OEB / HPAPI Assessment — Docetaxel

Provisional, screening-level. Requires qualified-toxicologist review.

HPAPI	OEB	Est. OEL (8-h TWA)	Confidence
Yes	4	1.5 ug/m3	Medium

1. Identity

Name	Docetaxel
CAS	114977-28-5
SMILES	CC1=C2[C@H](C(=O)[C@@]3([C@H](C[C@@H]4[C@]([C@H]3[C@@H]([C@@](C2(C)C)(C[C@@H]1OC(=O)[C@@H]([C@H](C5=CC=CC=C5)NC(=O)OC(C)(C)C)O)O)OC(=O)C6=CC=CC=C6)(CO4)OC(=O)C)O)C)O
PubChem CID	148124
ChEMBL	CHEMBL92
MW (g/mol)	807.9
Synonyms	docetaxel, 114977-28-5, Taxotere, Docetaxel anhydrous, Docetaxel Kabi, Docetaxel Winthrop
Sources	PubChem CID 148124; ChEMBL CHEMBL92

2. Toxicology / pharmacology justification

Endpoint	Value	Study type	Source	Relevance
GHS classification (all health H-codes)	H315 (causes skin irritation); H319 (causes serious eye irritation); H341 (suspected of causing genetic defects); H351 (suspected of causing cancer); H360 (may damage fertility or the unborn child); H361 (suspected of damaging fertility or the unborn child); H362; H372 (causes organ damage through prolonged/repeated exposure)	Aggregated supplier C&L; self-classification	PubChem GHS section (CID 148124) — aggregated supplier C&L; self-classification, NOT harmonized/CLH; suggestive, not authoritative	Suggestive, not harmonized/CLH. Cat-1 genotox/carc/repro and any sensitizer floor the OEB; Cat-2 'suspected' codes floor one band lower.
Mutagenicity (suspected)	Present	GHS Muta 2 (H341)	PubChem GHS section (CID 148124) — aggregated supplier C&L; self-classification, NOT harmonized/CLH; suggestive, not authoritative	Suspected mutagen — precautionary genotoxic handling; floors OEB 4.
Carcinogenicity (suspected)	Present	GHS Carc 2 (H351)	PubChem GHS section (CID 148124) — aggregated supplier C&L; self-classification, NOT harmonized/CLH; suggestive, not authoritative	Suspected carcinogen — floors OEB 4.

Endpoint	Value	Study type	Source	Relevance
Reproductive/developmental toxicity	1B	GHS Repr 1A/1B (H360)	PubChem GHS section (CID 148124) — aggregated supplier C&L; self-classification, NOT harmonized/CLH; suggestive, not authoritative	Confirmed reprotoxicant — floors OEB 4.
Reproductive toxicity (suspected)	Present	GHS Repr 2 (H361)	PubChem GHS section (CID 148124) — aggregated supplier C&L; self-classification, NOT harmonized/CLH; suggestive, not authoritative	Suspected reprotoxicant — floors OEB 3.
Target-organ toxicity (repeated exposure)	Present	GHS STOT-RE (H372/H370)	PubChem GHS section (CID 148124) — aggregated supplier C&L; self-classification, NOT harmonized/CLH; suggestive, not authoritative	Directly worker-relevant on repeated occupational exposure.
Pharmacological potency (aggregate median IC50/Ki/EC50)	100 nM (median of n=50 mixed assays)	ChEMBL bioactivity aggregate (mixed assay types)	ChEMBL CHEMBL92 bioactivity (median of 50 IC50/Ki/EC50, nM)	AGGREGATE median across mixed assay types (cell + biochemical); the true primary-target affinity may be far lower (often sub-nM). A soft HPAPI signal that does NOT change a dose-based OEL.
Development stage (ChEMBL max_phase)	4.0	-	ChEMBL CHEMBL92	Approved/late-stage drugs usually have a published ADE/PDE to prefer; investigational (max_phase < 4) rarely has a citable therapeutic dose or GHS record.
Mechanism of action	Tubulin stabiliser	ChEMBL mechanism	ChEMBL CHEMBL92 mechanism_of_action	Endocrine-active agents carry inherent reproductive/developmental hazard; targeted degraders (PROTAC/glue) act catalytically at low occupancy.
DailyMed (FDA SPL) lookup	*DATA GAP*	-	DailyMed (FDA SPL)	Not wired in this build; add SPL REST parse to fill clinical dose / warnings.
ECHA (REACH/CLH) lookup	*DATA GAP*	-	ECHA (REACH/CLH)	No open JSON API; add a scrape/registered-dossier lookup to fill DNEL/CLH.
EPA ToxValDB / CompTox Dashboard lookup	*DATA GAP*	-	EPA ToxValDB / CompTox Dashboard	Add CCD batch API or bulk export parse to fill NOAEL/LOAEL/LD50.

3. PDE / ADE / OEL derivation

Method: ICH Q3C(R8)/EMA 2014 adjustment-factor PDE

ADE/PDE: 15 ug/day **Derived OEL:** 1.5 ug/m3 (8-h TWA)

• POD = 0.75 mg/kg/day (NOAEL, rat 4-week IV (illustrative)), NOAEL.

• BW = 50.0 kg; worker inhalation V = 10.0 m3/shift; bioavailability beta = 1.0.

• F1(interspecies,rat)=5.0, F2(intraspecies)=10.0, F3(duration,subacute_28d)=5.0, F4(severity,teratogenic_or_genotox)=10.0, F5(LOAEL->NOAEL)=1.0; composite = 2500.

• GENOTOXICITY FLAG: a threshold-based PDE assumes a no-effect threshold that a genotoxic/mutagenic compound may not have. Treat this OEL as NON-conservative and apply a non-threshold (TTC/linear) assessment; the hazard override floors the OEB independently of this number.

4. HPAPI determination

Verdict: Yes. Meets 3 HPAPI criterion/criteria: Assigned OEB 4 >= 4 (HPAPI band); OEL 1.5 ug/m3 <= 10 ug/m3 (OEB >= 4); Reproductive toxicant (category 1B).

Hard criteria met: Assigned OEB 4 >= 4 (HPAPI band); OEL 1.5 ug/m3 <= 10 ug/m3 (OEB >= 4); Reproductive toxicant (category 1B)

Soft signals: Potent pharmacology (IC50/Ki ≈ 100 nM); Suspected mutagen (GHS H341, Cat 2) — precautionary genotoxic handling; Suspected carcinogen (GHS H351, Cat 2); Suspected reproductive toxicant (GHS H361, Cat 2); Target-organ toxicity on repeated exposure (GHS STOT-RE)

5. OEB classification & controls

OEB 4 — Highly potent (HPAPI onset) (1 - 10 ug/m3); basis: OEL-derived.

Containment: Closed handling; ventilated enclosures / split-butterfly valves; isolators for open ops.

PPE: Full gown, double gloves, PAPR / powered respirator.

6. Data gaps & confidence

Confidence: Medium. OEL derived from a repeat-dose NOAEL/LOAEL, but authoritative tox sources (DailyMed/ECHA/EPA ToxValDB) were not consulted in this build; confirm the POD and any hazard classification.

Data gaps: DailyMed (FDA SPL) lookup; ECHA (REACH/CLH) lookup; EPA ToxValDB / CompTox Dashboard lookup

8. Key references

Methodology references plus any hazard-specific citations triggered by this assessment. Verify against primary sources before formal use.

1. ICH Q3C(R8) (2021). Impurities: Guideline for Residual Solvents — PDE adjustment-factor method (F1-F5). International Council for Harmonisation.

2. EMA (2014, rev. 2020). Guideline on setting health-based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities (EMA/CHMP/CVMP/SWP/169430/2012).

3. NIOSH (2019). The NIOSH Occupational Exposure Banding Process for Chemical Risk Management. DHHS (NIOSH) Publication No. 2019-132.

4. Naumann BD, Sargent EV, Starkman BS, et al. (1996). Performance-based exposure control limits for pharmaceutical active ingredients. Am Ind Hyg Assoc J 57(1):33-42.

5. Sargent EV, Kirk GD (1988). Establishing airborne exposure control limits in the pharmaceutical industry. Am Ind Hyg Assoc J 49(6):309-313.

6. ISPE (2017). Risk-Based Manufacture of Pharmaceutical Products (Risk-MaPP), Baseline Guide Vol. 7, 2nd ed. — ADE/OEB framework.

7. ECHA/CLP Regulation (EC) No 1272/2008 — reproductive toxicity (Repr.) hazard classes.

8. ICH M7(R2) (2023). DNA-reactive (mutagenic) impurities — TTC/non-threshold assessment (applies to suspected mutagens pending data).
