Overview of EFSA Endocrine Disruptors assessment of pesticides active substances

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Outline of presentation

- Background:
  - Regulation (EC) No 2018/605: ED criteria
  - ECHA-EFSA Guidance to identify EDs
  - EFSA workflow to assess EDs

- Overview of pesticides active substances assessed by EFSA for EDs properties:
  - Human health
  - Non-target organisms

Background

Background: ED criteria and ED Guidance

- Commission Regulation (EC) No 2018/605, amending Annex II to Regulation (EC) No 1107/2009, set out scientific criteria for the determination of endocrine disrupting properties of pesticides active substances.

- Criteria entered into force and are applicable from 10 November 2018

- ECHA-EFSA Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009 was published on 07 June 2018.

- EFSA has always followed the Guidance when performing the ED assessment: request of additional data in line with the tiered approach outlined in the Guidance.

Background: EFSA workflow for ED assessment

Implementation of ED criteria for pesticides (amendment of Regulation 844/2012):

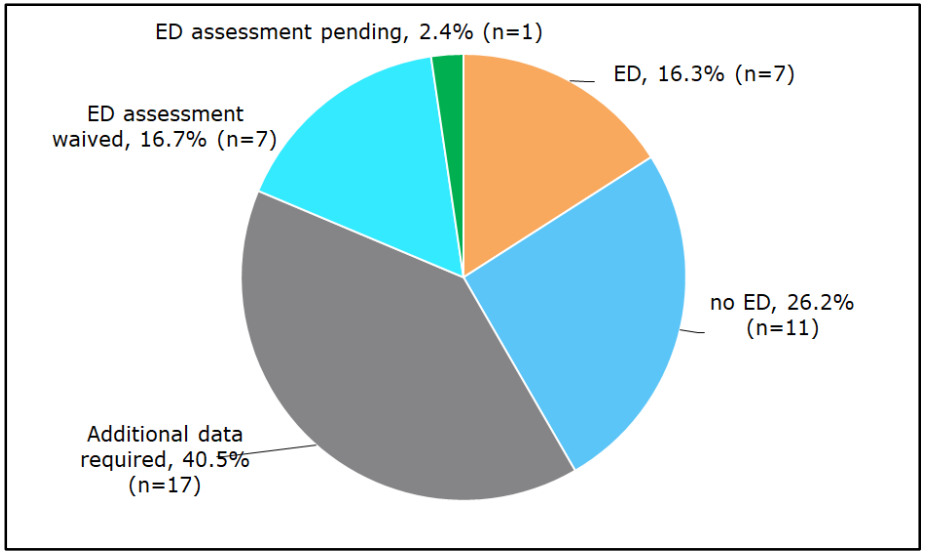
- Relevant to applications for approval/renewal of pesticides active substances, including pending applications:
  - For applications submitted **before 10 Nov 2018**: interim provisions apply, additional data may be requested:(3-30 months) except for new active substance
  - For applications submitted **after 10 Nov 2018**: initial dossier should contain ED assessment in line with ECHA/EFSA GD. No possibility to request for additional data

Overview of EFSA ED assessment

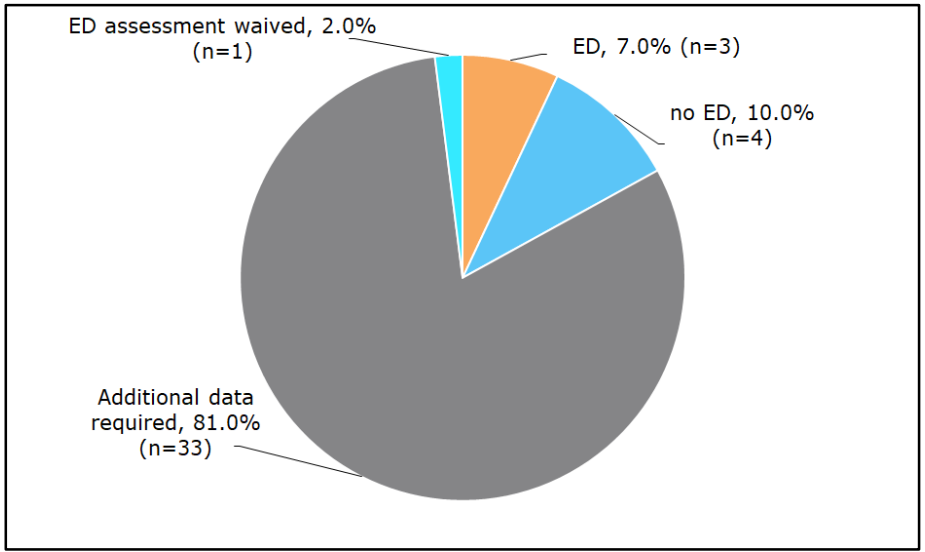
Summary of the ED assessments

- From late 2018 to present, 43 active substances have been assessed for human health and 41 for non-target organism

Human health (HH)

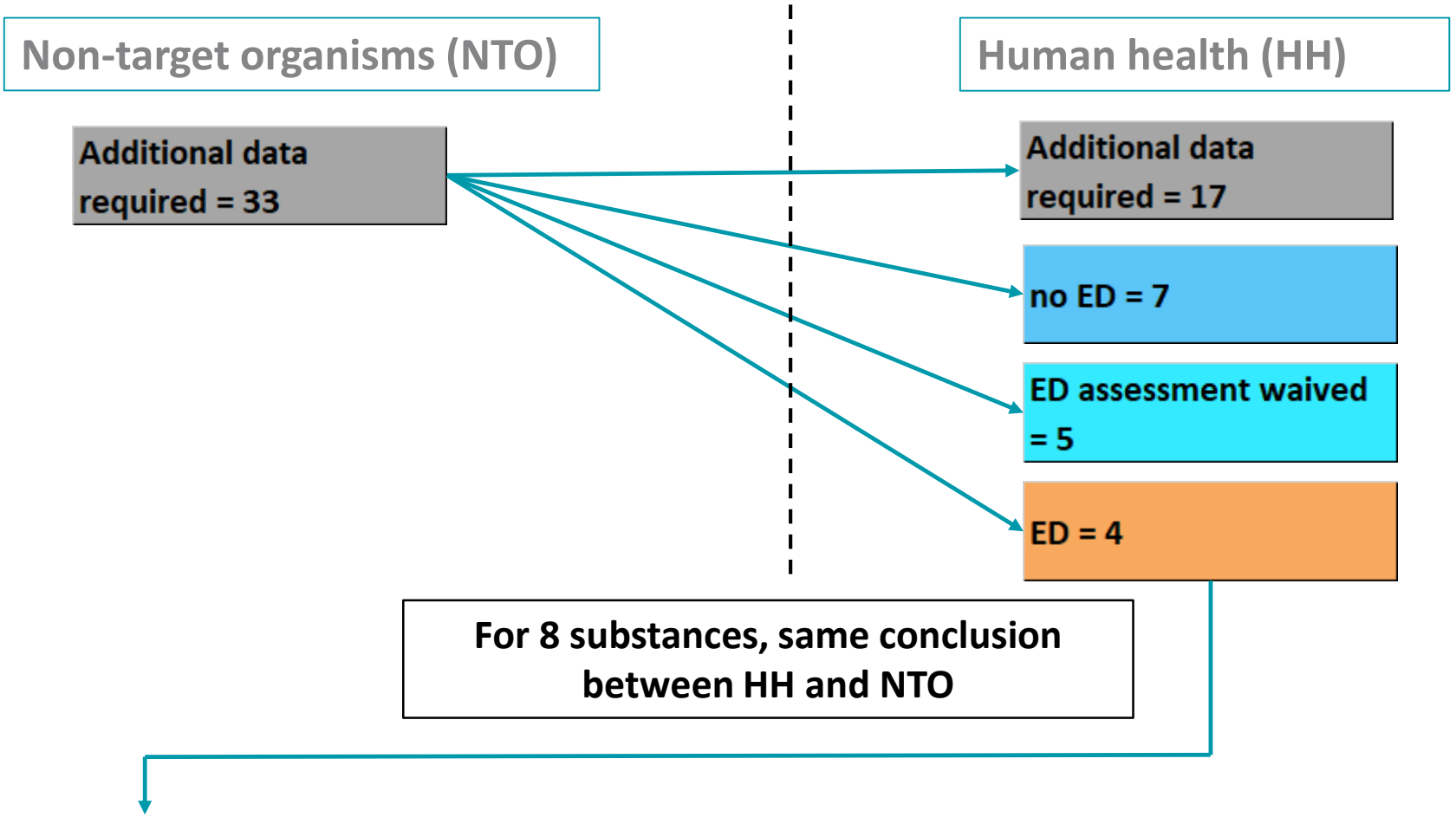


Non-target organisms (NTO)



Summary of the ED assessments

- Regarding the 41 active substances assessed for both HH and NTO, in 33 cases different conclusions were reached:



- For these substances, conclusion was not reached for NTO because of lack of data to assess population relevance.

Substances identified as EDs

- 7 out of 43 active substances have been identified as EDs:
  - 5 disrupt the Thyroid modality (2 both for HH and NTO)
  - 1 disrupts the Estrogen modality
  - 1 disrupts the Androgen modality (both HH and NTO)
- Regarding **Thyroid disruption**, all substances shared a similar MoA: changes of thyroid hormones leading to thyroid hyperthrophy/hyperplasia.
- Regarding **Estrogen disruption**, the relevant findings were increase estradiol level associate to uterine adenocarcinoma
- Regarding **Androgen disruption**, inhibition of androgen receptor leading to decrease ano-genital distance and delayed sexual maturation in males was the likely MoA.

In all cases, *in vivo* data from high level studies was the basis to conclude on EDs

Substances identified as no EDs

- 11 out of 43 active substances have been identified as no EDs (4 for both HH and NTO):

  - Regarding T-modality:

    the conclusion was always reached on the basis of no adversity observed *in vivo* for HH and on lack of endocrine activity based on level 3 studies for NTO.

    The only *in vitro* data were from ToxCast.

  - Regarding EAS-modalities:

    Both high level *in vivo* data and mechanistic information (*in vitro* and *in vivo*) were used to reach conclusion

ED assessment waived

*"There may be cases in which due to the knowledge on the **physico-chemical and (eco)toxicological properties** of the substance an **ED assessment does not appear scientifically necessary or testing for this purpose not technically possible**. In such cases, it should be justified for PPPs"*

- For 7 active substances the ED assessment was waived for humans health based on:
  - 3 substances: potent cholinesterase inhibition
  - 2 substances: irritant properties at the site of contact
  - 1 substance: metaemoglobin formation
  - 1 substance (waiving also for NTO): approved as iron food supplement

Conclusions

- ECHA-EFSA Guidance was always followed to assess ED properties of pesticides active substances.
- The ECHA-EFSA Guidance provides a framework to ensure consistency between assessments (and also between pesticides and biocides) and experience in its use has been gained by Member States.
- Differences in the assessment between human health and non-target organism (availability of data, in vitro information, population relevance).
- Most of the active substances are on clock stop (3-30 months): additional data required to support ED assessment.

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