Consent	*Will patients be included requiring non-standard informed consent procedures, such as children or patients (temporarily) unable to give consent due to cognitive disorders?* *Are trial specific procedures needed to screen patients for eligibility, that would require pre-screening consent?* *Are there any unusual aspects in the informed consent process for this trial?*
Privacy	*Will any personal data be collected centrally, such as e-mail or address for distribution of patient questionnaires?*
Safety	
Compliance to safety measures	*Does the protocol require additional or more frequent procedures (pregnancy test, blood chemistry test etc) for safety reasons, compared to standard practice?* *Does the study drug or study product require specific storage conditions or preparation to warrant its quality, that is different or more stringent compared to standard practice, or that the site staff may be unfamiliar with or unaware of?* *Are there any other required safety measures that may be difficult to comply with?*
Safety reporting	*Are there any Adverse Events of special interest that require expedited (immediate) reporting by the site, even if they do not qualify as an SAE?* *Does the trial require reporting of (S)AEs that are commonly exempt from reporting in HOVON trials? Such as progression of disease under study, nausea, CTCAE grade 1 AEs.* *Are there any unusual or complex safety reporting procedures in the trial*

Safety management	*Are there multiple parties and/or multiple countries involved in the trial with different requirements regarding the handling and reporting of safety information? Is there a risk that these requirements will not be met?* *Are there any unusual or complex safety management procedures in the trial?* *Is the trial blinded?* *Is there a clear and robust procedure regarding unblinding for SAE and SUSAR reporting?*
Protocol compliance	
Eligibility	*Does confirmation of eligibility require complex or time-consuming or unusual assessments?*
Treatment schedule	*How different is the protocol treatment schedule from standard practice?* *Are there many or complex decision points?* *Do decision points require a complex or unfamiliar assessment?*
Test procedures	*Does the protocol require complex or time-consuming or unusual assessments compared to standard practice?* *Does the assessment of any of the endpoints require central sample collection? Are any of the requirements for the collection (method, timing) or storage or handling or shipping of the samples complex or time-consuming or unusual?* *Are the sites compensated by the sponsor for the costs of additional assessments?*
Data validity	
Timely data collection	*Is there an increased trial specific risk that data are not collected within the required timelines?*
Accurate CRF completion	*Is the CRF extensive (many data) or complex?* *Are sites participating that are unfamiliar with the sponsor's data collection form design, e-CRF system or procedures?* *Does the trial require collection of data that may be difficult to extract from the source data or that need interpretation of source data (medical judgment)?*

Blinding	*Is there a risk, also in an open-label trial, that investigators are exposed to aggregate data or reports that may prematurely reveal (interim) results concerning the endpoints?* *Is there a risk that a patient requires emergency treatment by a physician not involved in the trial?* *Is there a risk that an investigator is unable to get an emergency unblinding for a patient?* *Are all involved site staff aware of the emergency unblinding procedure?* *Are instructions how to perform an emergency unblinding readily available at the site?* *Are all people involved in the emergency unblinding procedure aware of their responsibilities?* *Is the emergency unblinding procedure robust with regards to 24/7 availability of the service?* *Is the emergency unblinding procedure complex?* *Is there a risk that the blind is intentionally broken for a patient without it being reported or detected?* *Is there a risk that the blind is inadvertently broken? And is there a risk that this happens without it being reported or detected?* *Could a clinical event inadvertently break the blind?*
GCP compliance	
Qualifications	*Are there non-standard procedures in the trial that require additional training?*
Other	*Are there any other aspects of the trial or the trial sites that may pose a risk for GCP compliance?*
Other	
Other	*Are there any other aspect of the trial that may pose a risk to patient safety or to the validity of the trial results?*

Appendix 2 - Examples of risk mitigation strategies

Please note that these are only examples. Other solutions or variations on the examples may be more suitable for your trial specific risks.

Trial aspect at risk	***Possible risk mitigation strategies***
Informed Consent	Additional training of site staff on ICF form and procedures. Partial or complete review of trial specific signed ICFs on-site (trial specific monitoring visits).
Privacy	Robust design of systems and procedures used for collecting personal data, including testing of system security.
Compliance to safety measures	Training of site staff on patient safety measures and/or product handling. Partial or complete review of CRF data to verify protocol compliance, including eligibility. Periodic or triggered (from data review) phone calls to site to review/request feedback on protocol compliance or product handling issues Partial or complete central collection and review of drug accountability records and/or patient diaries (NB privacy)
Safety reporting	Additional training of site staff on safety data collection forms and reporting procedures. Periodic review and follow up of timely safety data collection (AE CRF, DLT CRF, SAE follow up) Review of collected safety data for discrepancies and/or signals of missed reports, internal (AE CRF discrepancy checks) or cross-check (AE-SAE, SAE-DLT, etc). Partial or complete review of complete and accurate safety reporting on-site (trial specific monitoring visits with source data verification) Either scheduled or triggered (for cause visit, from data review)
Safety management	Investigate, discuss and record trial specific safety management requirements. Periodic review of safety database by safety desk coordinator for compliance to sponsor safety assessment procedures and SUSAR reporting timelines.

Protocol compliance in general *(including eligibility, treatment schedule, test procedures)*	Review of adequate site facilities for protocol procedures and/or site acceptance of protocol procedures including acceptance of available reimbursement of additional costs, by site selection questionnaire and/or pre-study site visit. Additional training of site staff on critical protocol procedures. Review of CRF data to detect recurrent issues with protocol compliance on site or trial level. Note: requires timely and accurate data collection. Partial or complete review of trial specific protocol compliance on-site (trial specific monitoring visits with source data verification) Either scheduled or triggered (for cause visit, from data review) Periodic or triggered (from data review) phone calls to site to review/request feedback on protocol compliance issues Central review or central assessment of complex assessments (NB privacy), either prospective or retrospective.
Timely data collection	Periodic central review and follow up of timely data collection.
Accurate CRF completion	Additional training of site staff on CRF completion and reporting procedures. Partial or complete review of complete and accurate data reporting on-site (trial specific monitoring visits with source data verification) Either scheduled or triggered (for cause visit, from data review e.g. number of queries)
Blinding	Robust (trial specific) procedures for maintaining the blind. Robust (trial specific) emergency unblinding procedure, training of site staff on emergency unblinding procedure. Provide written instructions for emergency unblinding for site staff. Publish on publicly accessible part of HOVON website. Provide patient wallet cards with instructions in case of an emergency (phone number) NB EC approval. Review of adherence to blinding and unblinding procedures and review of records on-site at the facility providing the service. Partial review to assess general process or complete review for all patients