

Index

A

Ames bacterial mutagenicity test, 194
Ames test, 50, 61–63, 66

B

Bioassay, 5, 15, 23, 24, 26, 27, 29, 30, 45, 61, 76, 96–99, 101, 102, 105, 106, 111, 126, 130, 132, 139, 160, 164, 168, 184, 185, 194, 197, 198
history, 96–97
Biotechnology-derived pharmaceuticals, 6

C

Cancer risk assessment, 71, 160, 171
Carcinogenicity, 2–8, 15–18, 20, 22–24, 26–30, 36–38, 45, 46, 51, 57, 60–69, 76, 97, 99–105, 109–122, 125–149, 159–180, 184–186, 188, 191, 192, 194, 195, 198, 200
evaluation, 110, 121
testing, 2, 3, 5, 6, 15, 26–29, 109–122, 126–128, 188
Clastogenicity, 14, 37, 38, 49, 60, 63, 191
Clinical tumor, 8, 190
Comet assay, 3, 16, 39, 40, 46, 49, 50, 69, 77–80, 82–84, 86

D

DNA damage, 14, 16, 26–28, 36, 40, 46, 47, 49, 50, 52, 59, 76–79, 83–86
DNA-reactive impurities, 4, 59–60

F

FDA CAC, 100–101
Follow-up testing, 16, 44–50, 69, 70, 79, 82

G

Genotoxic impurities, 4, 50, 55–72, 82
Genotoxicity, 3, 4, 14–15, 22–23, 26–30, 35–52, 59, 62, 76–80, 82–86, 88, 89, 111, 112, 119, 130, 161, 177, 184, 194, 198
GLP-1 agonists, 113, 136, 175–180

H

HESI alternatives to carcinogenicity testing, 99
High-throughput, 15, 16, 25, 42, 136
Human risk assessment, 97, 99, 104, 120, 166, 172, 174, 190

I

ICH. *See* International Conference on Harmonization (ICH)
ICH Guidance, 4, 112, 122
ICH S2(R1), 3, 36, 38–40, 42, 44–47, 49, 77, 79, 80, 85
Immunomodulators, 126
Impurities in pharmaceuticals, 55–72
In silico assessment, 63, 64
Insulin, 128, 129, 133–136, 143, 148–149, 187, 191
International Conference on Harmonization (ICH), 3–5, 14, 38–39, 56, 58, 59, 76, 99, 110, 112, 117, 119, 120, 122, 127, 160, 191
carcinogenicity guidelines, 15, 119

L

Liver micronucleus, 4, 77, 82–83

M

Modeling, 17–22, 30, 89, 137

N

NOGEL. *See* No-observed genotoxic effect level (NOGEL)

Nonclinical, 6, 36, 101, 103, 119, 129–131, 160, 161, 165, 174, 175, 177–180, 183–200

evaluation, 126

models, 139, 188, 189, 198

No-observed genotoxic effect level (NOGEL), 38, 89

P

Pharmaceuticals, 1–8, 14–16, 18, 21–25, 29, 30, 41, 47, 55–72, 76, 77, 79, 80, 83, 85, 96, 99–101, 104–106, 110–113, 117–122, 125–149, 160, 161, 164, 165, 167–169, 173, 184, 189

Pig-a assay, 51, 69, 70, 80, 82, 88

Positive, 3–5, 7, 8, 14–20, 22–25, 27, 28, 30, 37–40, 42–52, 60–62, 64–66, 69, 70, 79, 80, 82–86, 88, 96–99, 104, 112, 117–119, 121, 131, 139, 144, 148, 149, 159–180, 185, 186, 188–190, 195, 198

Q

Quantitative structure-activity relationship (QSAR), 3, 15, 17, 63–64, 105

R

Risk-assessment, 17, 25–29, 38, 60, 64–68, 70–72, 86, 89, 97, 99–101, 104, 117, 120, 127–131, 146, 160, 161, 164, 166, 170–174, 178, 190

Rodent bioassays, 5, 15, 23, 27, 30, 45, 61, 76, 96–98, 106, 130, 132, 160, 168, 184, 185, 194

T

TGR. *See* Transgenic rodent (TGR)

Tg.rasH2 transgenic mouse, 99, 121

Threshold of toxicological concern, 58, 60

Toxicogenomics, 3, 17, 25–30

Transgenic rodent (TGR), 4, 77, 84–85, 89

Tumor, 2, 4–8, 14, 15, 27, 29, 36, 61, 66, 67, 69, 71, 76, 96–99, 102–104, 113–119, 126–128, 131, 132, 134, 136, 138–142, 144, 147, 148, 160, 162–180, 184–200

progression, 147, 187, 193–195

promotion, 4, 8, 130, 188–190, 193, 195, 198, 200