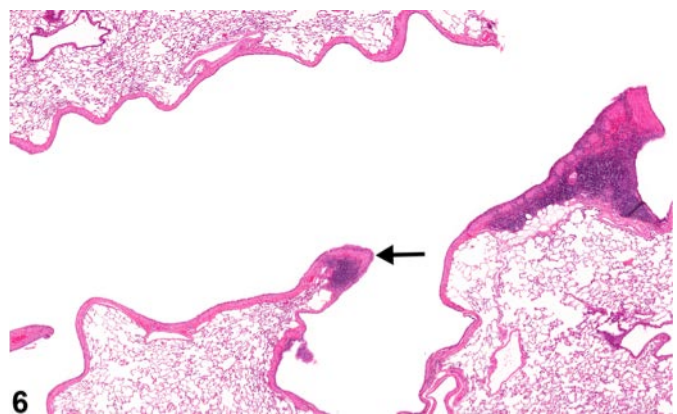
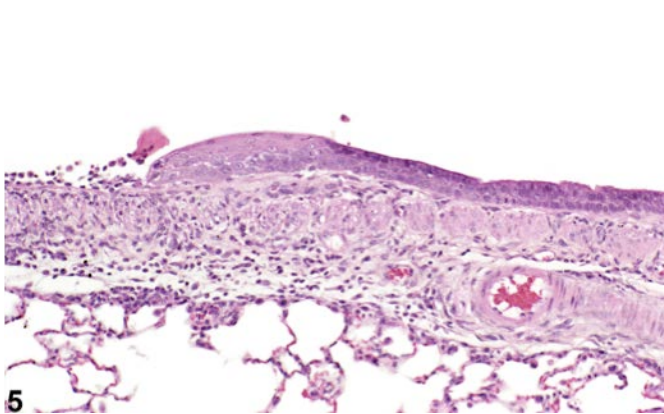
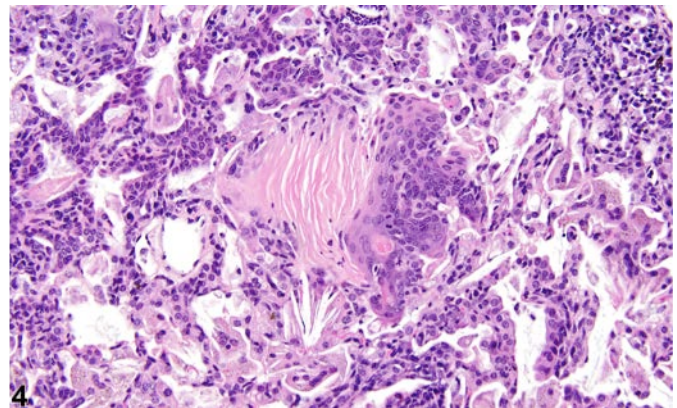
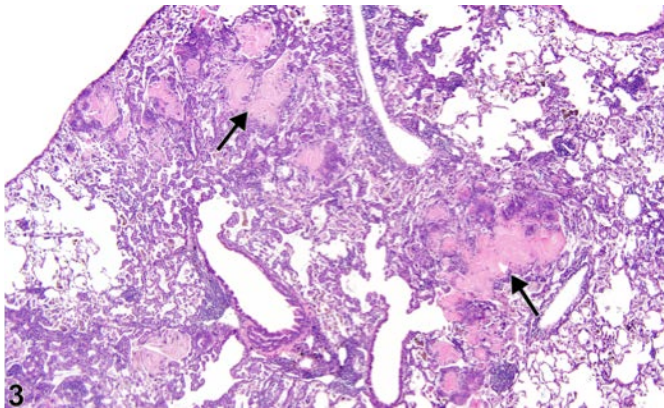
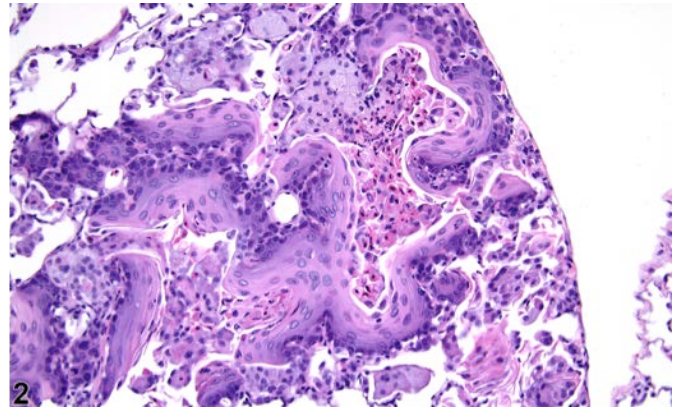
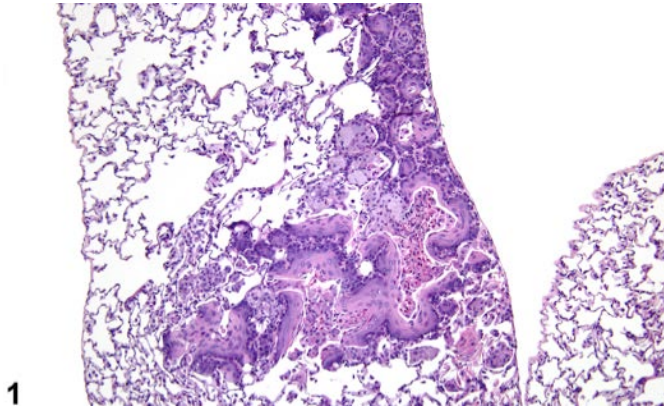
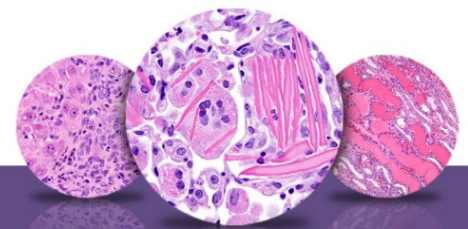




NTP Nonneoplastic Lesion Atlas

Lung – Metaplasia, Squamous





NTP Nonneoplastic Lesion Atlas

Lung – Metaplasia, Squamous

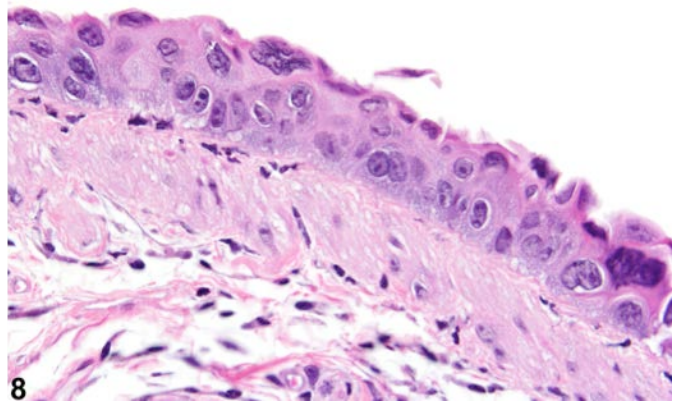
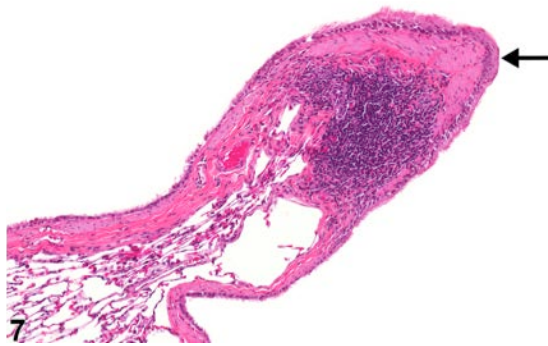
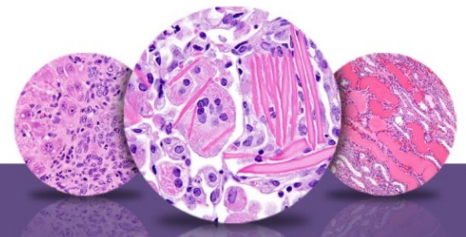


Figure Legend: **Figure 1** Lung, Alveolus - Metaplasia, Squamous in a female Harlan Sprague-Dawley rat from a subchronic study. The normal alveolar epithelium has been replaced by squamous epithelium. **Figure 2** Lung, Alveolus - Metaplasia, Squamous in a female Harlan Sprague-Dawley rat from a subchronic study (higher magnification of Figure 1). The metaplastic epithelium matures normally from basal cells to squamous epithelial cells. **Figure 3** Lung, Alveolus - Metaplasia, Squamous in a female Harlan Sprague-Dawley rat from a chronic study. The normal alveolar epithelium has been replaced by squamous epithelium, which can be identified by the lakes of eosinophilic keratin (arrows). **Figure 4** Lung, Alveolus - Metaplasia, Squamous in a female Harlan Sprague-Dawley rat from a chronic study (higher magnification of Figure 3). The metaplastic epithelium is keratinized; there is also hyperplasia of the alveolar epithelium. **Figure 5** Lung, Bronchiole - Metaplasia, Squamous in a male F344/N rat from an acute study. The normal bronchiolar epithelium has been replaced by squamous epithelium adjacent to an ulcer. **Figure 6** Lung, Bronchus - Metaplasia, Squamous in a male F344/N rat from a subchronic study. The normal bronchiolar epithelium at the bifurcation of an airway has been replaced by squamous epithelium (arrow). **Figure 7** Lung, Bronchus - Metaplasia, Squamous in a male F344/N rat from a subchronic study (higher magnification of Figure 6). The normal bronchiolar epithelium has been replaced by squamous epithelium (arrow). **Figure 8** Lung, Bronchiole - Metaplasia, Squamous, Atypical from a male B6C3F1 mouse in a subchronic study. The cells on the epithelial surface are squamous, but the cells in the deeper layers are disorganized, and there is anisocytosis and anisokaryosis.

Comment: Squamous metaplasia of the alveolar epithelium (Figure 1, Figure 2, Figure 3, Figure 4, Figure 5, Figure 6, Figure 7, and Figure 8) is characterized by replacement of type I and type II



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Lung – Metaplasia, Squamous

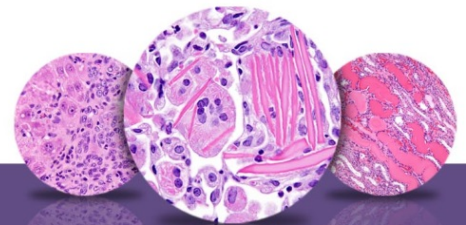
pneumocytes with squamous epithelium. Squamous metaplasia of the airway epithelium is characterized by replacement of bronchiolar or bronchial epithelium with squamous epithelium. Squamous epithelium is a stratified epithelium with orderly progression of cell maturation from cuboidal basal cells at the basement membrane to flattened squamous cells at the surface. The epithelium may be keratinized, and the cells may contain keratohyalin granules. Early squamous metaplasia, where only the surface cells are flattened, can be difficult to identify. Squamous metaplasia should not be confused with regeneration, since regenerating epithelial cells can assume a flattened morphology (stretching out to cover a denuded basement membrane). Generally, more than one layer of cells is present in squamous metaplasia. Squamous metaplasia can be seen as a response to chronic irritation or injury and is thought to be an adaptive change, as the squamous epithelium is more resistant to injury than is respiratory or alveolar epithelium. Consequently, squamous metaplasia is often accompanied by inflammation, fibrosis, necrosis, ulceration, and areas of epithelial hyperplasia. Though not typically considered preneoplastic, under some conditions squamous metaplasia may give rise to neoplasia (cystic keratinizing epithelioma or squamous cell carcinoma). Metaplastic epithelium in which there are atypical cells (Figure 8) may be preneoplastic.

Recommendation: Lung - Metaplasia, Squamous should be diagnosed whenever present and assigned a severity grade. A site modifier (i.e., alveolus, bronchiole, or bronchus) should be included in the diagnosis to indicate the location of the lesion. Associated lesions, such as inflammation, fibrosis, necrosis, or hyperplasia, should be diagnosed separately. If atypia is present, then the modifier “atypical” should be added to the diagnosis.

References:

Boorman GA, Eustis SL. 1990. Lung. In: Pathology of the Fischer Rat: Reference and Atlas (Boorman GA, Eustis SL, Elwell MR, Montgomery CA, MacKenzie WF, eds). Academic Press, San Diego, CA, 339-367.

Renne R, Brix A, Harkema J, Herbert R, Kittle B, Lewis D, March T, Nagano K, Pino M, Rittinghausen S, Rosenbruch M, Tellier P, Wohrmann T. 2009. Proliferative and nonproliferative lesions of the rat and mouse respiratory tract. *Toxicol Pathol* 37(suppl):5S-73S.
Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/20032296>



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References:

Sells DM, Brix AE, Nyska A, Jokinen MP, Orzech DP, Walker NJ. 2007. Respiratory tract lesions in noninhalation studies. *Toxicol Pathol* 35:170-177.

Walker NJ, Yoshizawa K, Miller RA, Brix AE, Sells DM, Jokinen MP, Wyde ME, Easterling M, Nyska A. 2007. Pulmonary lesions in female Harlan Sprague-Dawley rats following two-year oral treatment with dioxin-like compounds. *Toxicol Pathol* 35:880-889.

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