

no. 10406) has been subsumed into the term "Isolated ossification site" which is located under specific skull bones (e.g., basisphenoid, exoccipital, interparietal, etc.).

In Version 2, the number of observational findings presented in the tables has been greatly increased from Version 1. The rationale for this change was that technical scientists have often been forced to create their own terminology for findings when a description of these findings was not presented in the tables. This had the potential for creating inconsistencies in applied terminology across laboratories and/or across studies, and defeated the intended objective of a harmonized nomenclature. The International Nomenclature Committee carefully considered the applicability and appropriateness of each term that was added to the findings. Judgment was applied in deciding whether it was likely that specific findings would be observed in practice. Those that were considered unlikely to occur or were judged to be rarely observed or reported were not included in the tables. For these rarer occurrences, the practitioner is encouraged to apply the principles illustrated in the current presentation to construct a suitable description.

In order to clarify the organization and content of Version 2, a number of issues and considerations specific to each of the tables are addressed below:

3.1. External abnormalities (Table 1)

Omphalocele vs. umbilical hernia

Omphalocele is the result of failure of return of the intestinal loops into the body cavity, such that some of the intestines remain protruding through a defect in the ventral abdominal wall, usually at the umbilicus. The protruding intestines are covered by a thin transparent membrane, through which the loops can be easily seen. While this membrane may occasionally rupture, a remnant of the membrane will usually still be visible.

In umbilical hernia, the intestines return normally into the body cavity, but the ventral abdominal wall fails to close completely at the umbilical ring, allowing a varying amount of the intestines to protrude from the umbilical area. In contrast to omphalocele, the protruding intestines in umbilical hernia are covered by skin, not just a transparent membrane. The intestines are less easily seen in this defect, therefore, and it often presents superficially just as a bulge or protrusion in the umbilical region, covered by skin.

Since both defects are characterized by the protrusion of intestine through the umbilicus, omphalocele might sometimes be mistakenly described as umbilical hernia and vice versa. The simplest way to differentiate these two defects is to note that in omphalocele, the intestine is typically covered by a transparent membrane, while in umbilical hernia it is covered by non-transparent skin.

3.2. Visceral abnormalities (Table 2)

Lung and liver lobation

Flexibility is provided in the visceral table to allow both general and specific descriptions for the fetal lung and liver. Some laboratories may use, "liver" or "lung" as general terms, to describe various abnormalities in these organs. However, other laboratories may go further and describe the alterations detected in specific lobe(s).

3.3. Skeletal abnormalities (Table 3)

Structural change versus ossification state

A major change to the skeletal table is the incorporation of an additional column (following the Observation column) that identifies each observation term as "S" or "O." It is hoped that this will stress the importance of trying to distinguish between skeletal changes that are the result of structural abnormality and those

that are a change from the expected ossification state (i.e., a delayed or accelerated progression of the normal ossification process, relative to gestational age) in an otherwise normal structure/bone. It is not only important that these differences are correctly detected at the bench level but also that appropriate terminology is used to describe them. "S" has been used to denote terms that are recommended to describe a structural changes (e.g., changes in size or shape of the bone) and "O" has been used to denote terms that are recommended to describe changes in the state of ossification.

Cartilage evaluation

The structural terms (S) are appropriate for cartilage as well as ossified bone evaluation. According to in-house protocol, individual laboratories might choose to further qualify either the nomenclature (as listed in the 'Region/Organ/Structure' column) for the affected structure or the structural observation term (S) to indicate that the finding has been observed in a structure that was at least in part visualized as cartilage. Examples are: "Cartilaginous vertebral centrum, dumbbell-shaped" or "Ribs 9, 10 cartilaginous fusion."

"Supernumerary site" or "isolated ossification site"

A further enhancement intended to clarify the distinction between structural change and ossification state has been the replacement of "extra ossification site" (Version 1 term) by two separate terms, "supernumerary site" and "isolated ossification site." The former is a structure (S) term and describes an extraneous localized bone (or cartilage) "island," such as a sutural bone. The latter is an ossification (O) term, intended to describe an ossification site within the expected margins of a normal precursor of that bone but separated from the main ossified (alizarin red stained) area.

Supernumerary ribs

In Version 1, supernumerary ribs were described as "cervical rib", "full supernumerary rib" and "short supernumerary rib" and these observations were included in the main "Rib" section of the skeletal table. In Version 2, supernumerary ribs have been presented in a separate section that follows the main rib section and the terminology options have been expanded to include three categories (designated "full", "short" and "cartilaginous") for both cervical ribs and supernumerary (thoracolumbar) ribs and to accommodate the use of a new naming scheme proposed by Chernoff and Rogers [8]. In this latter publication, it was shown that both supernumerary cervical and supernumerary thoracolumbar ribs fall into two categories; these were named as "supernumerary ribs" and "ossification sites". "Supernumerary ribs" are larger (longer) structures with distal cartilage present and are likely to be permanent, ultimately remaining as distinct ribs; "ossification sites" are smaller (shorter) structures without distal cartilage and are likely to be transient, ultimately becoming part of the lateral processes of the adjacent vertebra. In accordance with this scheme, new synonyms for cervical rib are "CR" ("cervical rib", now listed for "supernumerary rib cervical full") and "COS" ("cervical ossification site", now listed for "supernumerary rib cervical short"), a new synonym for full supernumerary rib (now listed as "supernumerary rib thoracolumbar full") is "LR" ("lumbar rib") and a new synonym for short supernumerary rib (now listed as "supernumerary rib thoracolumbar short") is "LOS" ("lumbar ossification site").

Malpositioned pelvic girdle

An additional observation included in the skeletal table concerns evaluation of the position of the pelvic girdle relative to the number of prepelvic vertebrae (i.e., the number of vertebrae cranial to the point of pelvic articulation). The "expected" number of prepelvic vertebrae in all of the common rat, mouse and rabbit strains is 26. However, variations in the development of the axial skeleton can

Pre-pelvic vertebrae ^a	Rat/Mouse			Rabbit			
	Expected	Possible variations		Expected	Possible variations		
Cervical	7	7	7	7	7	7	7
Thoracic	13	14	12	12	13 ^b	13 ^b	12
Lumbar	6	6	6	7	6	7	6
Total	26	27	25	26	26	27 ^b	25

^a Also see Appendix D.

^b In the rabbit, the incidence of 13th rib and 27th pre-pelvic vertebra differs quite markedly between strains and within the same strain from different sources

Fig. 1. Typical vertebral configurations in rodents and rabbits.

lead to changes in this number (usually to 25 or 27) and occur in a proportion of control animals in all of these species.

Changes in the expected proportions of animals with different configurations in treated groups can provide a sensitive indicator of treatment effect. Typical vertebral configurations in rodents and rabbits are shown in Fig. 1.

Further considerations in animals showing variation in vertebral configuration are associated variations in the number and/or type of ribs. Typically, an increased number of prepelvic vertebrae is associated, in the same fetus, with a supernumerary rib at the thoracolumbar border and, in some cases, an increased number of "true" or "vertebrosternal" ribs (ribs with costal cartilages directly attached to the sternum) and a long costal cartilage on rib number 10 or 11. Conversely, the presence of a supernumerary cervical rib can be associated with fewer (usually 12) thoracic ribs, fewer (usually 6) vertebrosteral ribs, fewer (usually 25) prepelvic vertebrae and short costal cartilage on rib number 9 or 10.

Cartilage staining facilitates easier evaluation of costal cartilage, which allows further characterization of vertebral/rib configuration through clear identification of "true" ("vertebrosternal") ribs and "false" ribs. True ribs are upper thoracic ribs (normally numbers 1–7, associated with thoracic vertebrae 1–7) that are attached directly to the sternum. False ribs (and false floating ribs) are those that are not attached directly to the sternum. In the case of the common laboratory animals, these are normally ribs 8–13 in the rat and mouse and ribs 8–12 in the rabbit. Of these, ribs 8–9 or 10 (dependent upon species/strain) usually have long costal cartilages almost reaching the sternum and the remainder (numbers 10, or 11–12, or 13) usually have short costal cartilages.

Consistent use of long/large and short/small

The revised terminology has adopted a consistent use of the terms "long," "large," "short," and "small". Only the term "long" is actually an addition to the previous Version 1 terminology. The terms "long" and "short" have been added to describe abnormalities of those structures that clearly have a prominent length dimension. The terms "large" and "small" are included to describe changes in size but within normal proportions. As defined in Appendix A, it

is noted that in the case of describing skeletal abnormalities, these terms are meant to be used only when the abnormality involves the bone precursor. Thus care must be used to differentiate, for example, a "short" femur from an "incompletely ossified" femur.

3.4. Maternal-fetal abnormalities (Table 4)

The table of "Maternal-Fetal Abnormalities" addresses findings of the amniotic fluid, placenta, and umbilical cord. These findings were relocated from the Version 1 external and/or visceral tables, since they are technically not fetal observations. Presenting these tissues and findings in a separate table also emphasizes the importance of their evaluation.

4. Appendices of additional information

Additional information has been included in Version 2 to guide and inform the user of this glossary:

As with Version 1, commonly used terminology is defined in Appendix A: "Common Descriptive Terminology Used More Than Once in the Glossary." It permits the removal of repetitive synonyms, *related terms*, and non-preferred terms from the glossary tables; however, it also requires that the user consult Appendix A simultaneously with the tables. This appendix has been revised to accommodate the recording of cartilage observations (generally visualized in specimens that have been "double stained" with alcian blue for cartilage and alizarin red for ossified bone), which are often helpful in distinguishing changes in ossification state from alterations in structure.

No single medical dictionary has been designated as the primary source for the definitions included in Appendix A. Rather, it is recognized that there are a number of relevant and useful anatomical textbooks that may provide such information (Fig. 2).

Appendix B presents "Syndromes and Combining Terms", which includes abnormalities with multiple affected structures. Most of the syndrome terms and some of the combining terms are considered diagnostic in nature, but there might not be a better descriptive term to use in cases of multiple anomalies.

Appendix C, "Nomenclature-Alternative Terms," provides alternative names for selected structures listed in the "Observation" column. For example, "cervical vertebra 1" may be called the "atlas."

In Appendix D, "Structural Differences - Rat, Mouse, and Rabbit," visceral and skeletal structures that are different among these three species are summarized.

Appendix E presents common skeletal foramina and processes. Although a detailed description of the foramina and processes of ossified bones is generally not needed in a typical skeletal evaluation for regulatory developmental toxicity studies, there may be situations in which such detail would be valuable in characterizing a particular anomaly of development. Appendix E includes harmonized nomenclature for the description of the most commonly

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Fig. 2. Bibliography of select anatomical textbooks.

described foramina and processes. This list is intended as a technical resource and not to imply any recommendation for the routine application of such detailed description.

5. Uses and misuses of the glossary

The basic concepts and tenets addressed in Version 1 remain applicable in Version 2. General principles that should be highlighted are:

1. It is not intended that all observations presented in the extensive lists that comprise the Version 2 terminology tables and appendices should necessarily be used in the *summarization* of data. The lists are provided as a resource for the selection of appropriate terminology when characterizing individual findings that are observed. Hence, the information provided in the tables and appendices is not intended to prescribe the level of detail required for each study.
2. The provided terminology is intended to be used in describing morphological changes from an observed "normal range." Thus, some terms are relative in nature, and consistent application will rely upon the judgment and experience of the observer.
3. Ranking or classification of terms into categories, such as "malformation" and "variation" is not included in the glossary. This approach to characterization of findings is commonly used in some laboratories, but the definitions of such classification and/or grading schemes, as well as the decision to apply such schemes, are left to the discretion of the user. The focus of this harmonized terminology is description and not diagnosis/interpretation.
4. It is beyond the scope of this glossary to specify the normal number of skeletal elements expected for each skeletal region. Nevertheless, some of this information has been incorporated into the tables, and there may be reasons for a particular laboratory to report such findings when characterizing anomalies.
5. Terminology in the glossary generally reflects the most basic observational description and does not describe severity or other modifiers (e.g., relating to symmetry or degree of change), unless it is a necessary aspect of the finding. Such information might, however, be integral to characterizing certain observations and should be considered.
6. In some cases, the merging of incidence data for developmental anomalies may be an appropriate approach to summarization/analysis (in addition to compiling each individual finding separately). The circumstances under which this might be applied, and possible candidates for such merging, are outside the general scope of this paper.
7. Scientific judgment is integral to appropriate application of the information in this glossary and to interpretation of the developmental findings.

6. Future activities

In continuation of this effort on harmonized terminology, and consistent with the approach taken for version 1, questions, comments, additions, and recommendations (either specific or general) from users of this terminology document are encouraged. Input of this nature will provide a strong basis and impetus for future revisions and updates.

In Versions 1 and 2, only the commonly used laboratory mammals (i.e., rats, mice, rabbits) are addressed. Inclusion of terminology specific to other laboratory species, such as primates, has not yet been fully considered. Such an expansion of the terminology will require a continuation of the international collaborative effort and might be a logical direction for Version 3.

An additional possible enhancement to the use of this document would be the availability of illustrative images. Although the value of such a tool for use at either the bench or regulatory level has long been recognized, implementation has remained outside the scope of the current effort. It is hoped that future efforts can be directed towards linking on-line versions of the terminology document with an openly available digital database that provides relevant illustrations of specific developmental abnormalities and descriptions.

It is recognized that over time, technological advances in mammalian fetal evaluation are inevitable. This may include, for example, the increased use of imaging technologies that have become relatively commonplace in human medicine, providing a very different level of anatomical detail and even enabling temporal evaluation of fetal development through non-invasive methods. It may also entail more automated and/or efficient collection, storage, and/or analysis of fetal data. Current terminological conventions may not adequately serve the new methodologies. Thus it is recognized that this internationally harmonized terminology document may at some point require reconsideration and/or updating to accommodate important scientific advancements in the field.

Finally, the broader use of this harmonized terminology is encouraged, in order to help provide a link and enhance understanding within and across scientific disciplines. For example, the harmonized terminology could be useful in characterizing developmental anomalies associated with the phenotypic profiles of genetic variants of laboratory animal strains used in research or in providing common descriptors in constructing computationally based approaches to screening level assessments of developmental toxicology.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

Acknowledgements

This effort was supported in part by the following organizations:

- (1) International Programme on Chemical Safety (IPCS), Project on Harmonization of Approaches to the Assessment of Risk from Exposure to Chemicals, Geneva, Switzerland
- (2) Bundesinstitut für Risikobewertung (BfR), DevTox Project, Berlin, Germany

The following organizations and individuals were instrumental in providing comments on preliminary drafts of Version 2; individual affiliations listed are relevant to the time of participation and may no longer be current:

MARTA/MTA colleagues: Bruce Beyer (Sanofi-Synthelabo Research); Chris Bowman, Carol Kopp (WIL Research Laboratories, Inc.); Gary Chmielewski (Pfizer, Inc.); Doreen Curtin (Wyeth); Ali Faqi (MPI Research); Kim Hilbish (Eli Lilly & Co.); Julia Hui (Abbott Laboratories); MaryAnn Jacobs (Bristol Myers Squibb Company); Connie Johnson, Joyce Rendemonte (GlaxoSmithKline Pharmaceuticals), Robert Palmer (Hoffmann La Roche, Inc.); Elise Lewis, Raymond York (Charles River Laboratories, PA); Thomas Marks (AstraZeneca Pharmaceuticals); Cherie Qualls (Schering-Plough Research Institute); Keith Robinson (ClinTrials BioResearch, Ltd.).

UK colleagues: Stephanie Clubb (Charles River Laboratories Edinburgh, Preclinical, UK); Julian M. French (Safety Assessment UK, AstraZeneca R&D); Mary E. Moxon, Dena Goodrich, Brian Trueman (Syngenta Central Toxicology Laboratory, Macclesfield, UK)

Association Francophone pour l'étude des Anomalies de la Reproduction Et du Développement (A.F.A.R.E.D.): Paul Barrow (MDS Pharma Services, Saint-Germain-Sur-L'Arbresle, France), Annick Chevalier (Organon, Riom, France), Elisabeth Elefant (CRAT, Paris, France), Oliver Foulon (CIT, Evreux, France), Pierre Guittin (Aventis Pharma, Vitry-Sur-Seine, France), Catherine Jausseley (Bayer Cropscience, Sofia Antipolis, France), Isabelle Leconte (Sanofi-Synthélabo Recherche, Porcheville, France), François Spézia (Pfizer Goba Research and Development, Amboise, France)
Japanese colleagues: Kazuhiro Chihara (Dainippon Sumitomo Pharma Co., Ltd.); Yuko Izumi (Takeda Pharmaceutical Company Limited); Yasuko Kato (Daiichi-Sankyo Co., Ltd.); Mineo Yasuda (Hiroshima International University)

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Table 1
External abnormalities.

Region/Organ/Structure	Observation	Generalized	Synonym or Related Term	Non-preferred Term	Definition	Note	Version 1 Code No.
General	Subcutaneous edema		Anasarca		An accumulation of interstitial fluid in subcutaneous connective tissue		10001
	Conjoined twins	Localized	<i>Omphalosite</i>		Localized accumulation of fluid		10005
	Fetus or pup/neonate	Discolored	<i>Skin discolored</i>		Monozygotic twins with variable incomplete separation into two during cleavage or early stages of embryogenesis	Site and extent of fusion should be described	10002
		Large Pale			Generalized or localized region of abnormal color (other than pale)	See also "General – Fetus or pup/neonate Pale" and "Skin – discolored"	New
	Subcutaneous hemorrhage	Small	Runt Petechia, Purpura, Ecchymosis, Hematoma		Generalized absence of color when compared to a normal specimen	Relative to normal	New
	Skin	Absent	Cutis aplasia, <i>Adermia</i>		An accumulation of extravasated blood beneath the skin	Relative to normal	New 10004
		Discolored			Localized region of no skin development		10003
		Lesion			Localized region of abnormal color	See also "General – Fetus or pup/neonate Discolored"	New
Head/neck	Acephalostomia	Tag	Cutis lesion		Localized region of abnormal skin		New
	Anencephaly			Acrania	Small appendage of skin		10008
	Cranial meningocele			Acrania	Absence of head but with the presence of mouth-like orifice in the neck region		10010
	Cranioschisis				Absence of the cranial region of the head, with the brain absent or reduced		10016
	Exencephaly				Herniation of meninges through a defect in skull		10011
	External aural fistula			Acrania	Fissure of the cranial region of the head with varying degrees of the brain exposed		10013
					Brain protrudes outside the skull due to absence of all or part of the cranial vault	Erosion of brain tissue has not occurred as in anencephaly	New
	Head	Absent Domed	Acephaly		An opening to a cyst produced by a persistent lateral cervical sinus or reduplicated 1st pharyngeal cleft usually located ventral to the ear		10009 10012
		Large	Macrocephaly		Absence of the head	May or may not be associated with hydrocephaly	10015
		Missshapen			Cranial region of head appears more elevated and rounded than normal		New
					Disproportionately large head		

Table 1 (Continued)

Region/Organ/Structure Head/neck Cont.	Observation	Small	Synonym or Related Term	Non-preferred Term	Definition	Note	Version 1 Code No.
Ear	Iniencephaly		Leptocephaly, Microcephaly, Nanocephaly		Disproportionately small head		10018
	Meningo-encephalocele		Encephalomeningocele	Cephalocele, Craniocoele, Encephalocele	Exposure of occipital brain and upper spinal cord tissue; involves extreme retroflexion of the head	May or may not be covered by skin	10014
	Meningohydro-encephalocele				Herniation of brain and meninges through a cranial opening		10017
	Narrow head		Craniostenosis		Herniation of brain, cerebral ventricle, and meninges through a defect in skull		New
	Pinna	Absent Fused	Anotia Synotia		Absence of external ear		10406
		Large	Long pinna, Macrotia		Fusion or abnormal approximation of pinnae below the face		10019 10024
		Malpositioned Missshapen Small	Low set pinna Microtia, Short pinna	Ear tab	Disproportionately large external ear		10020
	Cryptophthalmia		Cryptophthalmos		Disproportionately small external ear	May be associated with micro- or anophthalmia	10021 10023 10022
	Cyclopia		Monophthalmia, Single eyeball, Synophthalmia		Skin continuous over eye(s) without formation of eyelid(s)		10026
	Eye	Malpositioned Open Protruding	Exophthalmos, Exophthalmia, Proptosis	Ablepharia Pop-eye	Single median orbit; eyeball(s) can be absent, completely or incompletely fused	Snout may be absent or appear as a frontonasal appendage (proboscis) above the orbit	10030 10033 10029
Eye	Eye bulge	Absent					10025
		Large					10028
		Small					10035
	Eyelid	Fissure	Palpebral coloboma		A notch or fissure of the eyelid		10034
		Short	Microblepharia		Short vertical dimension of eyelid		10031
	Face	Cleft	Prosopochisis		Fissure of the face		10036
	Jaw, lower (Mandible)	Absent	Agnathia				10047
	Jaw, lower (Mandible)	Large	Gnathochisis, Split mandible Mandibular macrognathia, Long lower jaw, Protruding lower jaw, Prognathia	Exognathia	Excessive protrusion of the eyeball	Check for abnormalities of eye prior to opening of the eyelid	10056 10057
		Small	Brachygnathia, Micromandible, Short lower jaw			May be associated with macrophthalmia	10035
	Jaw, upper (Maxilla)	Cleft	Gnathochisis, Split maxilla	Exognathia		May be associated with microphthalmia	10034
Face	Jaw, upper (Maxilla)	Large	Maxillary macrognathia, Long upper jaw, Protruding upper jaw, Prognathia				10058
		Small	Micromaxilla, Short upper jaw				New
	Lip	Cleft	Maxillary micrognathia				10059
	Mouth	Absent	Micromaxilla, Short upper jaw				10060
		Large	Chelioschisis	Harelip	Fissure of the upper lip		10051 10050 10055
		Missshapen	Macrostomia, Wide mouth				New

Table 1 (Continued)

Region/Organ/Structure	Observation	Synonym or Related Term	Non-preferred Term	Definition	Note	Version 1 Code No.	
Face Cont.	Naris	Small				10062	
		Absent	Microstomia			10042	
	Palate	Fused	Atretic				New
		Malpositioned					10039
		Single	Mononaris				10044
		Small					New
		Cleft	Palatoschisis, Uranoschisis		Fissure of the palate		10052
		High-arched			Roof of mouth higher than normal		10053
	Palatal rugae	Absent			Absence of one or more rugae		New
		Interrupted					New
Papillae	Misaligned	Asymmetrically aligned				10063	
		palatal rugae, Irregular					
	Missshapen	palatal rugae					10064
		Bifurcated palatal rugae,					
		Discontinuous palatal rugae,					
		Interrupted palatal rugae,					
	Short palatal rugae						
	Supernumerary						
		Absent			Dermal projections, generally associated with whiskers		New
	Proboscis	Fused					New
Malpositioned				Tubular projection replaces the snout		New	
Snout	Absent					10038	
	Large	Arhinia				10037	
Tongue	Malpositioned	Long				10040	
	Misshapen					10041	
	Small	Short				10045	
	Absent	Aglossia			May be generalized or localized; location and description should be provided	10046	
Altered surface texture						New	
Tongue, frenulum	Large	Macroglossia, Long tongue				10054	
	Misshapen					New	
	Protruding					10065	
	Small	Microglossia, Short tongue				10061	
Tooth	Split		Forked tongue			New	
	Fused to floor of mouth	Ankyloglossia	Tongue-tie	Shortness or absence of the frenulum of the tongue; tongue fused to the floor of the mouth	May be protruding	10048	
Tooth	Absent	Anodontia, Edentia		Absence of one or more teeth		10049	
	Asymmetric					New	
	Bent					New	
	Discolored					New	
	Erupted					New	
	Fused					New	
	Large	Long tooth				New	
	Malpositioned					New	
Whiskers	Not erupted					New	
	Small	Short tooth				New	
Limb (fore- or hind-)	Absent		Ectromelia	Absence or shortening of the distal segment(s) of limb	May be further characterized, at skeletal examination, e.g., as being fibular, radial, tibial, or ulnar	10068	
				Complete absence of one or more limbs	Fleshy tab may be present	10066	

Table 1 (Continued)

Region/Organ/Structure	Observation	Phocomelia	Bent	Fused	Hyperextension	Synonym or Related Term	Non-preferred Term	Definition	Note	Version I Code No.
Limb (fore- or hind-) Cont.						<i>Symmetria</i>		The excessive extension or straightening of a limb or a joint	Limb cannot be flexed, joint can be specified	10067 10075 10069
						Flexed limb	Arthrogyposis	The excessive flexion or bending of a limb or a joint	Limb cannot be straightened, joint can be specified	10070
						Macromelia, Long limb		Limb turned toward the center (i.e., inward rotation) or the periphery (i.e., outward rotation)		10071 10072
						<i>Brachymelia</i> , <i>Micromelia</i> , <i>Nanomelia</i> , <i>Storl limb</i> , <i>Ectromelia</i>	<i>Acromelia</i>	Reduction or absence of proximal portion of limb, with the paws being attached to the trunk of the body		10073
						<i>Adactyly</i>		Absence of all digits	See Digit, few (Ectrodactyly) for absence of some but not all digits	10077
						Ectrodactyly, Oligodactyly		Absence of one or more, but not all, digit(s)	Expected skeletal alterations include absence of all phalanges in each affected digit	10080
						Ankylodactyly, Syndactyly, Webbed digits, Dactylo-megaly, Long digit, Macroductyly		Partial or complete fusion of, or webbing between, digits	Includes bony, cartilaginous, and/or soft tissue	10091
						Clinodactyly, Camptodactyly		Deflection of digit(s) from the central axis		10081
						<i>Brachydactyly</i> , <i>Microductyly</i> , <i>Short digit</i>		Digit attached by a thread of tissue	Includes fixed flexion deformity of digit(s). Confirmed by skeletal examination to exclude the possibility of artifact	10083
						Polydactyly				10085 New
						<i>Acheiria</i> , <i>Acheiro-podia</i> , <i>Apodia</i> , <i>Symphodia</i>			Expected skeletal alterations include absence or shortening of phalanx(es)	10079
							Clubbed paw, Talipes	Paw turned toward the center (i.e., inward) or the periphery (i.e., outward)	Can be pendulous	10088
								The excessive extension or straightening of a paw	Refers to distal-most tip, nail	10076
								The excessive flexion or bending of a paw	Refers to distal-most tip, nail	10082
									Refers to distal-most tip, nail	10089
										10078
									Refers to hind paws in bipeds	10092
										10084
									Carpus or tarsus cannot be flexed	10086
									Carpus or tarsus cannot be straightened	10087
										10090
										10093
										10094
										10097
										10095
Tail						<i>Acaudia</i> , <i>Anury</i> , <i>Angulated tail</i> , <i>Branched tail</i> , <i>Double-tipped tail</i> , <i>Forked tail</i>		Shaped like an angle Tail divided or split		
								Rounded or flat at the end, not tapered		

Table 1 (Continued)

Region/Organ/Structure	Observation	Synonym or Related Term	Non-preferred Term	Definition	Note	Version 1 Code No.
Tail Cont.		Curly tail		Curved into nearly a full circle, or coiled		10096
	Curled			Generalized or localized discoloration of tail		New
	Discolored			Small tag of tissue at tip of tail		10098
	Fleshy tab			Approximately 180 degree bend or curve of the tail		10099
	Hooked			Localized undulation(s) of the tail		10100
	Kinked					New
	Long					10101
	Malpositioned					New
	Misshapen					10102
	Narrow		Ring tail		Should be specified as entire length or localized	10103
	Small	Constricted tail			Should be specified as entire length or localized	10104
	Thread-like	Brachyury, Short tail			May be associated with absent/threadlike tail	10105
Trunk	Anus	Filamentous tail, Filiform tail		Absence or closure of the anal opening		New
	Absent	Anal atresia, Aproctia, Imperforate anus, Non-patent anus				10118
	Large					10107
	Small					10112
	Decreased			Shortened distance between anus and genital tubercle	AGD is sexually dimorphic	New
Anogenital distance (AGD)	Increased			Increased distance between anus and genital tubercle	AGD is sexually dimorphic	10109
Distended abdomen				Abdomen appears larger than normal	May be due to presence of fluid in abdomen or enlarged organs	New
Externalized heart		Ectopia cordis		Heart displaced outside thoracic cavity		10108
Gastrochisis		Laparochisis, Schistocelia		Fissure of abdominal wall, not involving the umbilicus, and usually accompanied by protrusion of viscera which may or may not be covered by a membranous sac	May be further defined as medial (gastrochisis) or lateral fissure (laparochisis)	10109
Genital tubercle	Absent					10106
	Large					New
	Misshapen					New
	Small					10119
Holorachischisis				Fissure of the entire spinal column		10110
Hypospadias				Urethra opening on the underside of the penis or on the perineum	Not readily apparent in fetuses or soon after birth	10111
Kyphosis			Humpback, Hunchback	Increased dorsal convexity in the curvature of the spinal column as viewed from the side		10113
Large intestine	Prolapsed			Protrusion of large intestine through anus	May be associated with large anus	New
Lordosis			Hollowback, Swayback, Saddleback	Increased dorsal concavity in the curvature of the spinal column as viewed from the side		10114

Table 1 (Continued)

Region/Organ/Structure	Observation	Synonym or Related Term	Non-preferred Term	Definition	Note	Version 1 Code No.
Trunk Cont						
	Omphalocele	Exomphalos	Umbilical hernia	A defect in the abdominal wall at the umbilicus, through which the intestines and other viscera protrude. These may or may not be covered by a thin, translucent sac.		10115
	Pelvic region			Hindlimbs located more medially than normal		New
	Scoliosis			Lateral curvature of the spinal column		10116
	Spina bifida	Spinal meningocele, Spinal myelomeningocele, Spinal myelomeningocele, Rachischisis		A family of defects in the closure of the spinal column	May be covered with skin (spina bifida occulta) or not covered with skin (spina bifida aperta); may involve protrusion of spinal cord and/or meninges	10120
	Thoracogastroschisis	Thoracoceloschisis		Fissure of thoracic and abdominal walls with thoracic and abdominal viscera, or major parts thereof, exposed ventrally		10121
	Thoracoschisis			Fissure of thoracic wall	Thoracic viscera may be exposed	10122
	Thorax	Thoracostenosis		Narrowness of the thoracic region		10123
	Trunk	Long trunk Short trunk				10117 10124
	Umbilicus		Omphalocele	Protrusion of a skin-covered segment of the gastrointestinal tract and/or greater omentum through a defect in the abdominal wall at the umbilicus; the herniated mass being circumscribed and covered with skin; or protrusion of skin-covered viscera through the umbilical ring with prominence of the navel		New

Table 2
Visceral abnormalities.

Region/organ/structure	Observation	Synonym or related term	Non-preferred Term	Definition	Note	Version 1 code no.
General	Abdomen	Ascites in abdomen, Hemorrhagic ascites in abdomen, Intra-abdominal hemorrhage, Red fluid in abdomen		Effusion and accumulation of red fluid or ascites (watery fluid) in abdomen	Nature of fluid (color, thickness) should be specified	New 10126
	Abdominal wall				Location and description should be provided	New
	Aneurysm			Localized sac formed by dilatation of an artery or vein that is filled with blood	Location and size should be defined	New
	Situs inversus			Mirror-image transposition of the abdominal viscera	May be generalized or localized	10125
	Thoracic wall			Mirror-image transposition of the thoracic viscera		New
	Thorax			Mirror-image transposition of the abdominal and thoracic viscera		New
	Thorax	Fluid in thorax, Hemorrhagic fluid in thorax, Intra-thoracic hemorrhage, Red fluid in thorax		Effusion and accumulation of red fluid or watery fluid in thorax	Location and size should be defined	New
Brain	Brain	Cyst		Appears as discrete 'hole' in fixed brain tissue; may appear as a fluid-filled cyst in fresh brain tissue	Location and description should be provided	New
	Cerebellar lobe				May be due to processing artifact in fixed tissue	New
	Cerebellum	Large Misshapen Small Absent			May be further defined as specific structure (e.g., flocculus, paraflocculus)	New
	Cerebellum	Discolored			May be generalized or localized	New
	Cerebellum	Large Small			May be generalized or localized	New
	Cerebellum	Discolored			May be generalized or localized	New
	Cerebral hemisphere	Large Misshapen Small				New
	Cerebrum	Large Small Discolored				10132 10134 New
	Cerebrum	Large Misshapen Small			May be generalized or localized	New
	Fourth ventricle	Large Misshapen Small Dilated			May be generalized or localized	New
	Fourth ventricle	Internal hydrocephaly (10131), Large fourth ventricle			See also Ventricles, dilated	New 10133 10135 New

Table 2 (Continued)

Region/organ/structure	Observation	Red material	Synonym or related term	Non-preferred Term	Definition	Note	Version 1 code no.
Brain Cont.	Lateral ventricle	Red material Dilated	Hemorrhagic Dilated cerebral ventricle. Internal hydrocephaly (10131). Large lateral ventricle			Involvement of anterior portion of lateral ventricle, within olfactory lobe, may also be noted. See also Ventricles, dilated	New 10128
	Olfactory lobe	Red material Absent	Hemorrhagic			To be used when laterality of absent lobe cannot be determined	New New
	Perimeningeal space	Large Single Small Large	External hydrocephaly (10131)		Increase in space between brain and skull	May be due to processing artifact	New New New New
	Pineal gland	Red material Large Small Absent Discolored	Hemorrhagic. Subdural hemorrhage		Blood between brain and skull	Not to be confused with blood within dural sinus	New New New New
	Pituitary gland	Large Malpositioned Misshapen Small Dilated				May be generalized or localized	New New New New
	Third ventricle	Dilated	Internal hydrocephaly (10131). Large third ventricle			See also Ventricles, dilated	New
	Ventricles	Dilated	Internal hydrocephaly (10131). Large ventricles			See also separate observations for dilated lateral, third, and fourth ventricles	New New New
	Spinal cord	Red material Absent Discolored	Hemorrhagic Interrupted			May be generalized or localized	New New New
		Double	Duplicated			May be generalized or localized; may be due to processing artifact	New
		Interrupted Large Narrow Short Discolored				May be generalized or localized	New New New New New
Ear	Inner ear	Malpositioned Misshapen Red material Small Discolored	Hemorrhagic			May be generalized or localized	New 10136 New New New
	Inner/middle ear	Malpositioned Misshapen				May be generalized or localized; use of "inner/middle ear" is appropriate if location cannot be definitively established	New New

Table 2 (Continued)

Region/organ/structure	Observation	Synonym or related term	Non-preferred Term	Definition	Note	Version 1 code no.
Ear Cont.	Middle ear	Red material				New
		Discolored	<i>Hemorrhagic</i>		May be generalized or localized	New
Eye	Aqueous chamber/humor	Malpositioned				New
		Misshapen	<i>Hemorrhagic</i>			New
	Red material				New	
	Small				New	
	Absent				New	
	Discolored				New	
	Large				New	
	Small				New	
	Opacity	Eye surface opacity		Cornea appears opaque, or, if in section, may be thickened. Opacity can be complete or focal	if seen at fresh examination, on surface of eye, may be called 'surface opacity' since location cannot be definitive	10137
	Eye		Anophthalmia		May be generalized or localized; may be further defined by location, e.g., aqueous chamber, vitreous chamber	New
Lens	Large	Macrophthalmia, Megalophthalmia (-mos)		Large eye, eyeball		10141
		Small				10142
	Malpositioned					10143
	Absent					10138
	Adhered to cornea					New
	Altered texture					New
	Discolored					New
	Double					New
	Large					New
	Misshapen					New
Opacity					New	
Optic nerve	Small					10144
	Absent					10139
Retina	Fissure					10147
	Fold					New
	Cataract, Eye internal opacity	Duplicated				10145
						10145
	Opacity of the crystalline lens					10145
	Coloboma, Interrupted, Split					10145
	Coloboma, Interrupted, Split					10145
	Coloboma, Interrupted, Split					10145
	Coloboma, Interrupted, Split					10145
	Coloboma, Interrupted, Split					10145
	Coloboma, Interrupted, Split					10145
	Coloboma, Interrupted, Split					10145
Coloboma, Interrupted, Split					10145	

Table 2 (Continued)

Region/organ/structure	Observation	Synonym or related term	Non-preferred term	Definition	Note	Version 1 code no.	
Eye Cont.	Vitreous chamber/humor (body)	Absent				New	
		Discolored					
		Large				May be generalized or localized	New
		Small					New
		Discolored					New
		Large					New
		Missshapen					New
		Small					10150
		Fused					New
		Large					10153
		Malpositioned					10148
		Missshapen					New
		Small					10151
Mouth	Gum (Periodontium) Nasal cavity Nasal conchae	Small				New	
		Absent				10154	
		Malpositioned				10149	
		Missshapen				10152	
		Not fused with palate	Bent				New
		Small					New
		Atretic					10155
		Interrupted					New
		Dilated	Large				New
		Missshapen					New
		Narrow					New
		Atretic					New
		Absent	Choanal atresia				10156
Discolored					New		
Thyroid gland	Posterior naris Thyroid gland	Large				New	
		Malpositioned				10157	
		Missshapen				New	
		Small				New	
		Supernumerary lobe				New	
		Absent					New
		Discolored					10156
		Large					New
		Malpositioned					New
		Missshapen					New
		Small					New
		Supernumerary lobe					New
		Thymus	Thymic cord Thymus	Partially undescended horn of thymus			
Absent						10158	
Discolored						New	
Fragmented							New
Large							New
Malpositioned							10160
Missshapen							10161
Small							10162
Split							10163
Supernumerary							10164
Absent							10165
Large							10177
Missshapen							10189
Small					10195		
Heart	Aortic valve	Multiple small fragments				New	
		Reduced size or remnant of thymus				New	
		Includes alterations in number of cusps				New	
		Includes reduced number of convolutions				New	
		Includes alterations in number of cusps				New	
		Includes alterations in number of cusps				New	
		Includes alterations in number of cusps				New	
		Includes alterations in number of cusps				New	
		Includes alterations in number of cusps				New	
		Includes alterations in number of cusps				New	
		Includes alterations in number of cusps				New	
		Includes alterations in number of cusps				New	
		Includes alterations in number of cusps				New	

Table 2 (Continued)

Region/organ/structure	Observation	Defect	Synonym or related term	Non-preferred term	Definition	Note	Version 1 code no.
Heart Cont.	Atrial septum				Postnatal communication between atria; includes defects of septa primum and secundum	Not to be confused with the foramen ovale which normally remains open until birth	10171
Atrium	Malpositioned Misshapen Large Small Persistent		Distended With no blood inside				New New New New 10194
A-V canal					Defects of endocardial cushions resulting in low atrial and high ventricular septal defects	A-V = atrioventricular	10179
A-V ostium	Dilated				Enlargement of an atrioventricular orifice	A-V = atrioventricular	10175
A-V septum	Defect				Inappropriate communication between atrium and ventricle		10166 New
Chordae tendinae	Absent	Premature closure				Foramen ovale is normally open in fetuses	New 10172 10186
Foramen ovale	Absent		Acardia Cardiomegaly Dextrocardia (right-sided heart)			Levocardia (left-sided heart) is abnormal only in situs inversus; right-sided heart, previous code # 10176	New 10188 10174
Heart	Large Malpositioned						10173
	Misshapen Small Three-chambered		Microcardia Cor trilobulare		Three-chambered heart with two atria and a ventricle or one atrium and two ventricles		
	Two-chambered		Cor bilobulare		Two-chambered heart with an atrium and a ventricle		
Left A-V valve	Absent Large Misshapen Small					A-V = atrioventricular, also known as bicuspid/mitral	10167
						A-V = atrioventricular, also known as bicuspid/mitral	10180
						A-V = atrioventricular, also known as bicuspid/mitral	10190
						A-V = atrioventricular, also known as bicuspid/mitral	10196
Papillary muscle Pericardium	Absent Blood-filled Fluid-filled		Intrapericardial hemorrhage Hydropericardium; pericardial effusion		Accumulation of fluid in the sac that envelops the heart		10168 New 10185
Pulmonary valve	Absent Large Misshapen					Includes alterations in number of cusps	10169 10181 10191
Right A-V valve	Small Absent Large Misshapen					A-V = atrioventricular, also known as tricuspid	10197 10170
						A-V = atrioventricular	10182
						A-V = atrioventricular, also known as tricuspid. Includes alterations in number of cusps	10192

Table 2 (Continued)

Region/organ/structure	Observation	Synonym or related term	Non-preferred Term	Definition	Note	Version 1 code no.
Heart Cont.	Ventricle	Small			A-V = atrioventricular; also known as tricuspid	10198
		Double outlet		Pulmonary trunk and aorta arise from same ventricle	Usually associated with right ventricle	New
		Large			See Ventricular chamber and Ventricular wall; only to be used when heart has not been cut for examination	New
		Small			See ventricular chamber and ventricular wall; only to be used when heart has not been cut for examination	New
	Ventricular chamber	Large				10183
	Ventricular septum	Small				10199
		Defect	<i>Incomplete VS, Membranous VSD, Muscular VSD, Perimembranous VSD</i>	An opening in the membranous and/or muscular septum between the ventricles	If known, membranous or muscular region may be defined (see 10187, 10193)	New
		Depression	<i>Diverticulum</i>	A non-patent localized recess in the membranous and muscular septum between the ventricles		New
	Ventricular wall	Misshapen				New
		Thick				10184
		Thin				New
	Aorta	Absent				New
		Atretic	<i>Thread-like</i>	Absence of patent communication between the ascending aorta and the ventricular mass which is usually grossly hypoplastic	May be total or partial	10200
		Dilated			May be generalized or localized	10201
		Double			See also Aorta origin, malpositioned	10202
		Malpositioned			May be generalized or localized	10203
		Narrow				10204
		Overriding				10205
	Aorta origin	Diverticulum		Biventricular origin of aorta		New
		Malpositioned	<i>Aneurism</i>	Outlet from heart displaced	See also Aorta, malpositioned	New
	Aortic arch	Absent				New
		Atretic			May be total or partial	10206
		Dilated	<i>Thread-like</i>		May be generalized or localized	10207
		Double				New
		High-arched		Aortic arch extends further upwards into neck		New
		Interrupted		Ascending aorta not connected to descending aorta		10208
		Malpositioned	<i>High-arched</i>		Use of related term 'high-arched' is recommended when arch extends further into neck	New
		Narrow			May be generalized or localized	10209

Table 2 (Continued)

Region/organ/structure	Observation	Synonym or related term	Non-preferred Term	Definition	Note	Version 1 code no.
Aortic arch Cont.						
		Retrosophageal				
Artery	Artery	Right-sided Supernumerary branch Supernumerary	Transposed Supernumerary artery	Additional artery arising from aortic arch	Aortic arch usually passes behind trachea as well as esophagus	10210 10211 New New
Carotid artery	Carotid [may be further defined as common carotid, external, or internal]	Absent Branching variation Dilated Malpositioned Narrow Retrosophageal Supernumerary branch Malpositioned		Variation in the arrangement of arteries arising from carotid artery	General term for use if identity cannot be determined	New 10212 New 10213 10214 10215 10216 New New
Ductus arteriosus	Ductus arteriosus	Absent Atritic Dilated Malpositioned Narrow Patent Right-sided Malpositioned	Thread-like	Additional artery arising from carotid artery Origin (from aortic arch or innominate artery) of Carotid artery, malpositioned	May be further specified by location (position/laterality of branches) May be generalized or localized See also Carotid artery origin, malpositioned May be generalized or localized Artery may pass behind trachea as well as esophagus	10217 New 10218 10219 10220 10221 New New
Great vessels		Fused vessel walls Transposition Defect	Persistent Transposed Not separated	Open and unobstructed Ductus arteriosus Outlet (to aorta) from Ductus arteriosus, malpositioned	See also Carotid artery, malpositioned. Includes carotid originating from aortic arch (i.e., absent innominate artery or common carotid trunk)	New 10224 10222
Innominate artery	Innominate artery (also known as brachiocephalic trunk)	Persistent Absent Dilated Long	Fistula, Confluence Truncus arteriosus communis	Origin of aorta from right ventricle and pulmonary trunk from left ventricle Communication between ascending aorta and pulmonary trunk A common aortic and pulmonary trunk	See also Ductus arteriosus, malpositioned	10223 New 10225 10226

Table 2 (Continued)

Region/organ/structure	Observation	Synonym or related term	Non-preferred term	Definition	Note	Version 1 code no.
Innominate artery Cont.						
		Malpositioned			See also Innominate artery origin, malpositioned	10227
		Narrow				10228
		Short				10229
		Supernumerary branch	Supernumerary artery	Additional artery arising from innominate artery	May be more than one	New
	Innominate artery origin	Malpositioned		Origin (from aortic arch) of innominate artery, malpositioned	See also Innominate artery, malpositioned	New
	Common carotid trunk	Absent		Common trunk that divides into the innominate and left common carotid arteries	Common carotid trunk is often present in rabbits, but there is no similar structure in normal rats (see Appendix D for species differences)	New
		Dilated				New
		Long				New
		Malpositioned			See also Common carotid trunk origin, malpositioned	New
		Narrow			Abnormality in rats and mice (see Appendix D for species differences) See also Common carotid artery origin, malpositioned	New
		Present				New
		Short				New
		Supernumerary branch	Supernumerary artery	Additional artery arising from common carotid trunk		New
	Common carotid trunk origin	Malpositioned		Origin (from aortic arch) of common carotid trunk, malpositioned	See also Common carotid trunk, malpositioned	New
	Pulmonary artery	Absent				New
		Atretic				New
		Common origin		Common origin of two arteries from pulmonary trunk		New
		Dilated				New
		Malpositioned branch				10230
		Narrow				New
		Malpositioned				New
	Pulmonary artery origin			Origin (from pulmonary trunk) of left/right pulmonary artery, malpositioned		New
		Absent			May be total or partial	New
		Atretic				10233
		Dilated				10231
		Malpositioned			See also Pulmonary trunk origin, malpositioned	New
		Narrow				10232
		Retrosophageal			Pulmonary trunk may pass behind trachea as well as esophagus	10234
	Pulmonary trunk	Right-sided				10235
		Short				New
		Diverticulum				New
		Malpositioned				New
	Pulmonary trunk origin		Aneurism			10236
		Absent		Outlet from heart displaced	See also Pulmonary trunk, malpositioned	New
		Branching variation		Variation in the arrangement of arteries arising from subclavian artery	May be further specified by location (position/laterality of branches)	New
Subclavian artery	Subclavian artery					

Table 2 (Continued)

Region/organ/structure	Observation	Synonym or related term	Non-preferred term	Definition	Note	Version 1 code no.	
Subclavian artery Cont.	Dilated	Malpositioned			See also Subclavian artery origin, malpositioned	10237	
		Narrow			Subclavian artery may pass behind trachea as well as esophagus	10238	
	Subclavian artery origin	Supernumerary	Supernumerary branch	Supernumerary artery			10239
		Malpositioned			Additional artery arising from subclavian artery. Origin (from aortic arch or innominate artery) of subclavian artery, malpositioned	10240	
Umbilical artery	Umbilical artery	Absent			See Appendix D for species differences	New	
		Bilateral			Normal in rabbits; see Appendix D for species differences	New	
	Cartilage rings	Malpositioned			See Appendix D for species differences	New	
		Transposed	Left-sided			New	
	Trachea	Cartilage rings	Absent			Seen in fixed fetuses; may be artifact	New
			Branched				New
		Fused				New	
		Indistinct				New	
		Trachea	Interrupted				New
			Misaligned				New
Tracheoesophageal fistula	Trachea	Reduced number			May be total or partial	New	
		Absent			May be generalized or localized	New	
	Atretic			May be generalized or localized	New		
	Collapsed lumen	Flat		May be an artifact	New		
Esophagus	Tracheoesophageal fistula	Dilated				10241	
		Diverticulum				10242	
	Esophagus	Fluid or other abnormal material			Communication between esophageal and tracheal lumen		
		Malpositioned					
	Esophagus	Narrow					
		Absent					
	Esophagus	Atretic					
		Dilated					
	Esophagus	Diverticulum	Fluid or other abnormal material			May be total or partial	10244
			Malpositioned			May be generalized or localized	10245
Esophagus	Narrow	Malpositioned			May be an artifact	10246	
		Narrow			May be generalized or localized	10247	
Esophagus	Narrow	Malpositioned			May be generalized or localized	10248	
		Narrow				10248	

Table 2 (Continued)

Region/organ/structure	Observation	Synonym or related term	Non-preferred Term	Definition	Note	Version 1 code no.	
Lung	Lung	Abnormal lobation		Global term for any abnormality	See Appendix D for species differences Further details of lobe(s) affected and change(s) observed may be specified in text It is recommended that this global term is not used if individual lobes are routinely described in the laboratory	10249	
		Absent	Apulmonism		May be generalized or localized.	10250	
		Discolored	Infarct		Color and affected lobe(s) should be specified. 'infarct' to be used only if confirmed histologically	10252	
		Large				10253	
		Malpositioned				10256	
		Misshapen				10257	
		Small				10259	
		Unexpanded	Atelectasis		Incomplete expansion of lung; may be due to collapse of pulmonary alveoli at birth	10251	
		Absent				New	
		Lobe [Affected lobe(s) should be specified; see also lung, abnormal lobation]				New	
Vein	Anterior (cranial) vena cava	Absent fissure		Fluid-filled sac	May be generalized or localized. Color should be specified. 'infarct' to be used only if confirmed histologically	New	
		Cyst	Infarct			New	
		Discolored				New	
		Fused	Not separated			New	
		Large				New	
		Malpositioned				New	
		Misshapen				New	
		Small				New	
		Supernumerary				New	
		Supernumerary fissure				10260	
Vein	Anterior (cranial) vena cava	Unexpanded		Incomplete expansion of lung lobe due to collapse of pulmonary alveoli at birth	May be generalized or localized to specific lobe(s)	New	
		Absent	Atelectasis			New	
		Dilated				10261	
		Interrupted				10264	
		Malpositioned				10266	
		Narrow				10270	
		Absent				10262	
		Bilateral	Supernumerary, Persistent		Azygos veins on both sides	See Appendix D for species differences. Indicate left or right, as appropriate	10272
		Malpositioned				Not to be used as alternative to 10273	New
		Persisting into abdomen				Transposed azygos vein	New
Transposed	Right-sided, Left-sided		Azygos vein on opposite side from normal for species	See Appendix D for species differences	10273		