QMRF CHAPTER TITLES	SECTION TITLES	MODEL DESCRIPTION (Fill in this column)
1. QSAR identifier		
	1.1. QSAR identifier (title): 1.2. Other related models:	Derek Nexus - mutagenicity Derek Nexus contains alerts for multiple endpoints, including mutagenicity, chromosome damage, carcinogenicity, hepatotoxicity, teratogenicity and skin irritation
	1.3. Software coding the model:	Derek Nexus v6.0 contains 132 active alerts for bacterial mutagenicity, together with reasoning rules and secondary functionality that evaluates potentially misclassified and unclassified features in compounds that do not activate bacterial mutagenicity alerts or examples.
2. General information		0.1000
	2.1. Date of QMRF: 2.2. QMRF author(s) and contact details:	2 June 2009 Kate Langton, Lhasa Limited, 22-23 Blenheim Terrace, Woodhouse Lane, Leeds, LS2 9HD, UK
	2.3. Date of QMRF update(s):	01 December 2017
	2.4. QMRF update(s):	Lilia Fisk, Lhasa Limited, Granary Wharf House, 2 Canal Wharf, Leeds, LS11 5PS, UK
	2.5. Model developer(s) and contact details:	1.3, 2.3, 2.4, 2.6, 4.5, 7.8 Lhasa Limited, Granary Wharf House, 2 Canal Wharf, Leeds, LS11 5PS
	2.6. Date of model development and/or	Derek Nexus 6.0 was released on 12 December 2017
	publication: 2.7. Reference(s) to main scientific papers and/or software package:	[1] Sanderson DM & Earnshaw CG (1991). Computer prediction of possible toxic action from chemical structure; The DEREK system. Human and Experimental Toxicology 10, 261-273, [2] Judson PN, Marchant CA & Vessey JD (2003). Using argumentation for absolute reasoning about the potential toxicity of chemicals. Journal of Chemical Information and Computer Sciences 43, 1364-1370, [3] Marchant CA, Briggs KA & Long A (2003). In silico tools for sharing data and knowledge on toxicity and metabolism: Derek for Windows, Meteor, and Vitic. Toxicology Mechanisms and Methods 18, 177–187. [4] Judson PN, Stalford SA & Vessey J (2013). Assessing confidence in predictions made by knowledge-based
	2.8. Availability of information about the model:	systems. Toxicology Research 2, 70-79. Derek Nexus is a proprietary, rule-based expert system for the prediction of toxicity. Its knowledge base is composed of alerts, examples and reasoning rules which may each contribute to the predictions made by the system. Each alert in Dere describes a chemical substructure believed to be responsible for inducing a specific toxicological outcome (often referred to as a toxicophore). Alerts are derived by experts, using toxicological data and information reging the biological mechanism of action. Where relevant, metabolism data may be incorporated into an alert, enabling the prediction of compounds which are not directly toxicity but are metabolised to an active species. The derivation of each alert is described in the alert comments along with supporting references and example compounds where possible. By reporting this information to the user, Derek provides highly transparent predictions. The use of structural alerts for the prediction of
	2.9. Availability of another QMRF for exactly the same model:	toxicity is both widely understood and the subject of many publications. No
3. Defining the endpoint - OECD	3.1. Species:	Predictions are made for the domain of bacteria and can be broken down into species (e.g. Salmonella typhimurium and
Principle 1	·	Escherichia coli). 4.Human health effects 4.10.Mutagenicity
	3.2. Endpoint: 3.3. Comment on endpoint:	*-Indian related effects 4.10.Widegenicity The Derek Nexus model for mutagenicity is developed from Ames test data in both S.typh and E.coli. Supporting data from transgenic rodent mutation assay, in vitro L5178Y TK+/- assay, in vitro HGPRT gene mutation assay, in vitro Na+/K+ ATPase gene mutation assay has also been considered for the development of a small number of alerts. Additionally, alert writers consider both mechanistic evidence and chemical properties (such as reactivity).
	3.4. Endpoint units:	Derek Nexus makes qualitative predictions for and against toxicity through reasoning. For the endpoint of mutagenicity, predictions for toxicity decrease in confidence in the following order: certains probable>plausible>equivocal. Predictions against toxicity increase in confidence in the following order: inactive (with unclassified and/or misclassified features)-cinactive-improbable. Likelihood levels have been shown to correlate with predictivity [Judson et al., 2013]. Multiple data sources (e.g., toxicity data from multiple assays and mechanistic evidence) are synthesised into the structure-activity relationships that underpins Derek Nexus predictions. An appreciation of the assay units applied by alert writers when building the alert training set. However, predictions are not quantitative and, as a result, do not include units.
	3.5. Dependent variable:	Data from the Ames test and mechanistic studies (e.g. measures of electrophilicity) are synthesised to arrive at an expert conclusion of whether compounds within the model training set is likely to be a mutagen.
	3.6. Experimental protocol:	The model is based primarily on data from the Ames test conducted following standard test protocol (OECD TG471). If
	3.7. Endpoint data quality and variability:	activity is observed in a non-standard assay or protocol this will be mentioned in the comments. Alert writers use all available and relevant information in the public domain (and proprietary data, where available) for alert development. Wherever possible, primary references are used as data sources: (i) the data are subject to expert assessment prior to inclusion in the alert training set using, amongst other criteria, OECD test guidelines and (ii) the references themselves are cited in the alert comments enabling users to conduct their own expert assessments on data quality.
4. Defining the algorithm - OECD Principle 2	4.1. Type of model:	Expert derived structural alerts for mutagenicity (2D SARs), physicochemical properties and associated reasoning. Following alert evaluation, Derek evaluates whether non-alerting query compounds contain any features that are either (i) also present in non-alerting mutagens in a large Ames test reference set (misclassified features) or (ii) not present in a large Ames test reference set (unclassified features).
	4.2. Explicit algorithm:	[1] Structural alerts, [2] logic of argumentation and [3] feature-based database search.
	4.3. Descriptors in the model:	[1] Markush structures encoding activating and deactivating features (known as patterns in the Derek Nexus knowledge base), [2] ClogP, [3] count of non-hydrogen atoms and [4] 2D structural fragments.
	4.4. Descriptor selection:	There is an a priori assumption that patterns and associated reasoning will be used to model toxicity within Derek Nexus. Further, experts identified that misclassified and unclassified features were useful descriptors for determining the reliability of negative predictions for non-alerting compounds.
	4.5. Algorithm and descriptor generation:	Alert writers design the patterns to describe the activating and deactivating features found during expert assessment of the alert training set. Misclassified and unclassified features are generated by processing a large Ames test reference set (comprising 4757 mutagens and 5210 non-mutagens) against Derek Nexus (v6.0) and fragmenting.
	4.6. Software name and version for descriptor	Alert writers use the Derek Knowledge Editor (v2.0) for the implementation of patterns. ClogP predictions generated using
	generation: 4.7. Chemicals/Descriptors ratio:	the BioByte model (v5.3). Fragmentation is completed using an in-house algorithm. This is not applicable to structural alerts as these are knowledge-based rather than statistically based.
5. Defining the		
3. Jenning tire applicability domain - OECD Principle 3	5.1. Description of the applicability domain of the model:	The scopes of the structure-activity relationships describing the mutagenicity endpoint are defined by the developer to be the applicability domain for the model. Therefore, if a chemical activates an alert describing a structure-activity for mutagenicity it can be considered to be within the applicability domain. If a compound does not activate an alert or reasoning rule then Derek makes a negative prediction. The applicability of the negative prediction to the query compound: can be determined by an expert, if required, by investigating the presence (or absence) of misclassified and/or unclassified features.
	5.2. Method used to assess the applicability domain:	The applicability domain of each alert is defined by the alert developer on the basis of the training set data and expert judgement on the chemical and biological factors which affect the mechanism of action for each alert. For non-alerting compounds, users should determine the applicability of negative predictions by evaluating the information supplied by Derek (i.e. the presence or absence of misclassified and/or unclassified features).
	5.3. Software name and version for applicability domain assessment: 5.4. Limits of applicability:	This is not applicable. Limits for individual alerts are mainly defined by restrictions in the scope of the alerts which are available for inspection within the software.
6. Internal validation -		1000
OECD Principle 4	6.1. Availability of the training set:	Non-proprietary elements of the training set are available through the references, and illustrated by the examples, within Derek Nexus. The illustrative examples are not available, due to the proprietary nature of Derek Nexus.

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