

S15015 15015_CVD_Resp_ApoE_SW- Submitted Data

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1. Purpose

The purpose of this file is to describe the submitted raw data files of the Philip Morris International Reduced Risks Products System Toxicology study S15015 CVD Resp ApoE SW.

2. File Types

The file extensions used are the following:

- *.txt and *.csv: can be opened with a text editor.
- *.xlsx: can be opened with Microsoft Excel.
- *.pdf: can be opened with Adobe Acrobat Reader.

3. Folders organization

The organization of files in folders is summarized below. Information on the data contained in the folders and/or files is given in brackets.

S15015

- ❖ **AN_CHEM** (endpoints measured by analytical chemistry, including biomarkers of exposure in blood and urine)
 - S15015-AN_CHEM-BOE.xlsx (carboxyhemoglobin measurements and biomarkers of exposure measured by ABF in blood and in urine.)
 - S15015-AN_CHEM-NicMet_Urine.xlsx (measurement of nicotine metabolites in urine performed by Singapore facility.)
- ❖ **ATM** (test atmosphere characterization)
 - S15015-ATM.xlsx (test atmosphere characterization: temperature, humidity and concentration of key constituents, including TPM, nicotine, acrolein, formaldehyde...)

❖ **BW** (body weight measurements)

- S15015-BW-Data.xlsx (weekly body weight measurement for each animal)
- S15015-BW-MetaData.xlsx (full metadata associated with body weight measurements, in Isa-Tab format, including the following tabs:
 - [i_Organism]: description of the overall study and of the methods used for exposure and body weight measurement
 - [s_Organism]: list of all animals included in the study with the protocols (exposure, measurements) that were applied to them
 - [A_Organism_BodyWeight]: lists all treated animals and gives the links to the raw data file)

❖ **CLIN_CHEM** (clinical chemistry measurements)

- S15015-CLIN_CHEM_Data.xlsx (measurement of a number of clinical chemistry parameters in blood, including glucose, cholesterol,...)
- S15015-CLIN_CHEM_MetaData.xlsx (full metadata associated with clinical chemistry measurements, in Isa-Tab format, including the following tabs:
 - [i_Organism]: description of the overall study and of the methods used for exposure and clinical chemistry measurements
 - [s_Organism]: list of all animals included in the study with the protocols (exposure, measurements) that were applied to them
 - [s_DP_Clinical_Chemistry]: lists all animals from which blood samples have been extracted to measure clinical chemistry parameters
 - [a_DP_Clinical_Chemistry]: lists all samples on which clinical chemistry parameters have been determined and gives the links to the raw data file)

❖ **FACS** (endpoints analyzed by fluorescence-activated cell sorting)

- S15015-BALF-FACS-Data.xlsx (measurement of free lung cells -FLCs- in bronchoalveolar lavage fluid -BALF- using fluorescent activated cell sorting -FACS-)
- S15015-BALF-FACS-MetaData.xlsx (full metadata associated with BALF FLC measurements, in Isa-Tab format, including the following tabs:
 - [i_Organism]: description of the overall study and of the methods used for exposure and FACS measurements
 - [s_Organism]: list of all animals included in the study with the protocols (exposure, measurements) that were applied to them
 - [s_DP_BALF]: lists all animals from which BALF samples have been extracted
 - [a_DP_BALF_FACS]: lists all samples on which FLCs in BALF were counted by FACS and gives the links to the raw data file)

❖ **HEMAT** (hematology measurements)

- S15015-HEMAT-Data.xlsx (measurement of blood cells and hemoglobin)
- S15015-HEMAT-MetaData.xlsx (full metadata associated with hematology measurements, in Isa-Tab format, including the following tabs:
 - [i_Organism]: description of the overall study and of the methods used for exposure and blood cells measurements
 - [s_Organism]: list of all animals included in the study with the protocols (exposure, measurements) that were applied to them
 - [s_DP_Hema]: lists all animals from which blood samples have been extracted for hematology analysis
 - [a_DP_Hema]: lists all samples on which blood cells and hemoglobin were evaluated and gives the links to the raw data file)

❖ **HISTO** (histopathology of nose, lung, and liver tissue and lung histomorphometry analyses - raw data corresponding to 15015_CVD_Resp_ApoE_SW_SR_Part5.pdf)

- S15015-Histo-Lung-Data.xlsx (histopathology severity scores and evaluation of individual lung tissue slides)
- S15015-Morpho-Lung-Data.xlsx (histomorphometry assessment of lung tissue slides)
- S15015-Histo-Lung-Metadata.xlsx (full metadata associated with lung histopathology and histomorphometry measurements, in Isa-Tab format, including the following tabs:
 - [i_Organism]: description of the overall study and of the methods used for exposure and histopathological evaluation
 - [s_Organism]: list of all animals included in the study with the protocols (exposure, measurements) that were applied to them
 - [s_DP_Histo]: lists all animals from which lungs have been extracted and processed for histopathology analysis
 - [a_DP_Histopathology]: lists all samples on which lung tissue was evaluated by a histopathologist and gives the links to the raw data file
 - [a_DP_Histomorphometry]: lists all samples on which histomorphometry assessment was conducted and gives the links to the raw data file)
- S15015-Histo-Nose-Data.xlsx (histopathology severity scores of individual nose tissue slides)
- S15015-Histo-Nose-Metadata.xlsx (full metadata associated with nose histopathology measurements, in Isa-Tab format, including the following tabs:
 - [i_Organism]: description of the overall study and of the methods used for exposure and histopathological evaluation

- [s_Organism]: list of all animals included in the study with the protocols (exposure, measurements) that were applied to them
 - [s_DP_Histo]: lists all animals from which nose have been extracted and processed for histopathology analysis
 - [a_DP_Histopathology]: lists all samples on which nose tissue was evaluated by a histopathologist and gives the links to the raw data file)
- S15015-Histo-Liver-Data.xlsx (histopathology severity scores of individual liver tissue)
- S15015-Histo-Liver-Metadata.xlsx (full metadata associated with nose histopathology measurements, in Isa-Tab format, including the following tabs:
 - [i_Organism]: description of the overall study and of the methods used for exposure and histopathological evaluation
 - [s_Organism]: list of all animals included in the study with the protocols (exposure, measurements) that were applied to them
 - [s_DP_Histo]: lists all animals from which livers have been extracted and processed for histopathology analysis
 - [a_DP_Histopathology]: lists all samples on which liver tissue was evaluated by a histopathologist and gives the links to the raw data file)
- ❖ **ITRAQ** (proteomics analysis using Isobaric tag for relative and absolute quantitation - ITRAQ - technology)
 - P15015_LI_PEX_PROCESSED.csv (Matrix of normalized protein expression data for all liver samples, obtained by ITRAQ technology)
 - P15015_LI_PEX_Metadata.xlsx (Metadata for all liver samples profiled by ITRAQ)
 - P15015_LLU_PEX_PROCESSED.csv (Matrix of normalized protein expression data for all lung samples, obtained by ITRAQ technology)
 - P15015_LLU_PEX_Metadata.xlsx (Metadata for all lung samples profiled by ITRAQ)
- ❖ **LF** (results from the respiratory physiology or lung function assessment)
 - S15015-LF-Data.xlsx (respiratory physiology measurements)
 - S15015-LF-MetaData.xlsx (full metadata associated with nose histopathology measurements, in Isa-Tab format, including the following tabs:
 - [i_Organism]: description of the overall study and of the methods used for exposure and respiratory physiology evaluation
 - [s_Organism]: list of all animals included in the study with the protocols (exposure, measurements) that were applied to them
 - [s_DP_Histo]: lists all animals from which livers have been extracted and processed for histopathology analysis

- [a_DP_Histopathology]: lists all samples on which liver tissue was evaluated by a histopathologist and gives the links to the raw data file)
- ❖ **MAP** (multianalyte profiling in blood and bronchoalveolar lavage fluid - raw data corresponding to 15015_CVD_Resp_ApoE_SW_SR_Part6.pdf)
 - S15015-MAP-BALF-Data.xlsx (multianalyte profiling -MAP- in bronchoalveolar lavage fluid -BALF-)
 - S15015-MAP-BALF-MetaData.xlsx (full metadata associated with BALF MAP measurements, in Isa-Tab format, including the following tabs:
 - [i_Organism]: description of the overall study and of the methods used for exposure and BALF MAP evaluation
 - [s_Organism]: list of all animals included in the study with the protocols (exposure, measurements) that were applied to them
 - [s_DP_BALF]: lists all animals from which BALF has been collected
 - [a_DP_BALF_MAP]: lists all samples on which BALF was analyzed by MAP and gives the links to the raw data file)
 - S15015-MAP-Serum-Data.xlsx (multianalyte profiling -MAP- in serum)
 - S15015-MAP-Serum-MetaData.xlsx (full metadata associated with Serum MAP measurements, in Isa-Tab format, including the following tabs:
 - [i_Organism]: description of the overall study and of the methods used for exposure and Serum MAP evaluation
 - [s_Organism]: list of all animals included in the study with the protocols (exposure, measurements) that were applied to them
 - [s_DP_SerumMAP]: lists all animals from which serum has been collected for MAP analysis
 - [a_DP_BALF_MAP]: lists all samples on which serum was analyzed by MAP and gives the links to the raw data file)
- ❖ **MMP_Act** (MMP enzymatic activity measured in the bronchoalveolar lavage fluid)
 - S15015-BALF-MMP_Act-Data.xlsx (MMP enzymatic activity measured in bronchoalveolar lavage fluid -BALF-)
 - S15015-BALF-MMP_Act-MetaData.xlsx (full metadata associated with BALF MMP activity measurements, in Isa-Tab format, including the following tabs:
 - [i_Organism]: description of the overall study and of the methods used for exposure and BALF MMP activity evaluation
 - [s_Organism]: list of all animals included in the study with the protocols (exposure, measurements) that were applied to them
 - [s_DP_BALF]: lists all animals from which BALF has been collected

- [a_DP_BALF_MAP]: lists all BALF samples on which MMP enzymatic activity was evaluated and gives the links to the raw data file)
- ❖ **MRNAMA** (transcriptomics profiles in multiple tissues obtained using microarray profiling)
 - **Lung (left lung -LLU-)**
 - P15015_LLUMRNA_PROCESSED.csv (Matrix of normalized gene expression data for all lung samples, obtained with microarrays. Each row is designating a gene symbol, while each column is a sample. The numbers are log2-expression values.)
 - P15015_LLUMRNA_Metadata.xlsx (Metadata for all lung samples profiled by microarray - Please note that in this file ZRH corresponds to THS2.2. The metadata includes the study design and the metadata collected during the laboratory process (from sample to Affymetrix CEL file). The column "Array.Name" describes the original CEL file name and is matching the headers of the PROCESSED file while the column "Array.Name.TXT" is matching the text export of the original CEL file (File extension .txt))
 - P15015_LLUMRNA_S-*.txt (Individual raw data CEL files converted to text files. The star represents the sample id for each sample)
 - **Nose (respiratory nasal epithelium -RNE-)**
 - P15015_RNEMRNA_PROCESSED.csv (Matrix of normalized gene expression data for all nasal epithelium samples, obtained with microarrays. Each row is designating a gene symbol, while each column is a sample. The numbers are log2-expression values.)
 - P15015_RNEMRNA_Metadata.xlsx (Metadata for all nasal epithelium samples profiled by microarray - Please note that in this file ZRH corresponds to THS2.2. The metadata includes the study design and the metadata collected during the laboratory process (from sample to Affymetrix CEL file). The column "Array.Name" describes the original CEL file name and is matching the headers of the PROCESSED file while the column "Array.Name.TXT" is matching the text export of the original CEL file (File extension .txt))
 - P15015_RNEMRNA_S-*.txt (Individual raw data CEL files converted to text files. The star represents the sample id for each sample)
 - **Blood (BLD)**
 - P15015_BLDMRNA_PROCESSED.csv (Matrix of normalized gene expression data for all blood samples, obtained with microarrays. Each row is designating a gene symbol, while each column is a sample. The numbers are log2-expression values.)

- P15015_BLD_MRNA_Metadata.xlsx (Metadata for all blood samples profiled by microarray - Please note that in this file ZRH corresponds to THS2.2. The metadata includes the study design and the metadata collected during the laboratory process (from sample to Affymetrix CEL file). The column "Array.Name" describes the original CEL file name and is matching the headers of the PROCESSED file while the column "Array.Name.TXT" is matching the text export of the original CEL file (File extension .txt))
 - P15015_BLD_MRNA_S-*.txt (Individual raw data CEL files converted to text files. The star represents the sample id for each sample)
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- **Liver (LI)**
 - P15015_LI_MRNA_PROCESSED.csv (Matrix of normalized gene expression data for all liver samples, obtained with microarrays. Each row is designating a gene symbol, while each column is a sample. The numbers are log2-expression values.)
 - P15015_LI_MRNA_Metadata.xlsx (Metadata for all liver samples profiled by microarray - Please note that in this file ZRH corresponds to THS2.2. The metadata includes the study design and the metadata collected during the laboratory process (from sample to Affymetrix CEL file). The column "Array.Name" describes the original CEL file name and is matching the headers of the PROCESSED file while the column "Array.Name.TXT" is matching the text export of the original CEL file (File extension .txt))
 - P15015_LI_MRNA_S-*.txt (Individual raw data CEL files converted to text files. The star represents the sample id for each sample)
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- **Heart (HRT)**
 - P15015_HRT_MRNA_PROCESSED.csv (Matrix of normalized gene expression data for all heart samples, obtained with microarrays. Each row is designating a gene symbol, while each column is a sample. The numbers are log2-expression values.)
 - P15015_HRT_MRNA_Metadata.xlsx (Metadata for all heart samples profiled by microarray - Please note that in this file ZRH corresponds to THS2.2. The metadata includes the study design and the metadata collected during the laboratory process (from sample to Affymetrix CEL file). The column "Array.Name" describes the original CEL file name and is matching the headers of the PROCESSED file while the column "Array.Name.TXT" is matching the text export of the original CEL file (File extension .txt))
 - P15015_HRT_MRNA_S-*.txt (Individual raw data CEL files converted to text files. The star represents the sample id for each sample)
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- **Thoracic aorta(TA)**

- P15015_TA_MRNA_PROCESSED.csv (Matrix of normalized gene expression data for all thoracic aorta samples, obtained with microarrays. Each row is designating a gene symbol, while each column is a sample. The numbers are log2-expression values.)
 - P15015_TA_MRNA_Metadata.xlsx (Metadata for all thoracic aorta samples profiled by microarray - Please note that in this file ZRH corresponds to THS2.2. The metadata includes the study design and the metadata collected during the laboratory process (from sample to Affymetrix CEL file). The column "Array.Name" describes the original CEL file name and is matching the headers of the PROCESSED file while the column "Array.Name.TXT" is matching the text export of the original CEL file (File extension .txt))
 - P15015_TA_MRNA_S-*.txt (Individual raw data CEL files converted to text files. The star represents the sample id for each sample)
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- **Kidney (KI)**
 - P15015_KI_MRNA_PROCESSED.csv (Matrix of normalized gene expression data for all kidney samples, obtained with microarrays. Note, that unlike other matrices, each row is designating a probeset, and not a gene symbol, while each column is a sample. The numbers are log2-expression values.)
 - P15015_KI_MRNA_Metadata.xlsx (Metadata for all kidney samples profiled by microarray - Please note that in this file ZRH corresponds to THS2.2. The metadata includes the study design and the metadata collected during the laboratory process (from sample to Affymetrix CEL file). The column "Array.Name" describes the original CEL file name and is matching the headers of the PROCESSED file while the column "Array.Name.TXT" is matching the text export of the original CEL file (File extension .txt))
 - P15015_KI_MRNA_S-*.txt (Individual raw data CEL files converted to text files. The star represents the sample id for each sample)
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- ❖ **PLAQUE** (measurements of atherosclerotic plaque in the aorta and aortic arch using different techniques - raw data corresponding in part to 15015_CVD_Resp_ApoE_SW_SR_Part8.pdf)
- S15015-Plaque-Digital-Data.xlsx
 - S15015-Plaque-MicroCT-Data.xlsx
 - S15015-Plaque-MetaData.xlsx (full metadata associated with atherosclerotic plaque measurements, in Isa-Tab format, including the following tabs:
 - [i_Organism]: description of the overall study and of the methods used for exposure and plaque evaluation
 - [s_Organism]: list of all animals included in the study with the protocols (exposure, measurements) that were applied to them

- [s_DP_Plaque_Size]: lists all animals from which plaques have been evaluated
- [a_DP_Plaque_Size_Digital]: lists all aortic arch samples on which plaque size was evaluated and gives the link to the raw data file
- [a_DP_Plaque_Size_microCT]: lists all aorta for which microCT data is available and gives the link to the raw data file)

4. Abbreviations

BALF: bronchoalveolar lavage fluid

BLD: blood

CAN: coded animal number

Isa-Tab: investigation-study-assay format

HRT: heart

ITRAQ: Isobaric tag for relative and absolute quantitation

LI: liver

LLOQ: lower limit of quantification

LLU: left lung

MAP: multianalyte

RNE: respiratory nasal epithelium

TA: thoracic aorta

UAN: uncoded animal number

ZRH: refers to THS2.2