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# 21 U.S. Code § 355-1

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## Risk evaluation and mitigation strategies

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### **(a) Submission of proposed strategy**

#### **(1) Initial approval**

If the Secretary, in consultation with the office responsible for reviewing the drug and the office responsible for postapproval safety with respect to the drug, determines that a risk evaluation and mitigation strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug, and informs the person who submits such application of such determination, then such person shall submit to the Secretary as part of such application a proposed risk evaluation and mitigation strategy. In making such a determination, the Secretary shall consider the following factors:

- (A) The estimated size of the population likely to use the drug involved.
- (B) The seriousness of the disease or condition that is to be treated with the drug.
- (C) The expected benefit of the drug with respect to such disease or condition.
- (D) The expected or actual duration of treatment with the drug.
- (E) The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug.
- (F) Whether the drug is a new molecular entity.

#### **(2) Postapproval requirement**

##### **(A) In general**

If the Secretary has approved a covered application (including an application approved before the effective date of this section) and did not when approving the application require a risk evaluation and mitigation strategy under paragraph (1), the Secretary, in consultation with the offices described in paragraph (1), may subsequently require such a strategy for the drug involved (including when acting on a supplemental application seeking approval of a new indication for use of the drug) if the Secretary becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug.

##### **(B) Submission of proposed strategy**

Not later than 120 days after the Secretary notifies the holder of an approved covered application that the Secretary has made a determination under subparagraph (A) with respect to the drug involved, or within such other reasonable time as the Secretary requires to protect the public health, the holder shall submit to the Secretary a proposed risk evaluation and mitigation strategy.

#### **(3) Abbreviated new drug applications**

The applicability of this section to an application under section 355(j) of this title is subject to subsection (i).

#### **(4) Non-delegation**

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Determinations by the Secretary under this subsection for a drug shall be made by individuals at or above the level of individuals empowered to approve a drug (such as division directors within the Center for Drug Evaluation and Research).

## **(b) Definitions**

For purposes of this section:

### **(1) Adverse drug experience**

The term “adverse drug experience” means any adverse event associated with the use of a drug in humans, whether or not considered drug related, including—

- (A) an adverse event occurring in the course of the use of the drug in professional practice;
- (B) an adverse event occurring from an overdose of the drug, whether accidental or intentional;
- (C) an adverse event occurring from abuse of the drug;
- (D) an adverse event occurring from withdrawal of the drug; and
- (E) any failure of expected pharmacological action of the drug, which may include reduced effectiveness under the conditions of use prescribed in the labeling of such drug, but which may not include reduced effectiveness that is in accordance with such labeling.

### **(2) Covered application**

The term “covered application” means an application referred to in section 355(p)(1)(A) of this title.

### **(3) New safety information**

The term “new safety information”, with respect to a drug, means information derived from a clinical trial, an adverse event report, a postapproval study (including a study under section 355(o)(3) of this title), or peer-reviewed biomedical literature; data derived from the postmarket risk identification and analysis system under section 355(k) of this title; or other scientific data deemed appropriate by the Secretary about—

- (A) a serious risk or an unexpected serious risk associated with use of the drug that the Secretary has become aware of (that may be based on a new analysis of existing information) since the drug was approved, since the risk evaluation and mitigation strategy was required, or since the last assessment of the approved risk evaluation and mitigation strategy for the drug; or
- (B) the effectiveness of the approved risk evaluation and mitigation strategy for the drug obtained since the last assessment of such strategy.

### **(4) Serious adverse drug experience**

The term “serious adverse drug experience” is an adverse drug experience that—

- (A) results in—
  - (i) death;
  - (ii) an adverse drug experience that places the patient at immediate risk of death from the adverse drug experience as it occurred (not including an adverse drug experience that might have caused death had it occurred in a more severe form);
  - (iii) inpatient hospitalization or prolongation of existing hospitalization;
  - (iv) a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; or
  - (v) a congenital anomaly or birth defect; or
- (B) based on appropriate medical judgment, may jeopardize the patient and may require a medical or surgical intervention to prevent an outcome described under subparagraph (A).

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