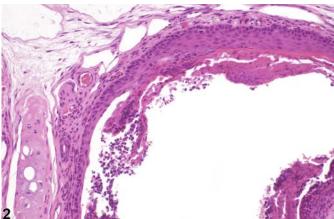
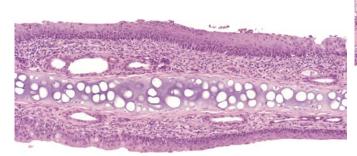
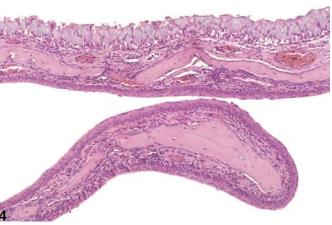


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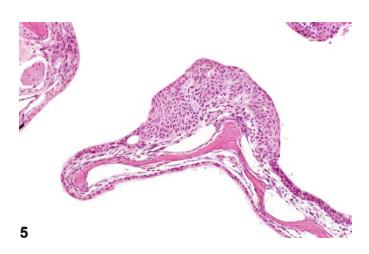








3







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Figure Legend: Figure 1 Nose, Respiratory epithelium - Metaplasia, Squamous in a male F344/N rat from a chronic study. The normal respiratory epithelium of the nasal septum has been replaced by squamous epithelium. Figure 2 Nose, Respiratory epithelium - Metaplasia, Squamous in a female B6C3F1/N mouse from a chronic study. The nasal mucosa has been replaced by keratinized squamous epithelium. Image provided courtesy of Dr. R. Miller. Figure 3 Nose, Respiratory epithelium - Metaplasia, Squamous in a male F344/N rat rom a chronic study. A thickened layer of squamous epithelium lines both sides of the nasal septum. Figure 4 Nose, Respiratory epithelium - Metaplasia, Squamous in a male F344/N rat from a chronic study. The respiratory epithelium on the turbinate and the transitional epithelium on the tip of the turbinate have been replaced by squamous epithelium.

Figure 5 Nose, Respiratory epithelium - Metaplasia, Squamous in a female B6C3F1/N mouse from a chronic study. A focal proliferation of squamous cells is present on a nasal turbinate.

Comment: Squamous metaplasia (Figure 1, Figure 2, Figure 3, Figure 4, and Figure 5) is defined as the replacement of transitional, respiratory, or olfactory epithelium by squamous epithelium. It is rarely seen in control animals but is relatively common in inhalation studies of irritants. Early changes include disorganization of the epithelial cells, with the superficial cells becoming oriented horizontally with respect to the basal lamina. This lesion must be differentiated from regeneration, which is typically 1 or 2 cell layers thick. However, in the transitional epithelium, which normally has only 2 or 3 cellular layers, this distinction can be difficult. The change in polarity of the superficial cells in the transitional epithelium may be the only indication of squamous metaplasia. In severe lesions, the metaplastic epithelium may be quite thickened, and there may be rete peg formation or keratinization. The metaplastic change can affect the ducts of subepithelial glands or the nasolacrimal ducts. Squamous metaplasia is considered an adaptive change, since squamous epithelium is more resistant to injury than are the other epithelial types. The metaplastic epithelium may contain areas of atypia, which may be preneoplastic. With cessation of exposure, squamous metaplasia may be reversible, but in chronic studies, depending on the nature of the test article, squamous metaplasia may give rise to squamous cell papilloma or squamous cell carcinoma.

Recommendation: Squamous metaplasia of the nasal epithelium should be diagnosed whenever present and assigned a severity grade. The affected epithelium should be included in the diagnosis as





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site modifier. Other lesions, such as inflammation, should be diagnosed separately when warranted by severity. If present, Bowman's gland dilation and olfactory nerve atrophy should be described in the narrative, unless the lesion is prominent enough to warrant a separate diagnosis (see Nose, Olfactory epithelium, Glands – Metaplasia). Keratinization may be a component of squamous metaplasia and need not be diagnosed separately; however, it should be described in the narrative. Metaplastic squamous epithelium may contain features of hyperplasia relative to unaffected squamous epithelium (e.g., thickening, rete peg formation), and these features should also be described in the narrative. If features of atypia are present, it should be should be diagnosed by adding the modifier, "atypical."

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