**Template #201: Intermediate effects - mechanistic information *(Version [6.2]-[July 2023])***

The following table gives a detailed description of the type of information prompted for by the data entry fields.

| **Line no.** | **Field name** | **Field type**  **Display type** | **Picklist**  **Freetext template** | **Help text** | **Remarks**  **Guidance**  **Cross-reference** |
| --- | --- | --- | --- | --- | --- |
|  | **Administrative data** | **Header 1** |  |  |  |
|  |  | Confidentiality  Display: Basic |  |  |  |
|  | Type of information | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - ex-vivo - in chemico - in silico - in vitro - not specified - other: | Select the appropriate type of study performed that provides the mechanistic information.  Select 'in vitro' for any type of in vitro study. Select 'in chemico' for assays using cell- / tissue-free laboratory models.  Select ‘in silico’ for e.g. a QSAR model.  If the information is taken from a handbook or review article, select the relevant item, e.g. ‘in vitro’, if this is provided in the information source. Otherwise, select ‘not specified’. Please note: In field ‘Reference type’ the option ‘review article or handbook’ should be selected. In general, the option 'not specified' should be selected if the submitter lacks the knowledge of the type of information.   The option 'other:' can be used if another than a pre-defined item applies, e.g. in case of an in vivo study or when reporting read across data. |  |
|  | Study period: start date | Date  Display: Basic |  | If applicable indicate the period during which the study was conducted, i.e. start and end date.   Note: independent of the study period, the in-life period (i.e. the phase of a study following treatment in which the test system is alive/growing) may have to be specified for some toxicology endpoints. |  |
|  | End date | Date  Display: Basic |  |  |  |
|  | Remark | Text (255 char.)  Display: Basic |  | If applicable indicate the period during which the study was conducted, i.e. start and end date, using an unambiguous date format, e.g. 'From 12 MAY 1999 to 15 AUG 2000' or 'From May 12, 1999 to Aug. 15, 2000'.  Note: Independent of the study period the in-life period (i.e. the phase of a study following treatment in which the test system is alive/growing) may have to be specified for some toxicology endpoints. |  |
|  | Reliability | List (picklist)  Display: Basic | **Picklist values:** - 1 (reliable without restriction) - 2 (reliable with restrictions) - 3 (not reliable) - 4 (not assignable) - other: | Enter an appropriate reliability score.  For further information go to: https://echa.europa.eu/documents/10162/13643/information\_requirements\_r4\_en.pdf  1 = reliable without restrictions: “studies or data [...] generated according to generally valid and/or internationally accepted testing guidelines (preferably performed according to GLP) or in which the test parameters documented are based on a specific (national) testing guideline [...] or in which all parameters described are closely related/comparable to a guideline method.”  2 = reliable with restrictions: “studies or data [...] (mostly not performed according to GLP), in which the test parameters documented do not totally comply with the specific testing guideline, but are sufficient to accept the data or in which investigations are described which cannot be subsumed under a testing guideline, but which are nevertheless well documented and scientifically acceptable.”  3 = not reliable: “studies or data [...] in which there were interferences between the measuring system and the test substance or in which organisms/test systems were used which are not relevant in relation to the exposure (e.g. non-physiological pathways of application) or which were carried out or generated according to a method which is not acceptable, the documentation of which is not sufficient for assessment and which is not convincing for an expert judgment.”   4 = not assignable: “studies or data [...] which do not give sufficient experimental details and which are only listed in short abstracts or secondary literature (books, reviews, etc.).”  The 'other:' option may be selected if a different scoring system is used. Consult any programme-specific guidance (e.g. OECD Programme, Pesticides NAFTA or EU REACH) on how to use this field.  Note: The term reliability defines the inherent quality of a test report or publication relating to preferably standardised methodology and the way the method and results are described. More clarity for the score can be provided in field 'Rationale for reliability score incl. deficiencies'. |  |
|  | Rationale for reliability incl. deficiencies | List sup. (picklist with remarks - 32,000 char.)  Display: Basic | **Picklist values:** - guideline study - [Reliability 1] - comparable to guideline study - [Reliability 1] - test procedure in accordance with national standard methods - [Reliability 1] - test procedure in accordance with generally accepted scientific standards and described in sufficient detail - [Reliability 1] - guideline study without detailed documentation - [Reliability 2] - guideline study with acceptable restrictions - [Reliability 2] - comparable to guideline study with acceptable restrictions - [Reliability 2] - test procedure in accordance with national standard methods with acceptable restrictions - [Reliability 2] - study well documented, meets generally accepted scientific principles, acceptable for assessment - [Reliability 2] - accepted calculation method - [Reliability 2] - data from handbook or collection of data - [Reliability 2] - significant methodological deficiencies - [Reliability 3] - unsuitable test system - [Reliability 3] - abstract - [Reliability 4] - secondary literature - [Reliability 4] - documentation insufficient for assessment - [Reliability 4] - results derived from a valid (Q)SAR model and falling into its applicability domain, with adequate and reliable documentation / justification - [Reliability 1 or 2] - results derived from a valid (Q)SAR model and falling into its applicability domain, with limited documentation / justification - [Reliability 2, 3 or 4] - results derived from a valid (Q)SAR model, but not (completely) falling into its applicability domain, with adequate and reliable documentation / justification - [Reliability 2 or 3] - results derived from a (Q)SAR model, with limited documentation / justification, but validity of model and reliability of prediction considered adequate based on a generally acknowledged source - [Reliability 2 or 3] - results derived from a valid (Q)SAR model, but not (completely) falling into its applicability domain, and documentation / justification is limited - [Reliability 3 or 4] - results derived from a (Q)SAR model, with limited documentation / justification - [Reliability 4] - other: | Select an appropriate standard justification from the picklist, e.g. 'Comparable to guideline study with acceptable restrictions'. Additional explanations (e.g. deficiencies observed) can be entered in the related supplementary text field. Particularly if reliability scores 2 or 3 are assigned, indicate the concrete arguments for defending a study or relevant deficiencies.  For example when the study considers all elements described in OECD guidance on Good In Vitro Method Practices (GIVIMP, OECD guidance document 286 in the series on testing and assessment), Reliability 1 ‘test procedure in accordance with generally accepted scientific standards and described in sufficient detail’ may be assigned.  For a reliability 1 it is presumed that documented information exists to demonstrate quality of the test material, test system and study performance.  For QSAR results (i.e. 'Type of information' is '(Q)SAR') some pre-defined phrases are provided for indicating if the prediction results are considered reliable based on the scientifically validity of the (Q)SAR model used, its applicability to the query substance, and the adequacy of reporting. Please note: If (Q)SAR results are flagged as key study in field 'Adequacy of study', the relevance of the model used for the regulatory endpoint should be documented in the field where the (Q)SAR model is described, i.e. 'Principle of the method’. | **Guidance for field condition:** Condition: Field active only if 'Type of information' is not 'experimental study planned' and not ‘experimental study planned (based on read-across)’. Condition 1: If 'Type of information' is not '(Q)SAR': - guideline study - [Reliability 1] - comparable to guideline study - [Reliability 1] - test procedure in accordance with national standard methods - [Reliability 1] - test procedure in accordance with generally accepted scientific standards and described in sufficient detail - [Reliability 1] - guideline study without detailed documentation - [Reliability 2] - guideline study with acceptable restrictions - [Reliability 2] - comparable to guideline study with acceptable restrictions - [Reliability 2] - test procedure in accordance with national standard methods with acceptable restrictions - [Reliability 2] - study well documented, meets generally accepted scientific principles, acceptable for assessment - [Reliability 2] - accepted calculation method - [Reliability 2] - data from handbook or collection of data - [Reliability 2] - significant methodological deficiencies - [Reliability 3] - unsuitable test system - [Reliability 3] - abstract - [Reliability 4] - secondary literature - [Reliability 4] - documentation insufficient for assessment - [Reliability 4] Condition 2: If 'Type of information' = '(Q)SAR': - results derived from a valid (Q)SAR model and falling into its applicability domain, with adequate and reliable documentation / justification - [Reliability 1 or 2] - results derived from a valid (Q)SAR model and falling into its applicability domain, with limited documentation / justification - [Reliability 2, 3 or 4] - results derived from a valid (Q)SAR model, but not (completely) falling into its applicability domain, with adequate and reliable documentation / justification - [Reliability 2 or 3] - results derived from a (Q)SAR model, with limited documentation / justification, but validity of model and reliability of prediction considered adequate based on a generally acknowledged source - [Reliability 2 or 3] - results derived from a valid (Q)SAR model, but not (completely) falling into its applicability domain, and documentation / justification is limited - [Reliability 3 or 4] - results derived from a (Q)SAR model, with limited documentation / justification - [Reliability 4] - other: |
|  | **Cross-reference** | **Block of fields (repeatable) Start** |  | The cross-reference feature can be used to refer to related information that is provided in another record of the dataset. This can be done either by entering just free text in the 'Remarks' field or by creating a link to the relevant record. The field 'Reason / purpose' allows for selecting a standard reason from the picklist and optionally to add free text explanation in the related supplementary text field.  Refer to the relevant legislation-specific guidance document as to the recommended use of cross-references. |  |
|  | Reason / purpose for cross-reference | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - adverse outcome pathway (AOP) - assessment report - defined approach - reference to other assay used for mechanistic information derivation - reference to other study - reference to same study - other: | Select the appropriate reason of the cross-reference, i.e.:  - adverse outcome pathway (AOP) (in case the mechanistic information is related to a key event that is part of an AOP). Consult the AOP wiki at: https://aopwiki.org) and provide the reference in the remarks field  - assessment report (for referring to a record that contains an assessment report as attachment)  - defined approach for combining with results from another in vitro method  - reference to other assay used for mechanistic information derivation (for optional indication in a study summarising if reference is made to the outcome of another assay)  - reference to same study (e.g. if different test systems/in vitro models were used and the results recorded in different records, or different test materials were assessed in the same study, using common reference and control items)  - reference to other study (e.g. if another study provides mechanistic information or key event relevant for the same Adverse Outcome Pathway or if another study is considered relevant in the interpretation of the test results)  - other: (to be specified) |  |
|  | Related information | Link to endpoint (single)  Display: Basic |  | As appropriate, select the record containing the related information, thus creating a link. | **Cross-reference:** AllSummariesAndRecords |
|  | Remarks | Text (32,768 char.)  Display: Basic |  | This field can be used for including any remarks. |  |
|  | **Cross-reference** | **Block of fields (repeatable) End** |  |  |  |
|  | Study objective(s) / purpose / aim | Text (32,768 char.)  Display: Basic |  | Specify the objective, purpose and/or aim of the study explaining clearly why the study was performed and what (regulatory) question is answered. For example:  - determination of skin sensitising properties of the test chemical by measurement of CD54 and CD86 expression in THP-1 cells after exposure to the CV75 concentration.  - gather information on mode of action.  - derive a point of departure. |  |
|  | **Data source** | **Header 1** |  |  |  |
|  | Reference | Link to lit. reference (multiple)  Display: Basic |  | Indicate the bibliographic reference of the study report or publication the study summary is based on. Provide general information such as Reference type, Title, Author, Year, Bibliographic source, Testing Facility, Report Number, Study number, Report date etc., as requested in the core template for literature search (https://www.oecd.org/ehs/templates/Generic%20elements%20for%20all%20OHTs.zip).   Always enter the primary reference in the first block of fields or sort it to the first position, if there are more than one reference to be cited. Copy this block of fields for specifying any other references related to this record (e.g. report of a preliminary study or other documentation). If results of a study report have been published, indicate the full citation of that publication(s) in addition to the reference of the original study.  In case of in-house data, select for reference type 'other company data' and provide the title of the document that contains the in house data. |  |
|  | Data access | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - data submitter is data owner - data submitter has Letter of Access - data no longer protected - data published - data submitter has permission to refer - not applicable - other: | Select appropriate indication for data access. Enter 'Not applicable' if the summary consists of information that is commonly accessible such as guidance on safe use.  Select 'data submitter has permission to refer' if the information requirement can be covered based on a permission to refer to old data as issued by the relevant regulatory agency. In addition, provide, in the adjacent free-text field, the statement according to instructions you received from the relevant regulatory authority together with the permission to refer. |  |
|  | Data protection claimed | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - yes - no - yes, but willing to share - yes, but not willing to share | Indicate as appropriate. Note: 'yes' should be selected only if 'Data submitter is data owner' or 'Data submitter has Letter of Access'. Options 'yes, but willing to share' or 'yes, but not willing to share' may be relevant for specific regulatory programmes where the submitter is requested to indicate whether he is willing to share studies conducted (e.g. with vertebrates).  In the supplementary remarks field, include an explanation as appropriate, i.e. justification for denial of sharing the corresponding study or refer to a document attached that provides justification (e.g. 'for justification see attached document X'). |  |
|  | **Effect identification** | **Header 1** |  | Describe the mechanism that can be measured with the method by providing a ‘Process’, ‘Object’ and ‘Action’. As a minimum, the ‘Process’ and ‘Action’ or the ‘Object’ and ‘Action’ must be identified. More than one combination can be provided (e.g. Cell Activation, CD54 molecule, increased & Cell Activation, CD86 molecule, increased). If both Process and Object are provided they have to be concordant with the chosen Action (e.g. both process and object are increased or decreased).  See Yves et. al (2017) https://www.liebertpub.com/doi/10.1089/aivt.2017.0017 and the website https://aopwiki.org/ for the concept and its implementation in practice, respectively.  If no suitable terms are available in picklist for Process and Object, please select ‘Other’ and introduce a new ontology- based term. Please consult the Ontology Lookup Service (OLS) to retrieve the terms that best describe the mechanisms you are reporting. OLS is a repository of the latest versions of biomedical ontologies and it is available at https://www.ebi.ac.uk/ols/index (Jupp S. et al. (2015) A new Ontology Lookup Service at EMBL-EBI. In: Malone, J. et al. (eds.) Proceedings of SWAT4LS International Conference 2015).  For each effect identified with a process, object and action (P/O/A), the results can be reported in the reporting section.  Please use the following P/O/A for existing OECD test guidelines and methods.  TG442C, DPRA, kinetic DPRA, and ADRA: protein binding / - / increase  TG442D, Keratinosens: keratinocyte activation / aldo-keto reductase family 1 member C2 (AKR1C2) / increase  TG442D, Lusens: keratinocyte activation / NAD(P)H dehydrogenase [quinone] 1 (NQ01) / increase  TG442E, h-CLAT: cell activation / CD54 molecule (intercellular adhesion molecule 1) / increase and cell activation / CD86 molecule / increase  TG442E, U-SENS: cell activation / CD54 molecule (intercellular adhesion molecule 1) / increase  TG442E, IL8 LUC: cell activation / interleukin 8 (IL8) / increase  TG455, ERTA STTA, VM7Luc and ERα CALUX: nuclear receptor activity / estrogen receptor alpha / increase, agonism and nuclear receptor activity / estrogen receptor alpha / decrease, antagonism  TG456, H295R Steroidogenesis Assay: steroid hormone biosynthetic process / estradiol / alteration and steroid hormone biosynthetic process / testosterone / alteration  TG458, ARTA STTA, AR-CALUX and 22Rv1/MMTV GR-KO: nuclear receptor activity / androgen receptor / increase, agonism and nuclear receptor activity / androgen receptor / decrease, antagonism  TG493, hrER binding FW assay and CERI assay: Nuclear receptor binding / estrogen receptor alpha / binder–non binder |  |
|  | **P/O/A details** | **Block of fields (repeatable) Start** |  |  |  |
|  | Process | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - apoptotic process - [GO:0008219] - biosynthetic process - [GO:0009058] - catalytic activity - [GO:0003824] - cell activation - [GO:0001775] - cell death - [GO:0008219] - cell differentiation - [GO:0030154] - cell migration - [GO:0016477] - cell proliferation - [GO:0008283] - gene expression - [GO:0010467] - keratinocyte activation - [GO:0032980] - metabolic process - [GO:0008152] - nuclear receptor activity - [GO:0004879] - nuclear receptor binding - [GO:0016922] - oxidative stress - [NCIT:C17741] - peroxidase activity - [GO:0004601] - programmed necrotic cell death - [GO:0097300] - protein binding - [GO:0005515] - protein iodination - [GO:0018077] - receptor activity - [GO:0004872] - receptor binding - [GO:0005102] - signalling - [GO:0023052] - steroid hormone biosynthetic process - [GO:0120178] - transporter activity - [GO:0005215] - other: | Process represents the dynamics of the underlying biological system (e.g., receptor binding) (Ives et al, 2017). The Process is also used to annotate Key events in the Adverse Outcome Pathway Wiki (https://aopwiki.org/) as described in Ives et al, 2017, doi:10.1089/aivt.2017.0017).  Select the process that best describes the mechanistic information observed or select ‘other’ to specify the Process and provide a term. Please consult the Ontology Lookup Service (OLS) which is available at https://www.ebi.ac.uk/ols/index to choose a Process term. If possible please select as Process one term belonging to the following ontology Gene Ontology (GO).  For most terms there will be several options. It is therefore important to also copy the preferred ontology identifier into the remarks field.  Cytotoxicity data should only be reported as a process (e.g. cell death) when it is the scope of the study to determine cytotoxicity. In cases where cytotoxicity is measured for supporting information e.g. for dose selection/elimination, it should not be considered as a process. Such data are reported as ‘Other observations’. |  |
|  | Object | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - aldo-keto reductase family 1 member C2 (AKR1C2) - [PR:000003904] - androgen receptor - [PR:000004191] - CD54 molecule (intercellular adhesion molecule 1) - [PR:000001467] - CD86 molecule - [PR:000001412] - cytochrome P450 - [CHEBI:38559] - estradiol - [CHEBI:23965] - estrogen receptor alpha - [OMIT:0023944] - estrogen receptor beta - [PR:000007205] - interleukin 8 (IL8) - [PR:000001395] - monocarboxylate transporter 8 (MCT8) - [PR:000014950] - NAD(P)H dehydrogenase [quinone] 1 (NQ01) - [PR:000011388] - nuclear factor erythroid 2–related factor 2 (Nrf2) - [PR:000011170] - sodium/iodide cotransporter (NIS) - [PR:000015171] - sulfotransferase 1A1 (SULT 1A1) - [PR:000015818] - testosterone - [CHEBI: 17347] - thyroid hormone receptor alpha - [PR:000003428] - thyroid hormone receptor beta - [PR:000016321] - thyroid peroxidase (TPO) - [PR:000016584] - thyrotropin receptor - [PR:000001677] - thyrotropin-releasing hormone (TRH) receptor - [PR:000050029] - thyroxine - [CHEBI:30660] - type I iodothyronine deiodinase (DIO1) - [PR:000006480] - tyrosine - [CHEBI:18186] - UDP-glucuronosyltransferase (UDP GT) - [PR:000024849] - other: | Object represents the subject of the (biological) effect observed, for example, a specific biological receptor that is activated or inhibited The Object is also used to annotate Key events in the Adverse Outcome Pathway Wiki (https://aopwiki.org/) as described in Ives et al, 2017, doi:10.1089/aivt.2017.0017).  It is optional to record both Process and Object. If both Process and Object are recorded they have to be concordant with the chosen Action.  Select the object that best describes the subject of the effect observed or select ‘other’ to specify the Object and provide a term. Please consult the Ontology Lookup Service (OLS) which is available at https://www.ebi.ac.uk/ols/index to choose a Process term. If possible please select as Object one term belonging to the following ontologies protein Ontology (PR) or Chemical Entities of Biological Interest (ChEBI).  For most terms there will be several options. It is therefore important to also copy the preferred ontology identifier into the remarks field.  More than one object can be provided e.g. when changes of more than one biomarker is measured. |  |
|  | Action | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - alteration - binder / non-binder - decrease - decrease, antagonism - disruption - down regulation - enhancement - increase - increase / decrease - increase, agonism - induction - inhibition - occurrence - up regulation - other: | Action represents the type of effect observed e.g. ‘‘decrease’’ in the case where a receptor is inhibited to indicate a decrease in the signalling by that receptor. Action is also used to annotate Key events in the Adverse Outcome Pathway Wiki (https://aopwiki.org/) as described in Ives et al, 2017, doi:10.1089/aivt.2017.0017). Action is used together with the field Process and/or Object.  The Action field is always required to describe the effect observed and it can form the following syntaxes “Process, Action” e.g. “gene expression, increase” or “Process, Object, Action” e.g. receptor activity, estrogen receptor, increase.  Select the Action that best describes the effect observed or select ‘other’ to specify the action and provide a term |  |
|  | **P/O/A details** | **Block of fields (repeatable) End** |  |  |  |
|  | Details on effect identification | Text (32,768 char.)  Display: Basic |  | Enter any relevant details concerning the Effect Identification. E.g. in case of selection of more than one triplet for “Process, Object, Action” or when a meaningful term was not found. |  |
|  | **Context** | **Block of fields (repeatable) Start** |  | This repeatable block of fields allows for indicating in which target system (on organ level) the observed effect(s) play a role. This may be used in the AOP / MOA building as appropriate.  Copy this block of fields for referring to different target systems if applicable. For a given system, multiple organs can be selected. |  |
|  | System | List (picklist)  Display: Basic | **Picklist values:** - autonomic nervous system - cardiovascular - central nervous system - ear - endocrine system - eye - female reproductive system - gastrointestinal tract - haematopoietic - hepatobiliary - immune system - integumentary - male reproductive system - musculoskeletal system - nervous system - peripheral nervous system - respiratory system: lower respiratory tract - respiratory system: upper respiratory tract - somatic nervous system - urinary - other: | Select the specific system where the observed effect(s) play a role. More than one 'Context' item can be created. |  |
|  | Organ | List multi. (multi-select list)  Display: Basic | **Picklist values:** - abdominal cavity - adrenal glands - alveolar duct - ampulla - aorta - appendix - bile duct - bladder - blood - blood vessel - bone - bone marrow - bronchi - bronchioles - bulbourethral gland - caput - carotid artery - cartilage - cauda epididymis - cervix - choroid - ciliary body - clitoral gland - coagulating gland - cochlea - colon - cornea - corpus - corpus penis - Cowper’s glands - diaphragm - dorsolateral prostate gland - duodenum - fallopian tubes - forebrain - gall bladder - gametes - glans penis - gonad - hard palate - heart - hindbrain - ileum - intestine - iris - islet of Langerhans - jejunum - kidney - lacrimal gland - larynx - lens - Levatorani plus bulbocavernous muscle complex - liver - lungs - lymph node - lymphoreticular tissue - mammary gland - mesenteric lymph node - midbrain - mucosa-associated lymphoid tissue - myofibres - myofilaments - nasal cavity - oesophagus - oral cavity - ovary - oviduct - pancreas - parathyroid gland - parotid gland - penile urethra - peritoneum - pharynx - pineal gland - pituitary gland - placenta - pleura - preputial gland - rectum - retina - salivary glands - sclera - seminal vesicle - seminiferous tubules - skin - skin associated lymphoid tissue - spinal cord - spleen - sternum - stomach - sublingual gland - submandibular gland - tendon - testes - thoracic cavity - thymus - thyroid gland - tongue - tooth - trachea - ureter - urethra - uterus - vagina - vas deferens - vascular system - ventral prostate gland - vestibular system - vitreous humour - zymbal gland - unknown - not specified - other: | Select from the multiple drop-down list the target organ(s) addressed. This field provides context-related picklist values depending on the selection made in the preceding field 'System'. | **Guidance for field condition:** Conditional picklist |
|  | Remarks | Text (32,768 char.)  Display: Basic |  | Include any remarks as appropriate. |  |
|  | **Context** | **Block of fields (repeatable) End** |  |  |  |
|  | **Materials and methods** | **Header 1** |  |  |  |
|  | **Method used** | **Header 2** |  | Indicate if the study was conducted according to a test guideline. If no test guideline was explicitly followed, but the methodology used is equivalent or similar to a specific guideline, you can indicate ‘equivalent or similar to guideline’ in the 'Qualifier' field preceding the field 'Method used'. |  |
|  | Qualifier | List (picklist)  Display: Basic | **Picklist values:** - according to guideline - equivalent or similar to guideline - no guideline followed | Select appropriate qualifier, i.e.:  - 'according to guideline' (if a given test guideline was followed);  - 'equivalent or similar to guideline' (if no test guideline was explicitly followed, but the methodology is equivalent or similar to a specific guideline);  - 'no guideline followed' (if a guideline was not available or an available guideline was not used. If so, fill in field 'Principle of the method'). |  |
|  | Method used | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - (Q)SAR - ADRA - ARTA 22Rv1/MMTV GR-KO - ARTA AR-CALUX® - ARTA AR-EcoScreen™ - DPRA - ERTA ERα CALUX® - ERTA STTA - ERTA VM7Luc - H295R Steroidogenesis Assay - IL-8 LUC assay - Keratinosens - kinetic direct peptide reactivity assay (kinetic DPRA) - LuSens - U-SENS - h-CLAT - hrER binding CERI assay - hrER binding FW assay - other: | The method names are only visible when 'according to guideline' is selected.   In the remarks field, you can enter the specific test guideline (if applicable) and version number,   In case 'equivalent or similar to guideline' was selected, provide any remarks as applicable, particularly:  - To indicate if the study was performed prior to the adoption of the test guideline specified;  - To indicate if the methodology used was based on an extension of the test guideline specified;  - To indicate what protocol was followed for methods that allow the optional determination of more than one parameter if this cannot be indicated in a distinct field of the Materials and methods section. |  |
|  | Deviations | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - yes - no - not applicable - not specified | In case a test guideline or other standardised method was used, indicate if there are any deviations. Briefly state relevant deviations in the supplementary remarks field (e.g. 'other test system used', 'different exposure duration'); details should be described in the respective fields of the section MATERIALS AND METHODS. |  |
|  | Principle of the method | Text template  Display: Basic | **Freetext template:  Option 1 Description of the in vitro, in chemico or other type of method used** Description of the in vitro, ex-vivo or other type of method used:  - Name / identifier of the method (if available): - Short description of the method and how it is relevant to the endpoint being investigated: - Parameters analysed / observed: **Option 2 Description of the (Q)SAR model** Description of the (Q)SAR MODEL  Upload the QMRF as an attachment or describe the model below:  1. DESCRIPTION OF THE (Q)SAR MODEL - Software tool(s) used including version: - Model(s) used (incl. version number): - SMILES or other identifiers used as input for the model: - Model description:  2. SCIENTIFIC VALIDITY OF THE (Q)SAR MODEL [Explain how the model fulfils the OECD principles for (Q)SAR model validation. Consider attaching the QMRF and/or QPRF or providing a link] - Defined endpoint: - Unambiguous algorithm: - Defined domain of applicability: - Appropriate measures of goodness-of-fit and robustness and predictivity: - Mechanistic interpretation:  3. APPLICABILITY DOMAIN [Explain how the substance falls within the applicability domain of the model] - Descriptor domain: - Structural domain: - Mechanistic domain: - Similarity with analogues in the training set: - Other considerations (as appropriate):  4. COMMENTS ON RELIABILITY OF QSAR PREDICTION [Explain how the prediction fits the purpose of classification and labelling and/or risk assessment] | For describing a (Q)SAR model it is recommended to provide the QMRF as attachment instead of using the free text template.  The QSAR Model Reporting Format (QMRF) is a harmonised template for summarising and reporting key information on QSAR models, including the results of any validation studies. The information is structured according to the OECD validation principles and can be compiled using the QMRF editor application.  The JRC QSAR Model Database is intended to help to identify valid (Q)SARs (e.g. for the purpose of REACH). It provides information on the validity of QSAR models and can be browsed for published QMRFs. |  |
|  | GLP compliance | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - yes (incl. QA statement) - yes - no - not specified | Indicate whether the study was conducted following Good Laboratory Practice or not. In case 'yes’ is selected, a Quality Assurance (QA) statement must be provided with the report. You can give an explanation in the supplementary remarks field, e.g. for explaining why GLP was not complied with or for specifying which (national) GLP was followed. |  |
|  | Other quality systems, standards or guidance followed | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - OECD Guidance Document no. 286 on Good In Vitro Method Practices (GIVIMP) - ISO/IEC 17025:2017, General requirements for the competence of testing and calibration laboratories. - not specified - other: | Indicate whether the study was conducted following a laboratory-specific quality system or standard such as the OECD guidance on Good In Vitro Method Practice (OECD GIVIMP). Other quality systems, not listed, may be added under 'other'.  When selecting OECD GIVIMP, the submitter ensures that the following elements (if applicable) are documented and/or reported:  The purpose of the study.  Test and control items: The chemical name, CAS-number lot/batch number of the test and control items. The purity, stability homogeneity, solubility and solvent/vehicle of the test and control item was stated or is traceable according to information given regarding manufacturer and lot/batch number. In case of mixtures, the composition of different constituents. In case of nanomaterials, clear identification of the tested nanomaterial (e.g. particle size, shape, particle size distribution, surface area, coating).  Test System: The in vitro test system (e.g. tissue or organ fragment / organ explant/ dissociated cells / primary cells culture/ continuous or finite cell line/ stem cells/ complex culture system/ re-differentiated cells/ sub-cellular fractions like cytosol and microsomes/ proteins) was described, justified and characterised to confirm/authenticate the identity. The source or supplier of the test system. Metabolic competence of the test system was described. The number of passages of the test system used,. The test system mass, volume, or dimensions. The type of media used. The use of serum or animal free chemically-defined alternatives. The use of growth factors was described. The use of antibiotics. The incubation temperature, humidity and CO2. All measures taken to avoid or screen for contamination by mycoplasma, bacteria, fungi and virus were described.  Apparatus, materials and reagents: The apparatus was described. The limit of detection or limit of quantitation of the apparatus. The materials and reagents. The culture dimensions (mm2 or ml). The use of animal-derived materials or reagents (e.g. Trypsin, antibodies, collagen, Matrigel etc.). The use of fully animal-free materials and reagents.  Test item treatment: The test item concentrations/dose levels. Biological fluid characterisation was described (quantification of proteins and cells/tissue present). Binding to biological fluid and culture material. Test system number, density, dimension, quantity used during treatment. The duration of treatment. The number of replicates per concentration/dose. The number of times the experiment was repeated (independent biological runs).  Data collection and analysis: The experimental design and layout (e.g. plate layout) and relevant acceptance criteria. The time points for data collection. The effect of the test item on cytotoxicity was measured. Other observations that may impact the results (e.g. autofluorescence, absorbance by the test system). Details on calculation of results. All results were clearly presented, including negative and failed runs. The statistical methods and software used. A clear description on how to interpret read outs, evaluation/data interpretation criteria and criteria for decision-making was given.  Funding and competing interests: The funding sources for the study. Any competing interests were disclosed or it was explicitly stated that the authors did not have any competing interests. Information on the overall availability of the IPR protected components, including whether they are commercially available or require a Material Transfer Agreement or other licensing agreements. (See OECD Guiding principles on good practices for the availability/distribution of protected elements in OECD test guidelines). |  |
|  | **Attached background material** | **Block of fields (repeatable) Start** |  |  |  |
|  | Attached document | Attachment (single)  Display: Basic |  | Attach any document that provides information on the method used, such as the SOP, protocol, QMRF or a scientific publication.  Upload file by clicking the upload icon. As appropriate, enter any additional information, e.g. language. The file name is displayed after uploading the document. |  |
|  | Remarks | Text (255 char.)  Display: Basic |  | As appropriate, include remarks, e.g. a short description of the content of the attached document if the file name is not self-explanatory. |  |
|  | **Attached background material** | **Block of fields (repeatable) End** |  |  |  |
|  | **Test material** | **Header 2** |  | The 'test material' used in the OHTs, is also known as 'test item' in other OECD documents, such as the OECD principles on Good Laboratory Practice (GLP) and OECD Good In Vitro Method Practice (GIVIMP). |  |
|  | Test material information | Link to entity (single)  Display: Basic |  | Select the appropriate TMI record. If not available in the repository, create a new one. You may also copy an existing TMI record, edit it and store it as new TMI.  To assign another TMI, click the Delete button, then the Link button and proceed as described above.  Depending on the purpose of the reporting or data submission, the information that must be provided may change. As a minimum, the chemical name, identifier and/or CAS number and molecular weight must be provided. | **Cross-reference:** TEST\_MATERIAL\_INFORMATION |
|  | Additional test material information | Link to entity (multiple)  Display: Basic |  | Select additional Test material information record if relevant. For example, in longer terms studies more than one batch of test material can be needed or there may be differences between the labelled and unlabelled test materials. | **Cross-reference:** TEST\_MATERIAL\_INFORMATION |
|  | Specific details on test material used for the study | Text template  Display: Basic | **Freetext template:** SOURCE OF TEST MATERIAL - Source (i.e. manufacturer or supplier) and lot/batch number of test material: - Purity, including information on contaminants, isomers, etc.:  MULTI-CONSTITUENT SUBSTANCES, UVCBs AND MIXTURES:  Characterised as far as possible by chemical identity (using the previous field), quantitative occurrence and relevant physicochemical properties of the constituents.  STABILITY AND STORAGE CONDITIONS OF TEST MATERIAL - Storage condition of test material: - Stability and homogeneity of the test material in the vehicle/solvent under test conditions (e.g. in the exposure medium) and during storage: - Stability in the medium, e.g.. sensitivity of the test material to hydrolysis and/or photolysis or volatility: - Solubility and stability of the test material in the solvent/vehicle and the exposure medium: - Reactivity of the test material with the incubation material used (e.g. binding to plastic ware or adsorption):  TREATMENT OF TEST MATERIAL PRIOR TO TESTING - Treatment of test material prior to testing (e.g. warming, grinding): - Preliminary purification step (if any): - Final nominal concentration of a dissolved solid, stock liquid or gel: - Final preparation of a solid (e.g. stock crystals ground to fine powder using a mortar and pestle):  FORM AS APPLIED IN THE TEST (if different from that of starting material) - Specify the relevant form characteristics if different from those in the starting material, such as state of aggregation, shape of particles or particle size distribution:  INFORMATION ON NANOMATERIALS - Chemical Composition: - Density: - Particle size & distribution: - Specific surface area: - Isoelectric point: - Dissolution (rate):  TYPE OF BIOCIDE/PESTICIDE FORMULATION (if applicable) - Description of the formulation, e.g. formulated product for foliar application; formulated product soil application; solution in organic solvent for soil application; formulated product seed treatment; solution in organic solvent seed treatment:  OTHER SPECIFICS - Other relevant information needed for characterising the tested material, e.g. if radiolabelled, adjustment of pH, osmolality and precipitate in the culture medium to which the test chemical is added: | It is recommended to consult the GIVIMP guidance document for the elements to be reported.  For stability of the test material under test conditions and reactivity with the incubation material used, please consult GIVIMP Annex H. Biokinetics and xenobiotic bioavailability. |  |
|  | Specific details on test material used for the study (confidential) | Text template  Display: Basic (Confidential) | **Freetext template:** SOURCE OF TEST MATERIAL - Source (i.e. manufacturer or supplier) and lot/batch number of test material: - Purity, including information on contaminants, isomers, etc.:  MULTI-CONSTITUENT SUBSTANCES, UVCBs AND MIXTURES:  Characterised as far as possible by chemical identity (using the previous field), quantitative occurrence and relevant physicochemical properties of the constituents.  STABILITY AND STORAGE CONDITIONS OF TEST MATERIAL - Storage condition of test material: - Stability and homogeneity of the test material in the vehicle/solvent under test conditions (e.g. in the exposure medium) and during storage: - Stability in the medium, e.g.. sensitivity of the test material to hydrolysis and/or photolysis or volatility: - Solubility and stability of the test material in the solvent/vehicle and the exposure medium: - Reactivity of the test material with the incubation material used (e.g. binding to plastic ware or adsorption):  TREATMENT OF TEST MATERIAL PRIOR TO TESTING - Treatment of test material prior to testing (e.g. warming, grinding): - Preliminary purification step (if any): - Final nominal concentration of a dissolved solid, stock liquid or gel: - Final preparation of a solid (e.g. stock crystals ground to fine powder using a mortar and pestle):  FORM AS APPLIED IN THE TEST (if different from that of starting material) - Specify the relevant form characteristics if different from those in the starting material, such as state of aggregation, shape of particles or particle size distribution:  INFORMATION ON NANOMATERIALS - Chemical Composition: - Density: - Particle size & distribution: - Specific surface area: - Isoelectric point: - Dissolution (rate):  TYPE OF BIOCIDE/PESTICIDE FORMULATION (if applicable) - Description of the formulation, e.g. formulated product for foliar application; formulated product soil application; solution in organic solvent for soil application; formulated product seed treatment; solution in organic solvent seed treatment:  OTHER SPECIFICS - Other relevant information needed for characterising the tested material, e.g. if radiolabelled, adjustment of pH, osmolality and precipitate in the culture medium to which the test chemical is added: |  |  |
|  | **Test system** | **Header 2** |  |  |  |
|  | Type of test system | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - bacteria - cellular fraction - complex biological test system - cell line - physical / chemical based - primary cells - tissue - yeast - other: | A test system is any biological, chemical or physical system or a combination thereof used in a study (OECD (2018), Guidance Document on Good In Vitro Method Practices (GIVIMP), OECD Series on Testing and Assessment, No. 286, OECD Publishing, Paris).  Examples of physical chemical based test systems: serum protein, peptide, enzyme.  Select complex biological test system for example in case of: 3D model, induced pluripotent stem cells, organ on a chip, co-cultures, etc.  Select 'other:' in case you don't find a suitable option, for example when your test system is a test kit or a lower in vivo organism. |  |
|  | Test system identity | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - AR-CALUX - AR-Ecoscreen - CHO-K1 - cystein peptide - cysteine derivative NAC - cytosol - ERα-CALUX - FTC-238 - GH3 - HaCaT human keratinocytes - Hepa-RG - hERα-HeLa-9903 - hrERα - human NCI-H295R adeno-carcinoma cell line - human hepatocytes - LuSens cells - lysine derivative NAL - lysine peptide - MDCK - microsomes - S9 - THP-1 cells - THP-G8 cells - U-937 cells - VM7Luc4E2 - 22Rv1/MMTV\_GR-KO cell line - other: | The test systems listed are those from existing test guidelines. Select the test system used or select other and provide the test system identity. Furthermore, provide information on:  - Source / supplier  - Catalogue / batch number  - Species and strain (as relevant) of the origin of the test system.  In case a co-culture of cell lines is used, or S9 mix or microsomes are used in combination with a cell line, the user is asked select 'other' and to provide the identity of all components under 'remarks'. In the later fields for 'details on the test system' and 'metabolic competence' the test system can be further described. |  |
|  | Genetic modification of the test system | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - genetically modified after purchase, prior to use - genetically modified by supplier - not applicable - not genetically modified - other: | When applicable, provide the following information on the genetic modification:  - Gene inserted  - Gene species (e.g. human, rat, mouse)  - Additional information on modification |  |
|  | Details of the test system | Text template  Display: Basic | **Freetext template:** TEST SYSTEM DESCRIPTION  Provide a short description of the test system, including (species, organ, tissue or cell type (e.g. human monocytoc leukemia cell line or human cryopreserved pooled liver tissue homogenate 9000 g fraction (S9):  For cell lines:  - Number of passages used, if applicable: - Cell cycle length, doubling time or proliferation index: - Measures taken for avoiding or screening for contamination by mycoplasma, bacteria, fungi and virus - Periodically checked for karyotype stability: [yes/no] - Differentiation performed [yes/no], describe:  MEDIA USED and incubation conditions  - Type and composition of media, including use of serum and antibiotics: - Incubation conditions such as CO2 concentration, humidity level, temperature, if applicable: | In this field further details on the in vitro model or strain can be provided. The free text template was developed on basis of the OECD GIVIMP guidance.  Include in the description for example when a combination was used of a cell line with a metabolically competent component such as S9 mix. |  |
|  | Metabolic competence of the test system | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - limited metabolic activity, specify - metabolic activity, specify - unknown metabolic activity - other information on metabolic competence, describe: - not applicable | Select the option that fits best and describe the knowledge about the metabolic competence (i.e. Phase I and/or II biotransformation capacity) of the test system under remarks.  For example, when the test system used is cryopreserved human pooled liver tissue homogenate 9000 g fraction (S9) procured from a commercial supplier, select “metabolic activity, specify” and specify:  contains phase I and II metabolic enzymes present in the microsomal (e.g. cytochrome P450s, Flavin-containing monooxygenase, uridine 5’-diphospho-glucuronosyltransferases, carboxylesterases) and cytosolic (e.g. sulfotransferases, glutathione S-transferases, methyltransferases, N-acetyl transferases, xanthine oxidase, aldehyde oxidase) fractions. |  |
|  | **Detection method** | **Header 2** |  |  |  |
|  | Detection method used | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - analytical method (e.g. LC/MS) - chromatography - complex detection methods (e.g. imaging) - fluorescence - luminescence - radioactivity - UV/VIS absorption - other: | Indicate the readout used. Select a detection method type from the picklist and provide the type of instrument (e.g. HPLC, Spectrophotometer, Flow cytometer) or chose 'other: and specify the type or equipment used / analysis performed. |  |
|  | Details on detection method | Text template  Display: Basic | **Freetext template:  Option 1 Semi or non-quantitative detection methods** SEMI OR NON-QUANTITATIVE DETECTION METHODS  Instrument type and model: **Option 2 Quantitative analytical methods** QUANTITATIVE ANALYTICAL METHODS  Instrument type and model:  COMPOUND (ANALYTE): ...  - Method ID: - Extraction solvent/technique: - Cleanup strategies: - Derivatisation (if any): - Instrument/detector (if further details): - Standardisation method: - Stability of standard solution: - Retention times: - Detection limit (Limit of Quantification) - Other:   INTERFERING SUBSTANCE(S):   STABILITY OF PARENT AND TRANSFORMATION PRODUCTS AT VARIOUS STAGES OF ANALYSIS:  PROBLEMS / PRECAUTIONS:  - Special problems encountered: - Precautions to be taken during: - analysis of samples: - handling of samples: - storage of samples:   TOTAL TIME FOR COMPLETION: | Quantitative analytical methods:  'Briefly describe further details on the principles of the method used to detect the analytes (to be specified, e.g. ''parent compound'', ''parent and transformation products'' or ''transformation product: .....'') in matrices. Use free text template and delete/add elements as appropriate. For example, add specific parameters in the case of inorganic chemicals. As an option you may include an excerpt from the study report.  Note: If a residue analytical method is recorded, the details for the so-called data collection or data-gathering method should be specified here. As to the terms ''data collection method'' and ''enforcement method'' see help text for field ''Instrument / detector''.  Enter any details that could be relevant for evaluating this study summary or that are requested by the respective regulatory programme. Consult the programme-specific guidance (e.g. OECD HPVC, Pesticides NAFTA or EU REACH) thereof. |  |
|  | **Test design** | **Header 2** |  |  |  |
|  | **Test material preparation** | **Header 3** |  |  |  |
|  | Vehicle / solvent | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - 1:1 mix, acetone:acetonitrile - 1:1 mix, water:acetonitrile - DMSO - X-VIVOTM 15 - acetone - acetonitrile - ethanol - isopropanol - mix DMSO:acetonitrile - not required - not specified - pH 7.5 phosphate buffer - saline - treatment/exposure medium - water - other: | If a vehicle or solvent was used, select the relevant item or use 'other:' and specify. You can give further relevant information in the supplementary remarks field, e.g. lot/batch no., purity, concentration, etc.  In case a solvent is used that is different from those recommended in the in vitro method Standard Operating Procedure or test guideline, a justification for the choice must be provided. |  |
|  | Dilution steps / dose intervals | Text template  Display: Basic | **Freetext template:** DILUTION STEPS PERFORMED  Provide the following information (where available):  - Dilution steps from ‘stock solution’ in the vehicle/solvent including the final % of vehicle/solvent in the exposure medium - Dose intervals in case of dose range - Number of concentrations prepared | Indicate if the test material was further diluted before exposure of the test system. In case of dose range, provide the amount of concentrations and dilution factor.  Example description: The test material was first diluted in 70% ethanol and subsequently diluted 500-fold in cell culture medium. Another 2-fold dilution was executed in the well to obtain a total of 1000-fold dilution and a final solvent concentration of 0.07%. |  |
|  | **Control and reference items** | **Header 3** |  |  |  |
|  | Controls / reference items used | List (picklist)  Display: Basic | **Picklist values:** - yes - no - not specified - not required | Indicate whether controls / reference substances were used. If 'yes' is selected, the details can be entered in the repeatable block 'Controls / reference substances'. |  |
|  | **Controls / reference items** | **Block of fields (repeatable) Start** |  | Indicate whether solvent/vehicle controls, negative controls, true negative controls (i.e. negative reference substances) and/or positive controls (i.e. positive reference substances) were tested concurrently. Repeat this block of fields as necessary.  In case of a robust study summary or as requested by the regulatory programme, also provide information in the supplementary remarks field, e.g. to the identity, supplier, lot and purity of the control substance(s) and the concentration / amount applied. | **Guidance for field condition:** Condition: Block of fields active only if 'Controls / reference substances used' is 'yes' |
|  | Type of controls used | List (picklist)  Display: Basic | **Picklist values:** - negative/untreated controls - positive control item - reference item - solvent / vehicle controls - true negative control item - other: | Select the type of control used to demonstrate the proper performance of the test system and therefore the validity of the experiments. More than one control/reference item can be provided.  See (GIVIMP, OECD guidance document 286 in the series on testing and assessment).  Solvent / vehicle controls consist of solvent or vehicle alone, without test item (test material), and otherwise treated in the same way as the treatment groups.  Negative / untreated controls consist of culture medium without solvent / vehicle or test item, and otherwise treated in the same way as the treatment groups.  True negative controls include items (e.g. chemicals) with known lack of activity.  Positive controls include items with known activity.   Reference items are substances with known activity, used as basis for comparison with the test item (test material). |  |
|  | Description of reference and control items used | List sup. (picklist with remarks - 2,000 char.)  Display: Basic | **Picklist values:** - 1-chloro-2,4--dinitrobenzene - [CAS 97-00-7] - 17α-estradiol - [CAS 57-91-0] - 17α-methyltestosterone - [CAS 58-18-4] - 17β-estradiol (E2) - [CAS 50-28-2] - 1:1 mix, acetone:acetonitrile - 1:1 mix, water:acetonitrile - 4-hydroxytamoxifen - [CAS 68047-06-3] - 4-nitrobenzyl bromide (4-NBB) - [CAS 100-11-8] - 5α-Dihydrotestosterone - [CAS 521-18-6] - DL-Lactic acid - [CAS 50-21-5] - DMSO - Di(2-ethylhexyl)phthalate - [CAS 117-81-7] - X-VIVOTM 15 - acetone - acetonitrile - bicalutamide - [CAS 90357-06-5] - bisphenol A - [CAS 80-05-7] - cinnamic aldehyde - [CAS 104-55-2] - combination of raloxifene hydrochloride, CAS 84449-90-1 and 17β-estradiol - [CAS 50-28-2] - corticosterone - [CAS 50-22-6] - cycloheximide - [CAS 66-81-9] - ethanol - ethylene glycol dimethacrylate (EGDMA) - [CAS 97-90-5] - flutamide - [CAS 13311-84-7] - forskolin - [CAS 66575-29-9] - hydroxyflutamide - [CAS 52806-53-8] - isopropanol - levonorgestrel - [CAS 797-63-7] - linuron - [CAS 330-55-2] - medium - mestanolone - [CAS 521-11-9] - methoxychlor - [CAS 72-43-5] - mix DMSO:acetonitrile - nickel sulfate - [CAS 10101-97-0] - norethindrone - [CAS 68-22-4] - norethynodrel - [CAS 68-23-5] - octyltriethoxysilane - [CAS 2943-75-1] - phenylacetaldehyde - [CAS 122-78-1] - picrylsulfonic acid, (2,4,6-trinitro-benzene-sulfonic acid, TNBS) - [CAS 2508-19-2] - prochloraz - [CAS 67747-09-5] - resveratrol - [CAS 501-36-0] - saline - squaric acid diethyl ester - [CAS 5231-87-8] - tamoxifen - [CAS 10540-29-1] - trans-cinnamic aldehyde - [CAS 14371-10-9] - water - other: | Select the reference or control item used or provide the name and identifier (e.g. CAS number), and in the remarks field the purity and concentration (range) used.  If 'other:' is selected, provide the name and identity (CAS number) in the additional text field.  For each selection (including the 'other:'), provide purity (%) and concentration (range or single concentration) in the field 'Remarks'. |  |
|  | Remarks | Text (32,768 char.)  Display: Basic |  | Additional information, such as solvents used. |  |
|  | **Controls / reference items** | **Block of fields (repeatable) End** |  |  |  |
|  | **Experimental conditions** | **Header 3** |  |  |  |
|  | Number of replicates | Text template  Display: Basic | **Freetext template:** NUMBER OF REPLICATIONS:  - Number of replicates per concentration (single, duplicate, triplicate) - Number of independent experiments | Provide the number of replicates per concentration and the number of independent experiments performed. For each experiment, valid or invalid, results should be reported. |  |
|  | Experimental conditions | Text template  Display: Basic | **Freetext template:** METHOD OF TREATMENT/ EXPOSURE:  - Concentration of the test system (e.g. cell density or number of cells used) - Description how the test material was added to the test system (e.g. in medium, in suspension)  TREATMENT AND HARVEST SCHEDULE:  - Pre-incubation period, if applicable - Exposure duration / duration of treatment - Frequency of administration, e.g. single, repeated or continuous - Harvest time after the end of treatment (sampling/recovery times) - Incubation conditions - Vessel type used for exposure  - OTHER: | Use free text template and delete/add elements as appropriate. Enter any details that could be relevant for evaluating this study summary or that are requested by the respective regulatory programme. Consult the programme-specific guidance (e.g. OECD Programme, Pesticides NAFTA or EU REACH) thereof.  Concentration of biological test systems is usually expressed as cell density (amount of cells/cm2 or cells/ml seeded) or confluence (%).  Concentration of physical chemical test systems is usually expressed in mg/ml or molarity.  Incubation conditions are e.g. temperature, CO2, concentration, humidity level, etc.  A vessel can e.g. be a test tube or cell culture plates with 24, 96 or 384 wells. |  |
|  | Additional analysis: e.g. cytotoxicity assay or other | List sup. (picklist with remarks - 2,000 char.)  Display: Basic | **Picklist values:** - ATP assay - BrdU or EdU incorporation into DNA - cell counting - cell death / apoptosis markers - LDH-release - mitochondrial depolarisation assay - neutral red uptake - observation of cell shape - other cytotoxicity assay, specify - other type of analysis, specify - penetration of dyes in non-viable cells (e.g. trypan blue, propidium iodide) - resazurin reduction assay (alamar blue or similar) - retention of dyes in viable cells (e.g. fluorescein diacetate or calcein-AM) - staining of proteins or DNA in the overall cell mass - tetrazolium dye reduction assays (MTT or similar) - no other analysis performed | This picklist was established on basis of GIVIMP annex I (OECD, 2018).  Select the viability assay used to measure cytotoxicity:   Select 'other cytotoxicity assay' in case another type of cytotoxicity assay was used. Select 'other type of analysis' in case another or another type of analysis was performed that is important for the interpretation of results (e.g. pH, autofluorescence, etc.).  In the remarks field any additional information can be provided. |  |
|  | **Data analysis** | **Header 3** |  |  |  |
|  | Acceptance criteria for the test material results | Text template  Display: Basic | **Freetext template:** Provide a description or list of the study acceptance criteria: | Add the criteria used to decide if the results of a test material are accepted or not (e.g. variability of triplicate values < 20% and minimum 6 valid concentrations). This is usually described in test guidelines and not in non-test guidelines.  Definition of Acceptance criteria: Criteria for when results can be accepted, i.e. a set of well-defined parameters describing aspects of the method such as range for positive and negative controls (GIVIMP, OECD, 2018).   For cell-based methods, the acceptance criteria should include the level of cytotoxicity or other type of interference that is accepted / not accepted.  Any free text explanation can be given to specify which criteria exist for acceptance of results, e.g. related to reference and control substances or vehicle/solvent control, cytotoxicity or other interference, capturing of full dose-response, minimum/maximum response to be observed or outliers. |  |
|  | Data calculation and statistics | Text template  Display: Basic | **Freetext template:** - Calculations performed - Statistical methods used - Where relevant, provide the method used to exclude outliers. | Provide the method used to calculate the results from raw data to the parameters calculated, such as normalisation, use of calibration curve, subtraction of control values, calculation of averages, Standard deviations etc.  List the statistical methods used to derive the parameters to be reported. Include a statement on the appropriateness of the statistical analysis used. Parameters, their explanation and values should be provided in the "Test results" section.  Example of data calculation and statistical analysis performed:  Relative Light Units raw data were copied to commercially available software Graphpad Prism for hill curve fitting (variable slope, four parameters). Subsequently, the EC50 value and its CV were calculated.  Specify if outlier analysis is performed and what (statistical) method was used to exclude values. |  |
|  | Evaluation / data interpretation criteria | Text template  Display: Basic | **Freetext template:** - Evaluation / data interpretation criteria: - Results will be expressed as: | Describe the evaluation criteria used in the study to judge if the test material is positive, negative or equivocal. For example:  When there is more than 10% binding to the androgen receptor (as expressed in relative light units) for more than two concentrations, the result is ‘positive’.  h-CLAT: When the RFI of CD86 is equal to or greater than 150% in at least one tested concentration (with cell viability ≥ 50%), the result for the test material is positive. The EC150 value is calculated where possible.  DPRA: The mean of cystein and lysine depletion is: Less than 6.38%: minimal reactivity.  Between 6.38% and 22.62%: low reactivity  Between 22.62% and 42.47%: moderate reactivity.  More than 42.47%: high reactivity.  Consider also precipitation and co-elution. |  |
|  | **Any other information on materials and methods incl. tables** | **Header 2** |  |  |  |
|  |  | Text (rich-text area)  Display: Basic |  | In this field, you can enter any information on materials and methods, for which no distinct field is available, or transfer free text from other databases. You can also open a rich text editor and create formatted text and tables or insert and edit any excerpt from a word processing or spreadsheet document, provided it was converted to the HTML format. You can also upload any htm or html document.  Here you may for example provide details on specific material or reagents used. In case of TG442E, h-CLAT you could provide the information on the type of antibodies used, as these are essential components of the method.  Note: One rich text editor field each is provided for the MATERIALS AND METHODS and RESULTS section. In addition the fields 'Overall remarks' and 'Executive summary' allow rich text entry. |  |
|  | **Results and discussion** | **Header 1** |  |  |  |
|  | **Test results** | **Header 2** |  |  |  |
|  | **Test results** | **Block of fields (repeatable) Start** |  | Report the parameters obtained and effective concentration(s) for the type of effect specified in the 'Test results' fields. Copy this field block for entering more than one experiment if necessary, e.g. for a test guideline or if different concentration ranges were tested.  One experiment may include more than one replicate for each tested concentration. An independent experiment is usually carried out with independently prepared controls, test system, reagents used for analysis and on a different time.  Set this flag if a key observation should be identified for the conclusion section. |  |
|  | Details of the effect identification | Link to repeatable entry  Display: Basic |  | Select the Process/Object/Action combination for which you will report the data. For each combination a dedicated results section can be completed. |  |
|  | Key result | Check box  Display: Basic |  | Set this flag if a key observation should be identified for the conclusion section. |  |
|  | Concentration selection of the test material | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - human exposure levels - interference with the detection method (e.g. auto fluorescence) - interference with the test system (e.g. cytotoxicity or pH) - maximum allowed concentration according to the test guideline - prior information of response (e.g. dose-range finding experiment) - solubility in exposure medium - solubility in solvent - unknown - other: | For data interpretation it is important to know on what basis the highest concentration tested was selected.  Prior information of response and interference with the test system can e.g. be obtained through literature or with experimental data in a dose-range finding experiment.  Example for TG442E (h-CLAT)  Highest concentration to be used is either of the following concentrations:  - 1.2-fold the CV75 concentration of the test chemical, i.e. the concentration where 25% of the cells is dead.  - Maximum 5000 µg/mL for non-cytotoxic test chemicals that dissolve or stably disperse in the solvent saline and subsequently in medium.  - Maximum 1000 µg/mL for non-cytotoxic test chemicals that dissolve in DMSO and subsequently in medium.  Any free text explanation can be given in the adjacent text field to justify the dose level selected. |  |
|  | Concentration range tested | Numeric range (decimal with picklist)  Display: Basic | **Lower numeric field [xx]:** - > - >= - ca. **Upper numeric field [xx]:** - < - <= - ca. **Picklist values:** - % - g/L - g/kg - mg/mL - mg/L - mg/kg - mmol/L - mol/L - ng/L - nmol/L - pg/L - pmol/L - ppb - ppm - µg/L - µg/kg - µmol/L - other: - s-1M-1 | Indicate the lowest and highest concentration tested.  Enter a single numeric value in the first numeric field if you select no qualifier or '>', '>=' or 'ca.'. Use the second numeric field if the qualifier is '<' or '<='. For a range use both numeric fields together with the appropriate qualifier(s) if applicable. |  |
|  | Number of replicates and outliers | Text template  Display: Basic | **Freetext template:** - Number of replicates: - Information on outlier removal: - Impact of outlier removal on the results: | Specify the number of replicates per concentration and if any values were excluded after outlier analysis. |  |
|  | **Parameter and result** | **Block of fields (repeatable) Start** |  |  |  |
|  | Parameter | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - % NAC depletion (each replicate) - % NAL depletion (each replicate) - % cystein depletion (each replicate) - % depletion (average) - % lysine depletion (each replicate) - Bmax - CD54 EC200 - CD86 EC150 - CD86 stimulation index - CV of luminescence readings for solvent/vehicle control - CV70 (cell viability) - CV75 (MTT assay) - CV75 (cell viability) - EC10 - EC20 - EC50 - IC20 - IC30 - IC50 - Kd - LOEC - NAC peak area (each replicate) - NAL peak area (each replicate) - NOEC - PC10 - PC50 - PC80 - PCMax - PCmin - RPCMax - RPCmin - TCxMax (maximum induction) - TCxMin (minimum induction) - arithmetic mean of cell viability and luciferase activity induction - average % cystein depletion - average % lysine depletion - average I max - coelution with NAC peptide - coelution with NAL peptide - coelution with cystein peptide - coelution with lysine peptide - fold luciferase activity induction - geometric mean of EC1.5 - geometric mean of IC30 (MTT assay) - geometric mean of IC50 (MTT assay) - highest fold induction - highest fold inhibition - induction of nlL8LA (Ind-IL8LA) - inhibition of GAPDH Luciferase Activity (Inh-GAPLA) - log EC10 - log EC20 - log EC50 - log IC20 - log IC30 - log IC50 - log Kmax - log Kow - log PC10 - log PC50 - maximum % induction - maximum % inhibition - mean % NAC depletion - mean % NAC depletion of the three replicate, SD and CV - mean % NAL depletion - mean % NAL depletion of the three replicate, SD and CV - mean % cystein depletion of the three replicate, SD and CV - mean % lysine depletion of the three replicate, SD and CV - mean fluorescence intensity - mean relative transcriptional activity to PC (1 nM of E2)logPC10 - mean value of the relative transcriptional activity to spike in control - normalised IL8 Luciferase Activity (nlIL8LA) - peak area (average) - peak area at 220 nm (each replicate) - presence of precipitate - reaction kinetic rate constants - relative binding affinity (RBA) - relative change with respect to solvent control - relative fluorescence intensity - relative peptide depletion in % - the 95% confidence interval of Ind-IL8LA - |CV| of logEC50 - |CV| of logIC50 - other: | This picklist displays either the parameters specific to the selected method, or general parameters in case another method is used.  Provide the relevant parameters, representative of the effect measured, that are calculated for your method. Existing test guidelines and OHTs for in vitro methods (e.g. OHT 66-1) may provide additional suggestions for other type of parameters.  For guideline methods, all relevant parameters are listed.  In case of a non-guideline method, the listed parameters are from existing OECD test guidelines, where the use of the parameters is explained. E.g. CV75 is the test chemical concentration that results in 75% cell viability. The PC value is obtained by interpolation in case a full dose response is not obtained for the test material.  Provide in the remarks field, other information that provides explanation of the parameter. E.g. when % depletion is selected, provide information on what is depleted (e.g. cysteine, lysine, etc.).  Explanation of some parameters:  EC 1.5, 150 and 200 represents the concentration where the test material triggers the effect at the limit (e.g. 1.5, 150 or 200) prescribed by the method used.  No-observed effect concentration (NOEC) is defined as the test concentration below the lowest concentration that did result in a significant effect in the specific experiment.  Lowest-observed effect concentration (LOEC) is the lowest concentration out of the tested concentrations at which a statistically significant difference from the control group is observed.  PC10, 50, 80 represents the concentration of a test material where the response is 10, 50 or 80% of the response induced by the reference chemical. PC values can be used when incomplete or ambiguous dose response curves are obtained and EC values cannot be calculated..  CL, in vitro, INT is in vitro intrinsic (metabolic) clearance. |  |
|  | Result for the parameter | Numeric (decimal including unit)  Display: Basic | **Unit [xx]:** - % - g/L - g/kg - mg/mL - mg/L - mg/kg - mmol/L - mol/L - ng/L - nmol/L - pg/L - pmol/L - ppb - ppm - µg/L - µg/kg - µmol/L - other: - s-1M-1 | Provide the result for the selected parameter and select the appropriate unit. |  |
|  | Remarks | Text (32,768 char.)  Display: Basic |  |  |  |
|  | **Parameter and result** | **Block of fields (repeatable) End** |  |  |  |
|  | **Other observations** | **Block of fields (repeatable) Start** |  |  |  |
|  | Observation | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - absorbance by the test material - auto fluorescence - co-elution - cytotoxicity - no other observations - pH change - precipitation - other: | Indicate other observations that are important for results interpretation such as information on cytotoxic concentrations, precipitation observed at specific concentrations, other parameters measured. Specify the observation and respective test concentration(s). Alternatively or in addition, use the field 'Any other information on results incl. tables'. If you refer to table(s), use appropriate table numbers (e.g. ‘… see Table 1’).  Note: Specific tables may be required. Consult the programme-specific guidance (e.g. OECD Programme, Pesticides NAFTA or EU REACH) thereof. |  |
|  | Concentration | Numeric range (decimal with picklist)  Display: Basic | **Lower numeric field [xx]:** - > - >= - ca. **Upper numeric field [xx]:** - < - <= - ca. **Picklist values:** - % - g/L - g/kg - mg/mL - mg/L - mg/kg - mmol/L - mol/L - ng/L - nmol/L - pg/L - pmol/L - ppb - ppm - µg/L - µg/kg - µmol/L - other: - s-1M-1 | Provide the result for other observations and select the appropriate unit. |  |
|  | **Other observations** | **Block of fields (repeatable) End** |  |  |  |
|  | Results for the test material | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - ambiguous - binder - borderline - data inconclusive - equivocal - high reactivity - inadequate - indication of UN GHS subcategory 1A for skin sensitisation - no indication of UN GHS subcategory 1A for skin sensitisation - low reactivity - minimal reactivity - moderate reactivity - negative - non-binder - positive - supposedly negative - technically compromised - not determinable - not interpretable - not specified - other: | The options in the picklist are derived from existing in vitro OECD test guidelines.  Indicate the result of the test conducted.  In the remarks field additional information can be added. For example when selecting binder additional information could be 'competitive', 'non competitive', 'specific' or 'non-specific'.  Example of results from TG442C, DPRA:  - Minimal reactivity  - Low reactivity  - Moderate reactivity  - High reactivity |  |
|  | Acceptance of results | List multi. (multi-select list with remarks)  Display: Basic | **Picklist values:** - minimum response by the test system obtained - negative control item - no acceptance criteria were used - positive control item - reference item - solvent / vehicle controls - test material - variability within replicate measurements - other: | Select the element for which acceptance criteria exist and indicate in the remarks field if the results are valid or invalid.  In case results are invalid, please describe in the next field 'Remarks on results' why the result is invalid (e.g. precipitation observed, toxicity of the test material, co-elution with the peptide, etc.), and what is the impact of invalid data on the results. |  |
|  | Remarks on results | Text (32,768 char.)  Display: Basic |  | This field can be used for:  - explaining expert judgement, in case it was applied;  - providing a justification;  - giving a qualitative description of results in addition to or if no numeric value(s) were derived;  - providing information in case a result may be over-estimated or under-estimated;  - giving a pre-defined reason why no numeric value is provided, e.g. by selecting 'not determinable' and entering free text explanation in the supplementary remarks field;  - explaining the impact on the results in case one or more acceptance criteria were not met;  - any additional information. |  |
|  | **Attached material** | **Block of fields (repeatable) Start** |  |  |  |
|  | Type of attachment | List multi. (multi-select list with remarks)  Display: Basic | **Picklist values:** - chromatogram - cytotoxicity results (where relevant) - data analysis file (calculation of parameters) - graph - picture - plate layout (where applicable) - raw data - table - other: | Choose the type of document from the picklist or select 'other:'.  For test guidelines that provide a reporting template (data analysis file), that file must be completed and can be uploaded here or in the overall results section.   Upload file(s) containing data or results by clicking the ‘Select files’ button. As appropriate, enter any additional information, e.g. language. The file name and the filename extension is displayed after uploading the document. |  |
|  | Attachment | Attachment (single)  Display: Basic |  | Attach the document indicated in the field "Type of attachment". |  |
|  | **Attached material** | **Block of fields (repeatable) End** |  |  |  |
|  | **Test results** | **Block of fields (repeatable) End** |  |  |  |
|  | **Overall remarks, attachments** | **Header 1** |  |  |  |
|  | Overall remarks | Text (rich-text area)  Display: Basic |  | In this field, you can enter any overall remarks or transfer free text from other databases. You can also open a rich text editor and create formatted text and tables or insert and edit any excerpt from a word processing or spreadsheet document, provided it was converted to the HTML format. You can also upload any htm or html document.  Note: One rich text editor field each is provided for the MATERIALS AND METHODS and RESULTS section. In addition the fields 'Overall remarks' and 'Executive summary' allow rich text entry. |  |
|  | **Attachments** | **Block of fields (repeatable) Start** |  | Attach any background document that cannot be inserted in any rich text editor field, particularly image files (e.g. an image of a structural formula).  Copy this block of fields for attaching more than one file. |  |
|  | Type | List (picklist)  Display: Basic | **Picklist values:** - full study report - illustration (picture/graph) - other: | Specify the type of attachment inserted, for example the 'full study report'. |  |
|  | Attached (confidential) document | Attachment (single)  Display: Basic (Confidential) |  | Provide any additional documents relevant for the submission, not already provided under the methods or results section or in the full study report. Choose the type of document from the picklist or select other.  Examples are:  - Scientific publication  - GLP documentation  - (Q)SAR: supporting information  - Data analysis file (calculation of parameters)  - Data supporting the reliability and sensitivity of the method  - Specific information on the test material or test system  - Justification  - Expert judgement  - Other  For test guidelines that provide a reporting template (data analysis file), that file must be completed and can be uploaded here if not yet done in the results section.  Upload file by clicking the upload icon. As appropriate, enter any additional information, e.g. language. The file name is displayed after uploading the document. |  |
|  | Attached (sanitised) documents for publication | Attachment (single)  Display: Basic |  | An electronic copy of a public (non-confidential) version of the full study report or other relevant documents can be attached. This attachment should be sanitised if needed. |  |
|  | Remarks | Text (255 char.)  Display: Basic |  | As appropriate, include remarks, e.g. a short description of the content of the attached document if the file name is not self-explanatory.  If required, an electronic copy of the full study report or QSAR QPRF reporting forms can be attached as WORD, pdf or other document type. |  |
|  | **Attachments** | **Block of fields (repeatable) End** |  |  |  |
|  | **Applicant's summary and conclusion** | **Header 1** |  |  |  |
|  | **Interpretation of results / observations** | **Header 2** |  |  |  |
|  | Overall results and conclusion | Text template  Display: Basic | **Freetext template:** Describe the overall result as:  a) based on observations O1, O2, …On b) the test material c) triggers/does not trigger d) a certain mechanism (process/object/action) e) on a certain biological level | Provide the overall result for the test material, on basis of one or more experiments and all observations reported in this template.  Convey a clear statement on the mechanistic information obtained.  Add the effect concentration in the next fields.  Example from h-CLAT: The RFI of CD86 is greater than 150% at 2 tested concentrations (with cell viability ≥ 50%) in 2 of 2 experiments. Therefore the test material is activating dendritic cells and is a possible skin sensitizer. |  |
|  | Type of result | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - quantitative - qualitative | Indicate if the results are qualitative when the result is yes/no or positive/negative or quantitative when dose-response information is obtained and an effect level (concentration) can be determined. |  |
|  | Effect concentration | List sup. (picklist with remarks)  Display: Basic | **Picklist values:** - EC 1.5 - EC10 - EC150 - EC20 - EC200 - EC50 - IC20 - IC30 - IC50 - LOEC - NOEC - PC10 - PC50 - PC80 - PCMax - PCmin - log EC10 - log EC20 - log EC50 - log IC20 - log IC30 - log IC50 - logKmax - log PC10 - log PC50 - not determined - other: | Where available, provide the effect concentration taking into account results from more than one experiment.  Explanation of some parameters:  EC 1.5, 150 and 200 represents the concentration where the test material triggers the effect at the limit (e.g. 1.5, 150 or 200) prescribed by the method used.  No-observed effect concentration (NOEC) is defined as the test concentration below the lowest concentration that did result in a significant effect in the specific experiment.  Lowest-observed effect concentration (LOEC) is the lowest concentration out of the tested concentrations at which a statistically significant difference from the control group is observed.  PC10, 50, 80 represents the concentration of a test material where the response is 10, 50 or 80% of the response induced by the reference chemical. PC values can be used when incomplete or ambiguous dose response curves are obtained and EC values cannot be calculated. |  |
|  | Concentration | Numeric range (decimal with picklist)  Display: Basic | **Lower numeric field [xx]:** - > - >= - ca. **Upper numeric field [xx]:** - < - <= - ca. **Picklist values:** - % - g/L - g/kg - mg/mL - mg/L - mg/kg - mmol/L - mol/L - ng/L - nmol/L - pg/L - pmol/L - ppb - ppm - µg/L - µg/kg - µmol/L - other: - s-1M-1 | Provide the effect concentration and select the appropriate unit. |  |
|  | Remarks | Text (32,768 char.)  Display: Basic |  | Include any remarks as appropriate. |  |
|  | **Executive summary** | **Header 2** |  |  |  |
|  |  | Text (rich-text area)  Display: Basic |  | If required by the respective national/regional programme, briefly summarise the relevant aspects of the study including the conclusions reached. If a specific format is prescribed, upload the respective free text template if available from the drop-down list or copy it from the corresponding document.  You may also provide information on other existing data or studies that confirm the results obtained.  Consult the programme-specific guidance (e.g. OECD HPVC, Pesticides NAFTA or EU REACH) thereof. |  |