FDA draft guidance - Nonclinical safety evaluation of the immunotoxic potential of drugs and biologics - February 2020

A comparison with the previous withdrawn guidance from 2002

FDA Guidance - Version 2002[b]	FDA Guidance - Draft Version 2020[a]
Guidance applicable to small molecules only	Guidance applicable to small molecules + some biologics (therapeutic proteins and recombinant/plasma-derived blood proteins)
Focuses mainly on immunosupression	Focuses also on immunostimulation (ex: TGN1412) with in vitro assays assessing immune activation, cytokine release and ligand-receptor interactions
No corresponding ICH guidelines except ICH S6 (1st version)	Refers to **ICH S8**[c] (2006), S11[d] (2020), S9[e] (2010), S5 R3[f] (2020) in addition to S6 R1[g] (2012)
Developmental immunotoxicity limited to standard DART studies	Juvenile Tox studies (all species) + NHP enhanced PPND study added in addition to standard DART studies
For TDAR : SRBC Plaque Assay was recommended as 1st choice	KLH is now the 1st choice for TDAR assay T-DAR is also proposed for increased IgM/G production in addition de decreased IgM/G production.
Dogs and monkeys were the only two NR species recommended	**Minipig** added in non rodent species in addition to dogs and NHPs
LLNA recommended	LLNA not recommended anymore (limits for this test) – In vitro tests recommended instead (OECD guidelines 2019 test No. 442C/D/E)

[a] FDA draft guidance for Nonclinical safety evaluation of the immunotoxic potential of drugs and biologics (February 2020) https://www.fda.gov/media/135312/download

[b] FDA guidance for Industry Immunotoxicology Evaluation of Investigational New Drugs (October 2002) https://www.fda.gov/media/72228/download

[c] ICH S8 Immunotoxicity studies for human pharmaceuticals (April 2006)

[d] ICH S11 Nonclinical Safety Testing in Support of Development of Paediatric Medicines (January 2019)

[e] ICH S9 Nonclinical Evaluation for Anticancer Pharmaceuticals – Questions and Answers (June 2018)

[f] ICH S5(R3) Detection of Toxicity to Reproduction for Human Pharmaceuticals (November 2017)

[g] ICH S6(R1) Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals (May 2012)