3.2.S DRUG SUBSTANCE
3.2.S.3.2 Characterization

All potential impurities should be listed in a tabular format as given below

Listing of Potential Impurities

IUPAC Chemical Name	Code #	Chemical Structure	Process /Degradation Impurity	Source/mechanism

Section 3.2.S.4.5- Justification of Specifications

In addition to other tests, controls for drug substance should include specifications for specified identified, specified unidentified, unspecified, and total impurities. Please refer to the ***Guidance for Industry ANDAs: Impurities in Drug Substances***

Specified Identified Impurities: Justification for the acceptance criteria (AC) for all specified identified impurities along with qualification threshold (QT) should be provided in a tabular format as given below:

Chemical Name	Code #	MDD	QT (%)	QT (TDI)	Regulatory QT Threshold (%)*	Proposed AC (%)	Justification if proposed AC (%) > Regulatory QT Threshold (%)**

*Based on lower intake of impurity from QT (%) or QT (TDI). If QT (TDI) is lower express as %.

**Reference the section if supportive data is provided for justification. This justification may include the following types of data and should be included directly in the application (not by reference to DMF):

1. The observed level and proposed acceptance criterion for the impurity do not exceed the level observed in the reference listed drug product.
2. The impurity is a significant metabolite of the drug substance.
3. The observed level and the proposed acceptance criterion for the impurity are adequately justified by the scientific literature.
4. The observed level and proposed acceptance criterion for the impurity do not exceed the level that has been adequately evaluated in toxicity studies.

If drug substance has a USP monograph that contains acceptance criteria for specified impurities, then all USP monograph impurities along with other potential impurities should be listed in drug substance impurities specifications.

Specified Unidentified Impurities: These should be listed by relative retention times and acceptance criteria for these impurities should not be more than regulatory IT threshold or higher level should be qualified by comparison with RLD.

Relative Retention Time	Code #	MDD	IT (%)	IT (TDI)	Regulatory IT Threshold (%)*	Proposed AC (%)	Justification if proposed AC (%) > Regulatory IT Threshold (%)

*Based on lower intake of impurity using IT (%) or IT (TDI). If IT (TDI) is lower express as %.

Unspecified Impurities: Acceptance criteria for these impurities should not be more than regulatory IT.

MDD	IT (%)	IT (TDI)	Regulatory IT Threshold (%)*	Proposed AC (%)	Not acceptable if proposed AC (%) > Regulatory IT Threshold (%)

*Based on lower intake of impurity from IT (%) or IT (wt). If IT (TDI) is lower express as %.

3.2.P DRUG PRODUCT
3.2.P.5.5 Characterization of Impurities

All potential degradation products should be listed in a tabular format as given below

Listing of Potential Degradation Products

IUPAC Chemical Name	Code #	Chemical Structure	Degradation product	Source/mechanism

Section 3.2.P.5.6- Justification of Specifications

In addition to other tests, controls for drug product should include specifications for specified identified, specified unidentified, unspecified and total degradation products. Please refer to the ***Guidance for Industry ANDAs: Impurities in Drug Products***

Specified Identified Degradation Products (Shelf Life): Justification for the acceptance criteria (AC) for all specified degradation products along with qualification threshold (QT) should be provided in a tabular format as given below:

Chemical Name	Code #	MDD	QT (%)	QT (TDI)	Regulatory QT Threshold (%)*	Proposed AC (%)	Justification if proposed AC (%) > Regulatory QT Threshold (%)**

*Based on lower intake of impurity from QT (%) or QT (TDI). If QT (TDI) is lower express as %.

**Reference the section if supportive data is provided for justification. This justification may include the following types of data and should be included directly in the application:

1. The observed level and proposed acceptance criterion for the degradation product do not exceed the level observed in the reference listed drug product.
2. The degradation product is a significant metabolite of the drug substance.
3. The observed level and the proposed acceptance criterion for the degradation product are adequately justified by the scientific literature.
4. The observed level and proposed acceptance criterion for the degradation product do not exceed the level that has been adequately evaluated in toxicity studies.

If drug product has a USP monograph that contains acceptance criteria for specified impurities, then all USP monograph impurities along with other potential degradation products should be listed in drug product degradation product specifications.

Specified Unidentified Degradation Products: These should be listed by relative retention times and acceptance criteria for these degradation products should not be more than regulatory IT threshold or higher level should be qualified by comparison with RLD.

Relative Retention Time	Code #	MDD	IT (%)	IT (TDI)	Regulatory IT Threshold (%)*	Proposed AC (%)	Justification if proposed AC (%) > Regulatory IT Threshold (%)

*Based on lower intake of impurity using IT (%) or IT (TDI). If IT (TDI) is lower express as %.

Unspecified Degradation Products: Acceptance criteria for these degradation products should not be more than regulatory IT threshold.

MDD	IT (%)	IT (TDI)	Regulatory IT Threshold (%)*	Proposed AC (%)	Not acceptable if proposed AC (%) > Regulatory IT Threshold (%)

*Based on lower intake of impurity from IT (%) or IT (wt). If IT (TDI) is lower express as %.