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## 2.6.6 Toxicology Written Summary

### GUIDANCE INFORMATION – DELETE WHEN COMPLETED:

- The sequence of the Toxicology Written Summary should be as follows:
  - Brief summary
  - Single-dose toxicity

- Repeat-dose toxicity
- Genotoxicity
- Carcinogenicity
- Reproductive and developmental toxicity
- Studies in juvenile animals
- Local tolerance
- Other toxicity studies
- Discussion and conclusions
- Tables and figures (either here or included in text)
- EMA Website

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#### 2.6.6.1 Brief Summary

GUIDANCE INFORMATION – DELETE WHEN COMPLETED:

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The principal findings from the toxicology studies should be briefly summarized in a few pages (generally not more than six). In this section, the extent of the toxicologic evaluation can be indicated by the use of a table listing the principal toxicologic studies (results should not be presented in this table), for example:

GUIDANCE INFORMATION – DELETE GRAPHIC WHEN COMPLETED:

<b>Toxicology Program</b>			
Study type and duration	Route of administration	Species	Compound administered*
Single-dose toxicity	po and iv	Rat and mouse	Parent drug
Single-dose toxicity	po and iv	Rat and mouse	Metabolite X
Repeat-dose toxicity			
1 month	po	Rat and dog	Parent drug
6 months	po	Rat	“ “
9 months	po	Dog	“ “

\* This column should be included only if metabolites are investigated.

## 2.6.6.2 Single-Dose Toxicity

GUIDANCE INFORMATION – DELETE WHEN COMPLETED:

Entry	Value	Date
Toxic 1	3542.2	11-Feb-2021
Toxic 2	4324354.99	01-Jan-2021

The single-dose data should be very briefly summarized, in order by species and by route. In some instances, it may be helpful to provide the data in the form of a table.



#### **2.6.6.3      Repeat-Dose Toxicity**

##### **GUIDANCE INFORMATION – DELETE WHEN COMPLETED:**

Studies should be summarized in order by species, by route, and by duration, giving brief details of the methodology and highlighting important findings (e.g., nature and severity of target organ toxicity, dose (exposure) and/or response relationships, no observed adverse effect levels). Nonpivotal studies can be summarized in less detail (pivotal studies are the definitive GLP studies specified by ICH guidance M3).

#### **2.6.6.4      Genotoxicity**

##### **GUIDANCE INFORMATION – DELETE WHEN COMPLETED:**

Studies should be briefly summarized in the following order:

In vitro nonmammalian cell system

In vitro mammalian cell system

In vivo mammalian system (including supportive toxicokinetics evaluation)

Other systems

#### **2.6.6.4.1      In Vitro Nonmammalian Cell System**



#### **2.6.6.4.2      In Vitro Mammalian Cell System**

#### 2.6.6.4.3 In Vivo Mammalian System



#### **2.6.6.4.4 Other Systems**

#### **2.6.6.5 Carcinogenicity**

##### **GUIDANCE INFORMATION – DELETE WHEN COMPLETED:**

A brief rationale should explain why the studies were chosen and the basis for high-dose selection. Individual studies should be summarized in the following order:

Long-term studies (in order by species), including range-finding studies that cannot appropriately be included under repeat-dose toxicity or pharmacokinetics)

Short- or medium-term studies (including range-finding studies that cannot appropriately be included under repeat-dose toxicity or pharmacokinetics)

Other studies

##### **2.6.6.5.1 Long-term Studies**



#### **2.6.6.5.2      Short- or Medium-term Studies**

#### **2.6.6.5.3      Other Studies**



#### **2.6.6.6      Reproductive and Developmental Toxicity**

##### **GUIDANCE INFORMATION – DELETE WHEN COMPLETED:**

Studies should be summarized in the following order, giving brief details of the methodology and highlighting important findings:

Fertility and early embryonic development

Embryofetal development

Prenatal and postnatal development, including maternal function

Studies in which the offspring (juvenile animals) are dosed and/or further evaluated if such studies have been conducted

If modified study designs are used, the subheadings should be modified accordingly.

#### **2.6.6.6.1 Fertility and Early Embryonic Development**



#### **2.6.6.6.2 Embryofetal Development**

#### **2.6.6.6.3 Prenatal and Postnatal Development**

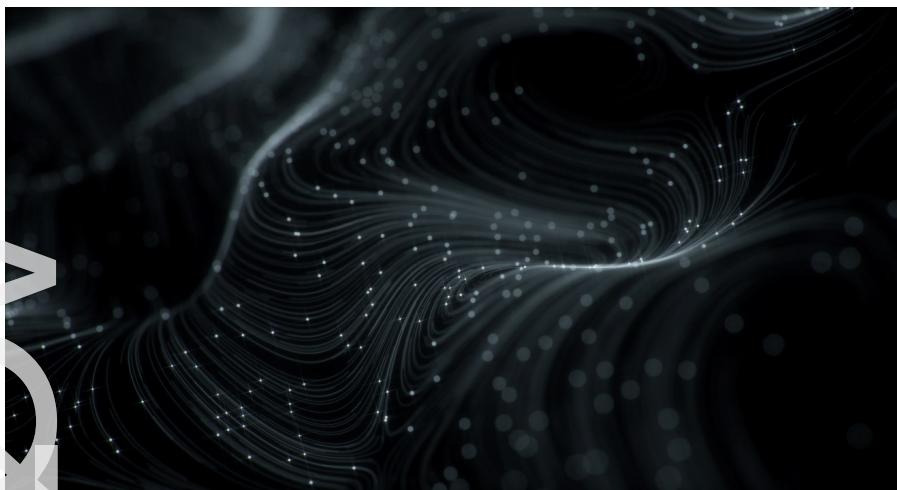


#### **2.6.6.6.4 Studies in Offspring**

#### **2.6.6.7 Local Tolerance**

**GUIDANCE INFORMATION – DELETE WHEN COMPLETED:**

If local tolerance studies have been performed, they should be summarized in order by species, by route, and by duration, giving brief details of the methodology and highlighting important findings.



#### 2.6.6.8        Other Toxicity Studies

##### **GUIDANCE INFORMATION – DELETE WHEN COMPLETED:**

If other studies have been performed, they should be summarized. When appropriate, the rationale for conducting the studies should be provided.

Antigenicity

Immunotoxicity

Mechanistic studies (if not reported elsewhere)

Dependence

Studies on metabolites

Studies on impurities

Other studies



#### **2.6.6.9      Discussion and Conclusions**

##### **GUIDANCE INFORMATION – DELETE WHEN COMPLETED:**

This section should provide an opportunity to discuss the toxicologic evaluation and the significance of any issues that arise. Tables or figures summarizing this information are recommended.



#### **2.6.6.10      Tables and Figures**

##### **GUIDANCE INFORMATION – DELETE WHEN COMPLETED:**

Text tables and figures can be included at appropriate points throughout the summary within the text. Alternatively, tables and figures can be included at the end of the summary.