

Supplementary Information for:

**Defining the molecular properties of N-nitrosodimethylamine (NDMA) precursors using
computational chemistry**

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This supplementary data document contains seven tables.

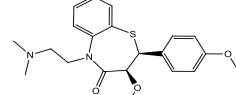
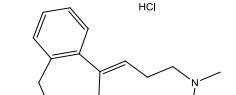
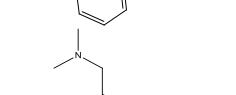
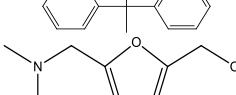
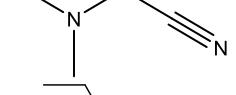
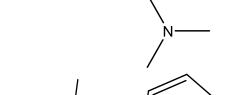
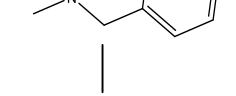
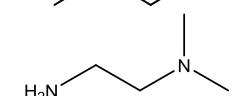
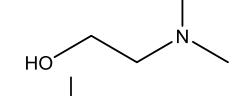
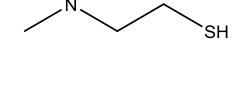
Table S1: NDMA formation potential conditions

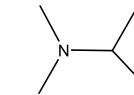
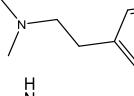
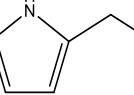
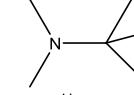
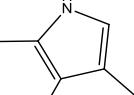
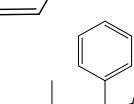
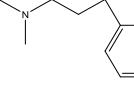
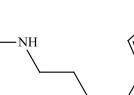
Chloramine dose	Contact time (days)	pH	Temperature (°C)	Comments	Reference
0.1 and 2 mM	10	6.9	Na		Mitch 2004 ⁹
0.4 mM	7	7	20	Matrix drinking water	Sacher ¹⁰
2 mM	10	6.8	Na		Mitch 2003 ¹¹
100 mg/L (1.4 mM)	5	7.5	22		Selbes ¹²
15- to 18-times excess (225– 270 µM).	na	8	na		Spahr ¹³
2.8 – 4.2 mM	5	8.5	20		Le Roux 2011 ¹⁴
28.4 mg/L (0.4 mM)	1	7	21		Shen ¹⁵
0.2 mM NH ₂ Cl + 2 µM precursor.	5	7	22		Gan ¹⁶
200-300 mg/L as Cl ₂ (2.8 – 4.2 mM)	1	8	20		Le Roux 2012 ²¹
3.45 mM	1-10	8	23		Chen ²²
2 mM	10	7	na		Kemper ²³
150 mg/L as Cl ₂	6	8	25		Hanigan ²⁴
3:1 Cl ₂ /N weight ratio.	3	8.4	25	Ammonia added first during chloramination	Leavey-Robuck ²⁵

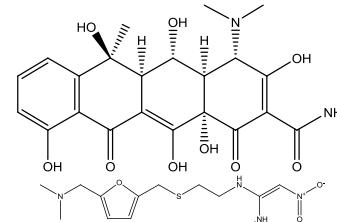
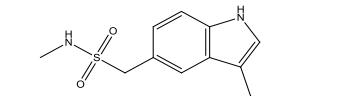
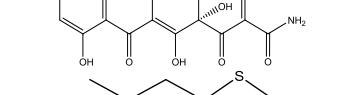
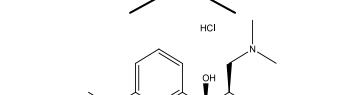
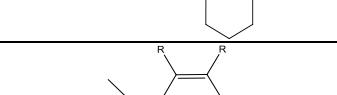
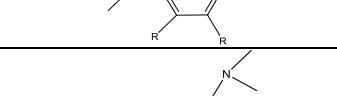
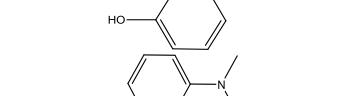
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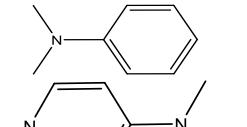
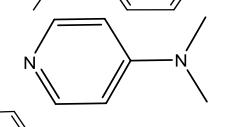
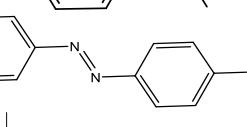
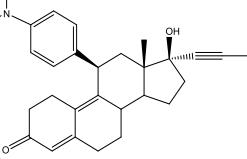
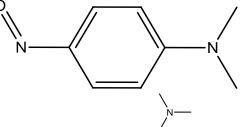
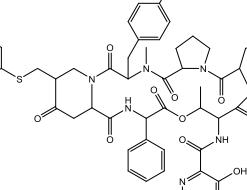
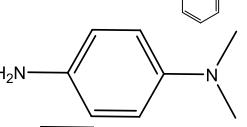
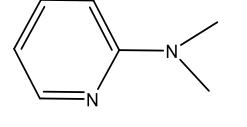
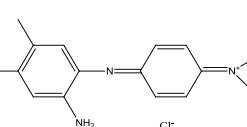
Table S2: Names and structures of NDMA precursors

Precursor	Abbreviation/ alternative name	NDMA formation (% M/M)	Reference/s	Structures
Dimethylamine	DMA	0.5 – 2.7 (0.8)	8-12	
Category 1: $(\text{CH}_3)_2\text{N-Alkyl-R}$				
Amitriptyline		1.2	15	
Carbinoxamine		1.0-1.4 (1.2)	15	
Chlorphenamine		5.2-5.5 (5.4)	15	
Chlortetracycline		0.9	25	
Clarithromycin		0.04	25	

Diltiazem		2.1-2.6 (2.4)	15	
Doxepin		2.3	14	
Doxylamine		8.0-9.7(8.9)	15	
5-(dimethylaminomethyl)furfuryl alcohol	DMfuryl	50.3-84.6 (50.3)	10, 12, 21	
Dimethylaminoacetonitrile	DMAAcCN	2.4	13	
<i>N,N</i> -dimethylbutylamine	DMBA	0.3	13	
<i>N,N</i> -dimethylbenzylamine	DMBzA	82.5-83.8 (83.5)	12, 13, 16	
<i>N,N</i> -dimethylethylamine	DMEA	0.5	13	
<i>N,N</i> -dimethylethylenediamine	DMEDA	0.8	13	
2-dimethylaminoethanol	DMEtOH	0.3	13	
2-dimethylaminoethanethiol	DMEtSH	0.8	13	

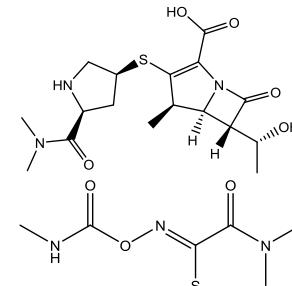
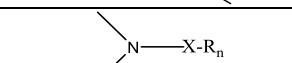
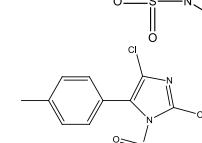
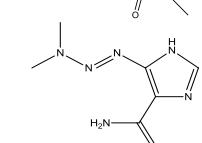
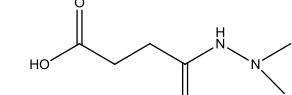
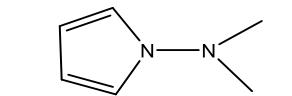
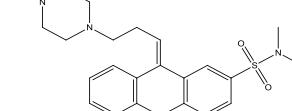
<i>N,N</i> -Dimethylisopropylamine	DMiPA	83.9	13	
<i>N,N</i> -dimethylphenethylamine	DMPhA	0.4	13	
<i>N,N</i> -dimethyl-1-(1 <i>H</i> -pyrrol-2-yl)methanamine	DMPMA	25	13	
<i>N,N</i> -dimethyltertbutylamine	DMtBA	6.2	13	
Gramine		2.9-5.6 (2.9)	10	
Methadone		70	24	
Nizatidine		4.5-4.9 (4.9)	10, 15	
Oleandomycin		0.04	25	

Oxytetracycline		1.4	25	
Ranitidine		62.9-94.2 (62.9)	10, 12-16	
Sumatriptan		6.1	15	
Tetracycline		0.5-1.7 (1.2)	10, 15, 16, 25	
N,N-dimethylthiophene-2-methylamine	DMthiophene	49.5 – 77.6 (49.5)	10, 13	
Trimethylamine	TMA	0.6 – 2.0 (0.6)	9, 13, 16	
Tramadol		0.6	15	
<hr/>				
Category 2: $(\text{CH}_3)_2\text{N-Aryl}$				
3-DMaminophenol		0.0-1.0 (0.0)	13, 21	
2-chloro-N,N-Dimethylaniline	2-Cl-DMAN	1.0	13	

<i>N,N</i> -dimethylaniline	DMAN	0.2	13	
4-dimethylaminopyridine	4-DMAP	0.1	13	
4-(dimethylamine)azobenzene	(Methyl yellow)	9.4	10	
Mifepristone		0.4	21	
<i>N,N</i> -dimethyl-4-nitrosoaniline	Nitrosoaniline	0.8	10	
Quinupristin		0.2	25	
<i>N,N</i> -dimethyl-p-phenylenediamine	DMphenylenediamine	0. 3 - 2.3 (2.3)	10, 16	
2-(dimethyl-amino) pyridine	DMpyridine	0.4	21	
Toluylene blue		1.1	10	

Category 3: $(CH_3)_2N-C=R_1(R_2)$

				$\begin{array}{c} R_1 \\ \\ N-C(=O)-R_2 \end{array}$
4-dimethylaminoantipyrine	4-DMAantipyrine	12.0	16	
Diphenamide	FDN or diphenamid	0.5	10	
Diuron		1.5	10, 22	
Dimethylformamide	DMform	0.4	10	
Dimethyldithiocarbamate	DMthiocarb	2.2 - 2.5 (2.5)	10, 16	
6-(dimethyl-amino) fulvene	DMfulvene	0.5	21	
Isoproturon		0.3	14	
Loperamide		0.8	10	

Meropenem	0.1	25		
Oxamyl	0.1	10		
Category 4: (CH₃)₂N-heteroatom				
N,N-dimethyl-N-(4-methylphenyl)-sulfamide (Ar-DMsulfamide)	0.4	10		
Cyazofamid	0.1	10		
Dacarbazine	1.6	10		
Daminozide	Alar	0.0 - 0.1 (0.1)	10, 16	
1-(dimethyl-amino) pyrrole	DMpyrrole	1.6	21	
Thiothixene		0.10	10	

N,N-Dimethylsulfamide	DMS	1.1	16	
Unsymmetrical dimethylhydrazine	UDMH	0.5	16	
Category 5: (CH₃)₂N⁺-R₂				
Tetramethylamine		0.0	23	
Choline		0.2	23	
Benzylidimethyldodecylamine (capped)	benzylIDM dodecylamine	0.3	23	

Table S3: Molecular descriptors for the DMA group in NDMA precursors

Precursor	Partial charge	Planarity (°)	Bond length (Å)	pK _a
DMA	-0.802	119.8	1.012	10.7
Category 1: (CH₃)₂N-Alkyl-R				
Amitriptyline	-0.481	121.6	1.459	9
Carbinoxamine	-0.376	123.1	1.457	9.7
Chlortetracycline	-0.107	125.7	1.489	4.3
Chlorphenamine	-0.37	121.7	1.459	8.9
Clarithromycin	-0.402	128.5	1.465	9.5
Diltiazem	-0.424	122.4	1.456	7.3
DMAAcCN	-0.415	121.8	1.453	6
DMBA	-0.424	121.7	1.461	10.1
DMBzA	-0.252	127.3	1.467	9.3
DMEA	-0.44	121.5	1.461	10.2
DMEDA	-0.527	121.7	1.458	9.5
DMEtOH	-0.508	121.7	1.456	9.1
DMEtSH	-0.417	121.8	1.459	9.1
DMfurfuryl	-0.384	122.6	1.454	8.7
DMiPA	-0.522	123.0	1.471	10.1
DMPhA	-0.469	121.6	1.46	9.4
DMPMA	-0.424	121.3	1.465	9.6
DMtBA	-0.543	127.8	1.489	10.4
DMthiophene	-0.379	122.1	1.461	8.9
Doxepin	-0.478	122.9	1.459	9.1
Doxylamine	-0.359	123.4	1.458	9.6
Gramine	-0.43	122.2	1.46	9.9
Methadone	-0.385	127.7	1.473	8.3
Oleandomycin	-0.449	123.3	1.469	9.1
Nizatidine	-0.389	122.6	1.454	6.9

Oxytetracycline	-0.286	126.9	1.414	6.5
Ranitidine	-0.439	122.6	1.455	8.4
Sumatriptan	-0.435	121.5	1.459	8.7
Tetracycline	-0.423	130.5	1.473	12.7
TMA	-0.392	121.8	1.454	10.3
Tramadol	-0.446	127.9	1.462	9.4

Category 2: (CH₃)₂N-Ar

2-Cl-DMAN	-0.471	131.7	1.411	3.9
3-DMaminophenol	-0.389	152.6	1.381	4.6
4-DMAP	-0.299	180	1.356	3.4
DMAN	-0.462	149.3	1.386	4.9
DMphenylenediamine	-0.557	132.9	1.417	6.3
DMpyridine	-0.401	154.2	1.372	4.6
Methyl yellow	-0.22	180	1.36	2.5
Mifepristone	-0.42	147.1	1.388	4.9
Nitrosoaniline	-0.18	180	1.348	0
Quinupristin	-0.437	146.6	1.389	4.2
Toluylene blue	-0.216	176.6	1.352	Cation

Category 3: (CH₃)₂N-C=R₁(R₂)

4-DMAantipyrine	-0.286	126.9	1.414	6.5
Diphenamide	-0.2	176.5	1.35	-1.2
Diuron	-0.205	169.4	1.359	1.3
DMform	-0.017	180	1.34	-1.1
DMfulvene	0.093	180	1.322	-0.4
DMthiocarb	0.22	179.4	1.326	-2.1
Isoproturon	-0.02	163.9	1.355	2.4
Loperamide	-0.225	172.2	1.354	0.4
Meropenem	-0.147	170	1.35	-0.6
Oxamyl	0.036	177.6	1.338	-1.5

Category 4: (CH₃)₂N-heteroatom

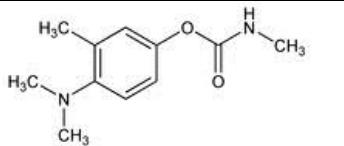
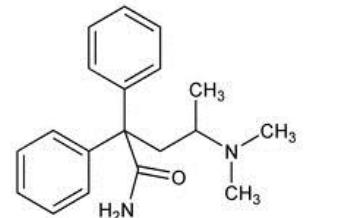
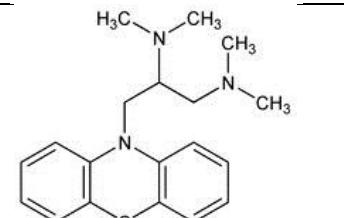
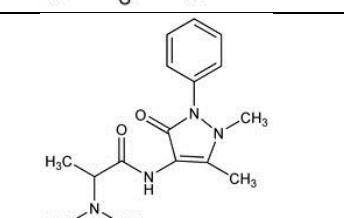
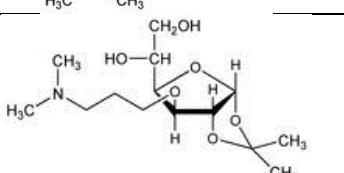
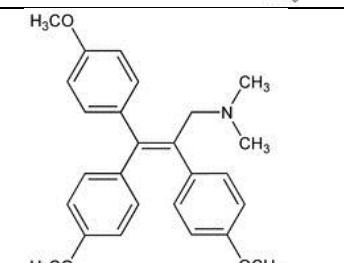
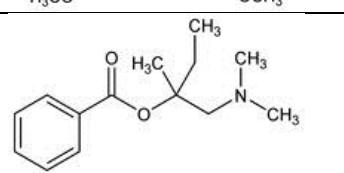
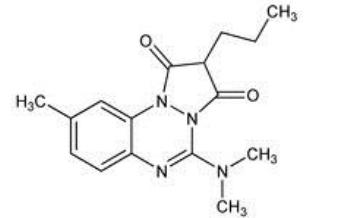
Ar-DMsulfamide	-0.342	131.7	1.644	0.8
Cyazofamid	-0.061	165.1	1.587	-6.1
Dacarbazine	0.295	178.5	1.298	0.8
Daminozide	-0.143	122.5	1.395	3.5
DMpyrrole	-0.445	123.9	1.402	3.3
DMS	-0.262	130.3	1.649	2.2
Thiotixene	-0.233	134.2	1.652	0
UDMH	-0.322	115.1	1.458	7.3

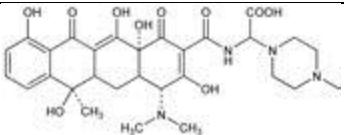
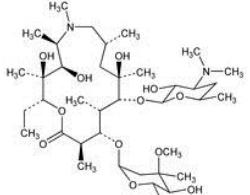
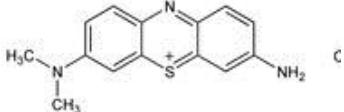
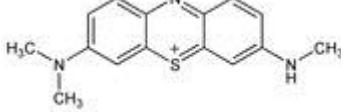
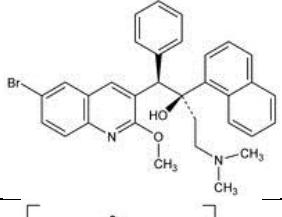
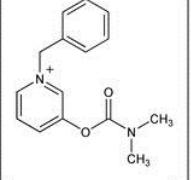
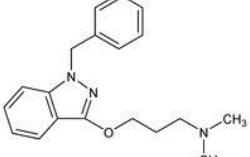
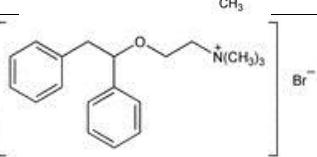
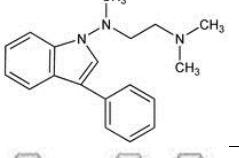
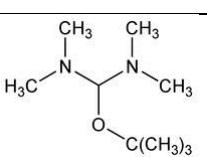
Category 5: (CH₃)₂N⁺-R₂

BenzylDMdodecylamine	0.27	121.4	1.526	Cation
Choline	0.071	123.2	1.503	Cation
Tetramethylamine	0.329	120	1.497	Cation

Table S4: List of potential NDMA precursors from Merck index search (n = 233)

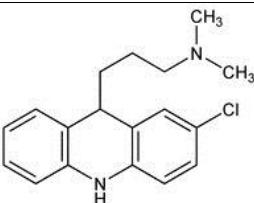
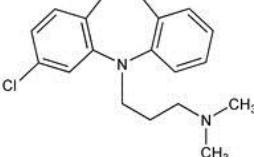
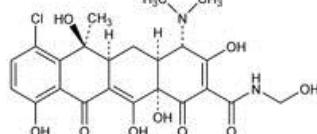
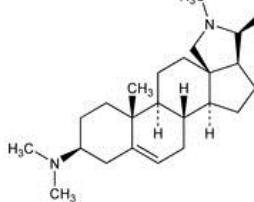
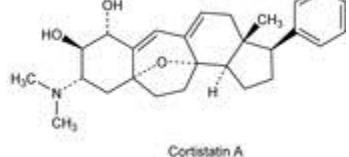
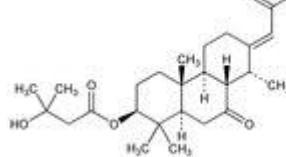
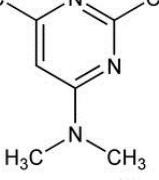
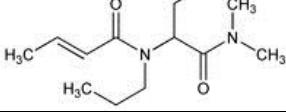
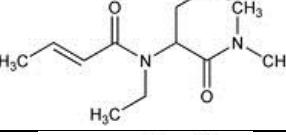
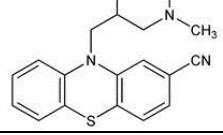
Name	Structure	Merck Number	Category	Comments
4-(Dimethylamino)-benzoic acid		M4524	2	Therapeutic
Acepromazine		M1303	1	Veterinary therapeutic
Aclacinomycins		M1374	1	Therapeutic. Antitumour antibiotic, produced by <i>Streptomyces galilaeus</i> .
Adinazolam		M1418	1	Therapeutic
Afatinib		M1439	1	Therapeutic
Ahistan		M546	1	Therapeutic
Alcian blue		M1482	3 and 5	Biological stain. Used in textiles.
Almotriptan		M1568	1	Therapeutic
Altretamine		M1586	2	Therapeutic. Insect chemosterilant.
Ambutonium bromide		M1651	5	Therapeutic

Amicetin		M1661	1	Antibiotic activity. Natural product.
Aminocarb		M1698	2	Insecticide.
Aminopentamide		M1725	1	Therapeutic. Veterinary therapeutic
Aminopromazine		M1733	1	Therapeutic. Veterinary therapeutic.
Aminopropylon		M33	1	Therapeutic
Amiprilose		M1750	1	Therapeutic
Amotriphene		M560	1	Therapeutic
Amylocaine		M1877	1	Therapeutic
Apazone		M1983	3	Therapeutic

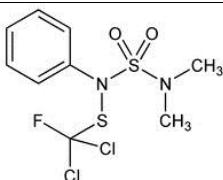
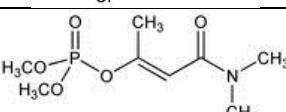
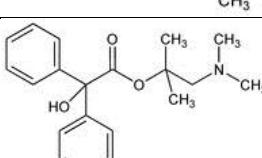
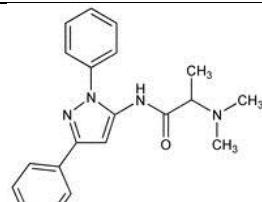
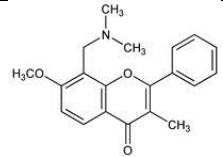
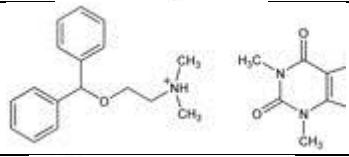
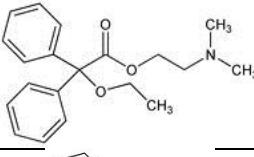
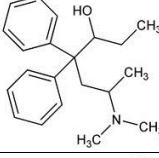
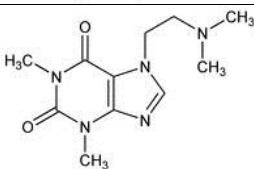
Apicycline		M53	3	Therapeutic (antibacterial).
Azithromycin		M2177	1	Therapeutic (antibacterial). Veterinary therapeutic (antibacterial).
Azure A		M2190	2	Biological stain
Azure B		M2191	2	Biological stain
Bedaquiline		M2288	1	Therapeutic
Benzpyrinium bromide		M73	1	Therapeutic
Benzydamine		M2395	1	Therapeutic and veterinary therapeutic
Bibenzonium bromide		M587	5	Therapeutic
Binedaline		M84	1	Possible therapeutic. Never marketed.
Bis(p-dimethylamino-benzylidene)benzidine		M1030	2	Chemical reagent
Bredereck's reagent		M2643	1	Chemical reagent

Bufofenine		M2753	1	Controlled substance
Butriptyline		M2805	1	Therapeutic
Cabergoline		M2876	1	Therapeutic. Veterinary therapeutic.
Calyculin A		M2996	1	Chemical reagent
Camostat		M3000	1	Therapeutic
Cartap		M3135	1	Insecticide
Cassaidine		M3160	1	Natural product
Cassaine		M3161	1	Natural toxin (e.g. used as arrow poison).
Cefotiam		M3206	1	Therapeutic
Cethromycin		M3288	1	Therapeutic
Chirald		M3332	1	Chemical reagent (Mosher's reagent).

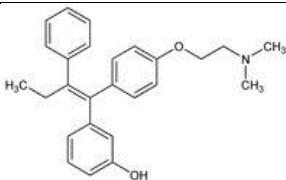
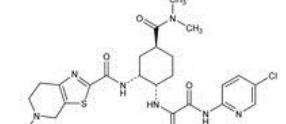
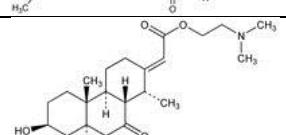
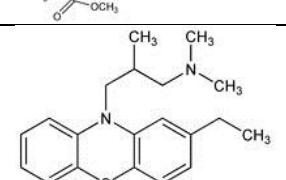
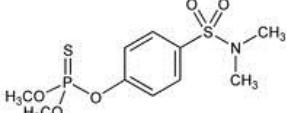
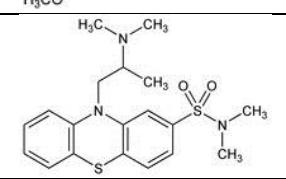
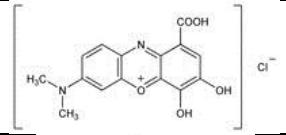
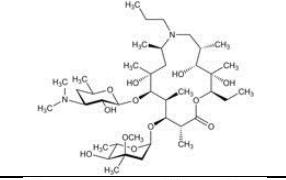
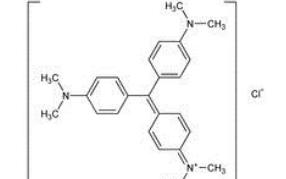
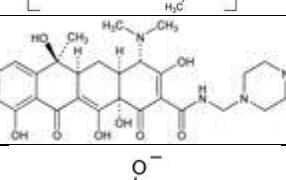
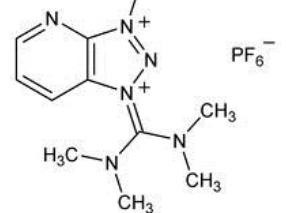
Chlophedianol		M3336	1	Therapeutic
Chloropyramine		M3434	1	Therapeutic
Chlorpromazine		M3461	1	Therapeutic. Veterinary therapeutic.
Chonemorphine		M114	1	Natural product (and antiparasitic agent).
Ciramadol		M653	1	Therapeutic
Citalopram		M3587	1	Therapeutic
Clentiazem		M3616	1	Therapeutic
Clobenzepam		M656	1	Therapeutic
Clobutinol		M3630	1	Therapeutic

Clomacran		M659	1	Therapeutic
Clomipramine		M3648	1	Therapeutic. Veterinary therapeutic.
Clomocycline		M1081	1	Therapeutic
Conessine		M3750	1	Natural product
Cortistatins		M3796	1	Natural product
Coumingine		M3823	1	Natural product
Crimidine		M668	2	Poison (used as rodenticide).
Cropropamide		M3852	1	Therapeutic
Crotethamide		M3856	1	Therapeutic
Cyamemazine		M3943	1	Therapeutic

Cyclopentolate		M4011	1	Therapeutic
Dalbavancin		M4070	1	Therapeutic
Dansyl chloride		M4083	2	Chemical reagent
DCM		M4111	2	Laser dye
Demanyl phosphate		M1103	1	
Demeclocycline		M4160	1	Therapeutic. Veterinary therapeutic.
Desosamine		M4200	1	Natural product. Component of macrolide antibiotics (therapeutic).
Desvenlafaxine		M4207	1	Therapeutic
Diamthazole dihydrochloride		M681	3	Therapeutic
Dibenzepin		M4282	1	Therapeutic

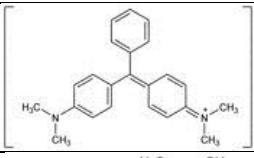
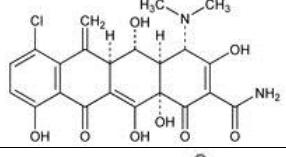
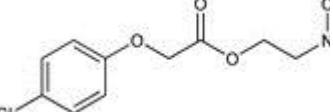
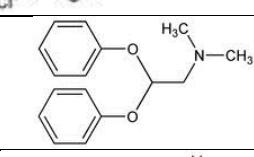
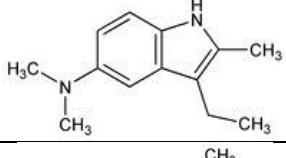
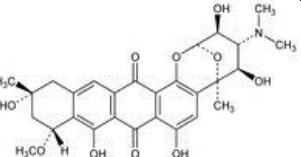
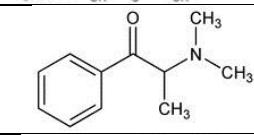
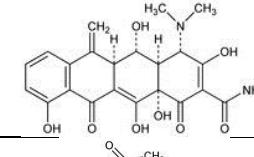
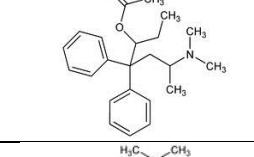
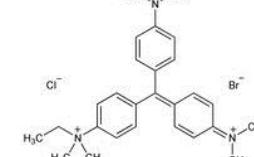
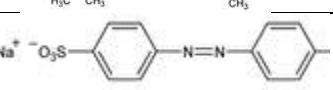
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Dicrotophos		M4367	1	Insecticide
Difemerine		M4422	1	Therapeutic
Difenamizole		M1113	1	Therapeutic
Dimefline		M4497	1	Therapeutic
Dimenhydrinate		M4500	5	Therapeutic
Dimenoxadol		M1116	1	Controlled substance (opioid).
Dimepheptanol		M695	1	Therapeutic and controlled substance (opioid).
Dimetacrine		M1117	1	Therapeutic
Dimethazan		M696	1	Therapeutic

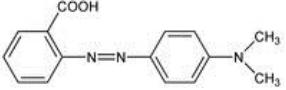
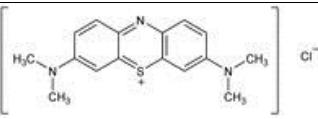
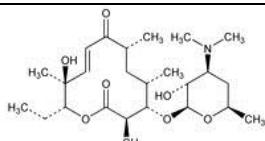
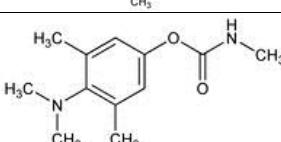
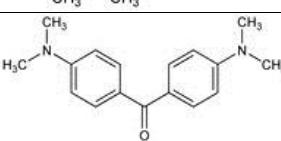
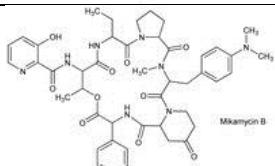
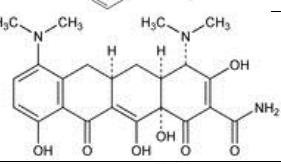
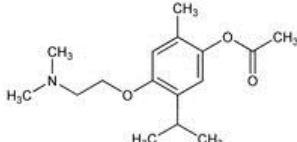
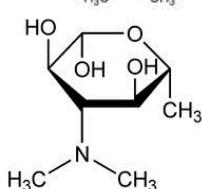
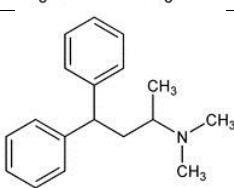
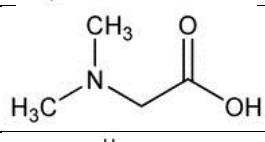
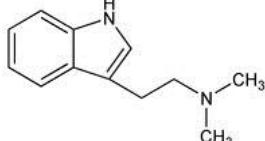
Dimethindene		M4508	1	Therapeutic
Dimethirimol		M4509	2	Fungicide
Dimethisoquin		M1118	1	Therapeutic
Dimethoxanate		M697	1	Therapeutic
Dimethylthiambutene		M1119	1	Controlled substance and veterinary therapeutic.
Dimetilan		M698	1	Insecticide
Dioxypyramidon		M704	1	Therapeutic
Dirithromycin		M4664	1	Therapeutic
DMAN		M4702	2	Chemical reagent
Doxycycline		M4758	1	Therapeutic and veterinary therapeutic.

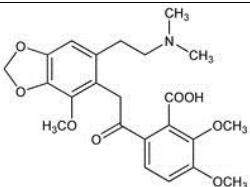
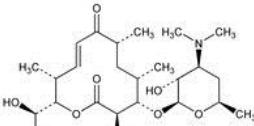
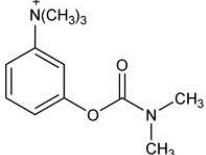
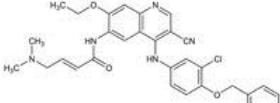
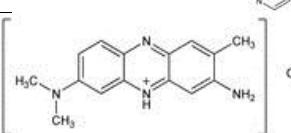
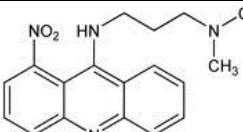
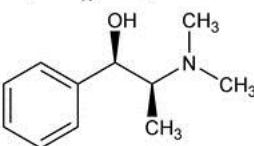
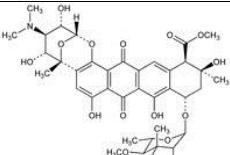
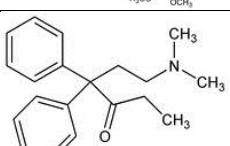
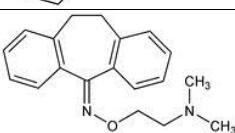
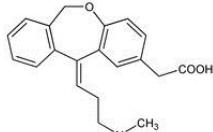
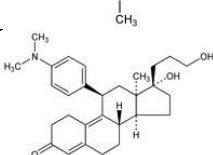
Droloxifene		M4765	1	Therapeutic
Edoxaban		M4832	1	Therapeutic
Erythrophlamine		M167	1	Natural product
Etymemazine		M728	1	Therapeutic
Famphur		M1150	4	Insecticide
Fonazine		M5528	1	Therapeutic
Gallocyanine		M5655	2	Dye. Chemical reagent.
Gamithromycin		M11761	1	Veterinary therapeutic
Gentian violet		M5700	2 and 5	Therapeutic. Veterinary therapeutic.
Guamecycline		M1182	1	Therapeutic
HATU		M5923	3	Chemical reagent

HBTU		M5924	3	Chemical reagent
Hexazinone		M6005	3	Herbicide
Holarrhenine		M235	1	Natural product
Hordenine		M6055	1	Natural product
Hydroxytetracaine		M6155	1	Therapeutic
Imipramine N-oxide		M6233	1	Therapeutic
Inosine pranobex		M6289	1	Therapeutic
Ipodate		M6385	3	Therapeutic
Iprindole		M6389	1	Therapeutic
Isoaminile		M6425	1	Therapeutic
Isomethadol		M785	1	Related to isomethadone (therapeutic).

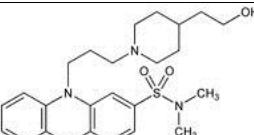
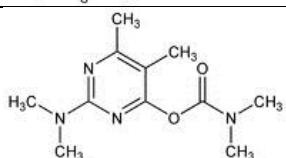
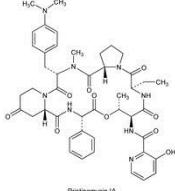
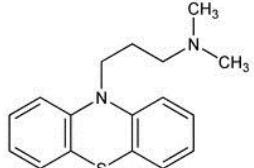
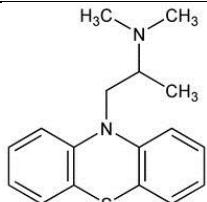
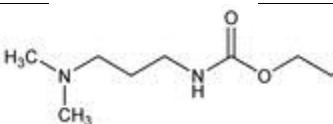
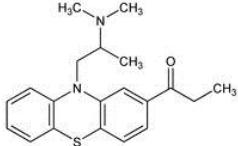
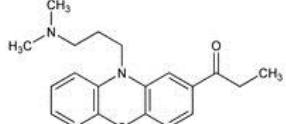
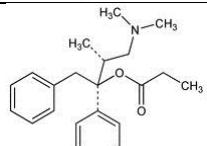
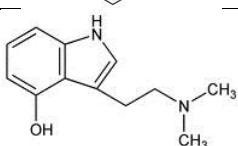
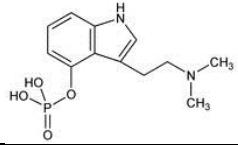
Isomethadone		M6500	1	Controlled substance (opiate).
Isopromethazine		M786	1	Therapeutic
Isothipendyl		M6543	1	Therapeutic
Itopride		M6561	1	Therapeutic
Janus green B		M6573	2	Dye. Biological stain.
Kurchessine		M256	1	Therapeutic
Kurcholessine		M257	1	Natural product. Therapeutic
Levomepromazine		M6788	1	Therapeutic
Levomethadyl acetate		M6789	1	Controlled substance (opiate). Therapeutic
Levopropoxyphene		M6793	1	Therapeutic
Lymecycline		M6959	1	Therapeutic
Macromerine		M6979	1	Natural product

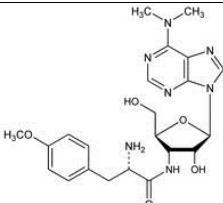
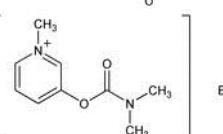
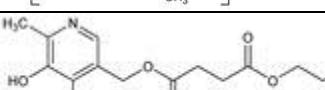
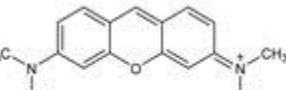
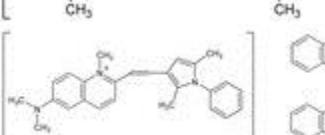
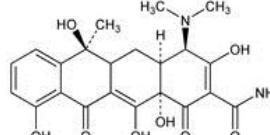
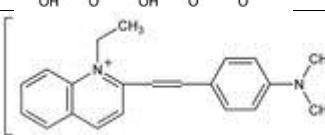
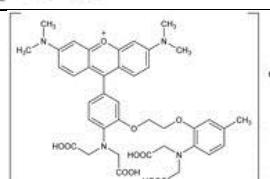
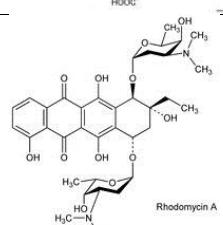
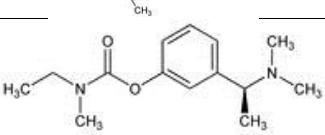
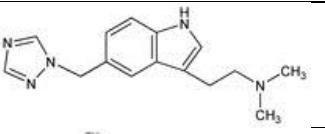
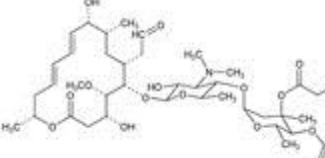
Malachite green		M7033	2 and 5	Dye. Biological stain. Veterinary therapeutic.
Meclocycline		M7119	1	Therapeutic
Meclofenoxate		M7121	1	Therapeutic. Plant growth regulator.
Medifoxamine		M7131	1	Therapeutic
Medmain		M302	2	
Melitracen		M7161	1	Therapeutic
Menogaril		M813	1	Therapeutic activity, but never developed for clinical use.
Metamfepramone		M321	1	Therapeutic, but never widely marketed.
Methacycline		M7285	1	Therapeutic
Methadyl acetate		M7287	1	Controlled substance (opiate).
Methyl green		M7424	5	Dye. Biological stain. Chemical reagent. Therapeutic. Veterinary therapeutic
Methyl orange		M7448	2	Dye. Chemical reagent.

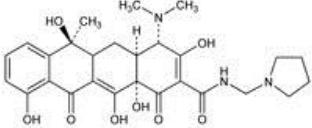
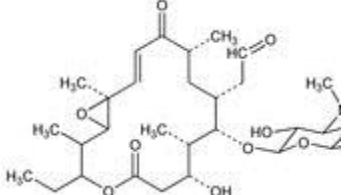
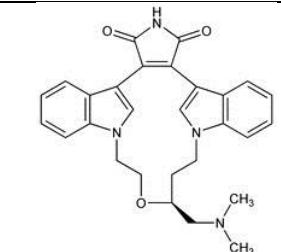
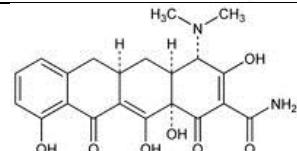
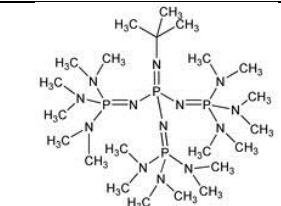
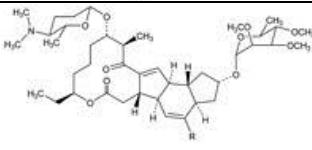
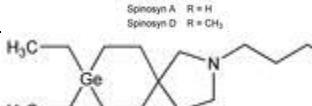
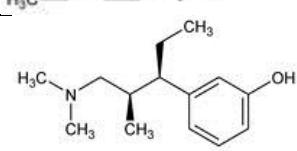
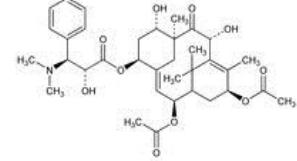
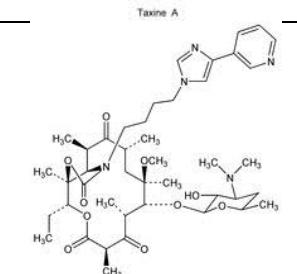
Methyl red		M7462	2	Dye. Chemical reagent
Methylene blue		M7402	2	Dye. Biological stain. Chemical reagent. Therapeutic. Veterinary therapeutic.
Methymycin		M7481	1	Natural product. Antibiotic.
Mexacarbate		M829	2	Pesticide (obsolete).
Michler's ketone		M7526	2	Used in dye manufacture.
Mikamycin		M352	2	Therapeutic
Minocycline		M7553	1 and 2	Therapeutic. Veterinary therapeutic.
Moxisylyte		M7648	1	Therapeutic
Mycaminose		M7672	1	Component of carbomycin, a therapeutic (antibiotic) and natural product.
N,N-1-Trimethyl-3,3-diphenylpropylamine		M507	1	Therapeutic
N,N-Dimethylglycine		M4539	1	Natural product
N,N-Dimethyltryptamine		M4558	1	Controlled substance

Narceine		M7774	1	Therapeutic
Neomethymycin		M7808	1	Natural product. Antibiotic.
Neostigmine		M7819	1	Therapeutic. Veterinary therapeutic.
Neratinib		M7827	1	Therapeutic
Neutral red		M7843	2	Chemical reagent. Dye. Biological stain.
Nitracrine		M7927	1	Therapeutic
N-Methylephedrine		M7410	1	Therapeutic
Nogalamycin		M8028	1	Natural product. Antibiotic therapeutic. No longer used clinically.
Normethadone		M8068	1	Controlled substance (opiate). Therapeutic.
Noxiptilin		M854	1	Therapeutic
Olopatadine		M8204	1	Therapeutic
Onapristone		M8212	2	Therapeutic

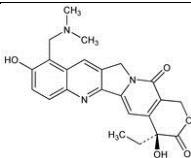
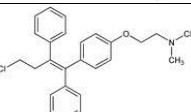
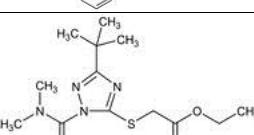
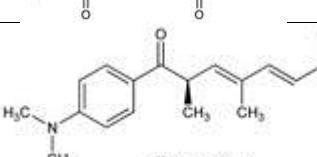
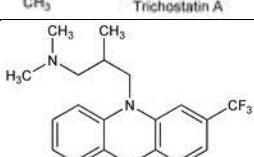
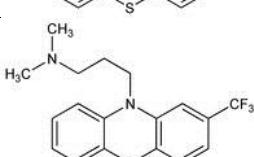
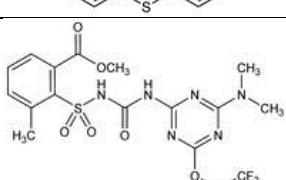
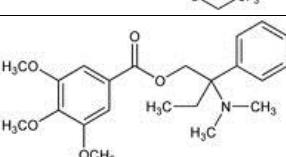
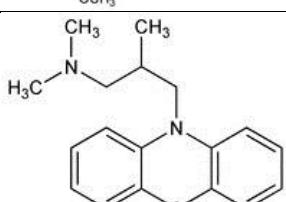
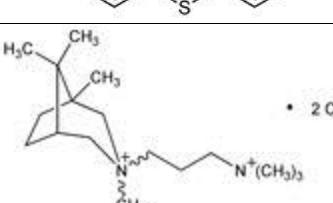
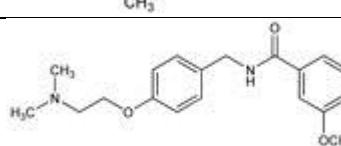
Opromazine		M8220	1	Metabolite of chlorpromazine, which is a therapeutic.
Oxapropanium iodide		M8292	5	Therapeutic
Oxomemazine		M8315	1	Therapeutic
Pactamycin		M8353	1	Natural product. Antibiotic.
p-Dimethylamino-benzaldehyde		M4522	2	Chemical reagent. Used to manufacture dyes.
p-Dimethylamino-benzalrhodanine		M4523	2	Chemical reagent
p-Dimethylamino-benzophenone		M4525	2	
Penimepcycline		M868	1	Antibiotic therapeutic
Picromycin		M8795	1	Natural product. Antibiotic.
Pipacycline		M8836	1	Therapeutic

Pipotiazine		M8865	4	Therapeutic
Pirimicarb		M8879	1	Insecticide
Pristinamycin		M9141	2	Natural product. Antibiotic therapeutic.
Promazine		M9168	1	Therapeutic. Veterinary therapeutic.
Promethazine		M9171	1	Therapeutic. Veterinary therapeutic
Propamocarb		M9182	1	Agricultural fungicide
Propiomazine		M9206	1	Therapeutic. Veterinary therapeutic.
Propionylpromazine		M9213	1	Veterinary therapeutic
Propoxyphene		M9222	1	Controlled substance (opiate).
Psilocin		M9304	1	Controlled substance
Psilocybin		M9305	1	Controlled substance. Therapeutic.

Puromycin		M9324	2	Chemical reagent
Pyridostigmine Bromide		M9360	1	Therapeutic. Veterinary therapeutic.
Pyrisuccideanol		M9374	1	Therapeutic
Pyronine Y		M9389	2 and 5	Bacterial and biological stain.
Pyrvinium Pamoate		M9406	2	Therapeutic
Quatrimycin		M9414	1	Antibiotic
Quinaldine Red		M9435	2	Chemical reagent
Rhod-2		M9575	2	Chemical reagent
Rhodomycins		M9585	1	Natural product. Antibiotic.
Rivastigmine		M9639	1	Therapeutic
Rizatriptan		M9640	1	Therapeutic
Rokitamycin		M9649	1	Therapeutic

Rolitetracycline		M9651	1	Therapeutic
Rosaramicin		M9662	1	Therapeutic
Ruboxistaurin		M9693	1	Therapeutic
Sancycline		M922	1	Antibiotic
Schwesinger P4 base		M9805	4	Chemical reagent
Spinosyns		M10147	1	Insecticide. Veterinary therapeutic.
Spirogermanium		M10155	1	Therapeutic
Tapentadol		M10459	1	Controlled substance (opiate). Therapeutic
Taxine		M10485	1	Natural product. Poison found in yew tree.
Telithromycin		M10531	1	Therapeutic

Tetracaine hydrochloride		M10603	1	Therapeutic. Veterinary therapeutic.
Tetrakis(dimethylamino)-ethylene		M10636	3	Chemical reagent.
Tetramethyl-diaminobutane		M10643	1	Natural product.
Thiazesim		M10727	1	Therapeutic
Thozalinone		M10803	3	Therapeutic
Tigecycline		M10858	1 and 2	Therapeutic
Tildipirosin		M11772	1	Veterinary therapeutic
Tilidine		M10864	1	Controlled substance (opiate). Therapeutic
Toldimfos Sodium		M10942	2	Veterinary therapeutic
Tolonium Chloride		M10949	2	Therapeutic. Dye. Biological stain.
Tolpropamine		M10952	1	Therapeutic

Topotecan		M10977	1	Therapeutic
Toremifene		M10979	1	Therapeutic
Triazamate		M11032	1	Pesticide
Trichostatin		M11084	2	Natural product. Antibiotic.
Trifluomeprazine		M11115	1	Veterinary therapeutic
Triflupromazine		M11123	1	Therapeutic. Veterinary therapeutic.
Triflusulfuron-methyl		M11127	2	Herbicide
Trimebutine		M11138	1	Therapeutic
Trimeprazine		M11143	1	Therapeutic. Veterinary therapeutic.
Trimethidinium methosulfate		M506	5	Therapeutic
Trimethobenzamide		M11147	1	Therapeutic

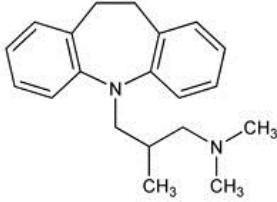
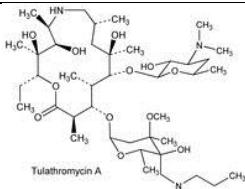
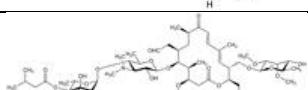
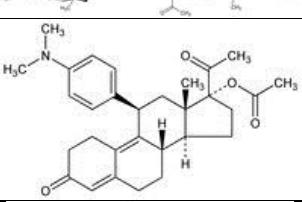
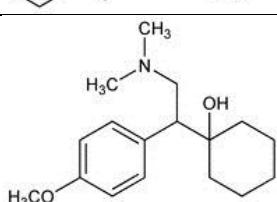
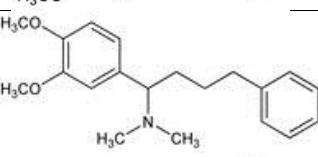
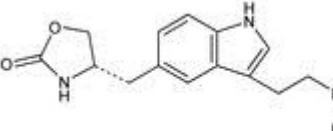
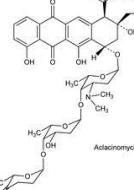
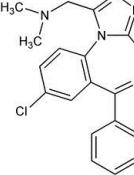
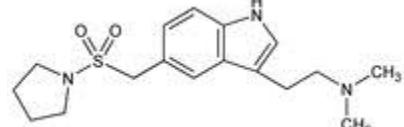
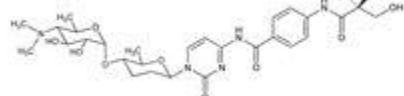
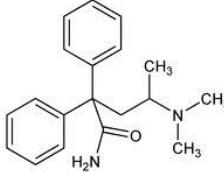
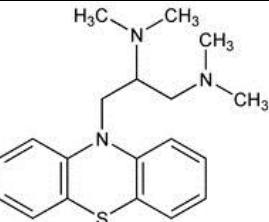
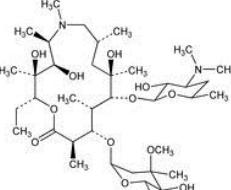
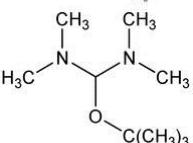
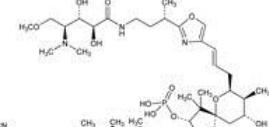
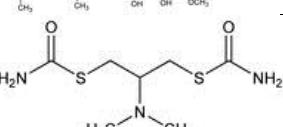
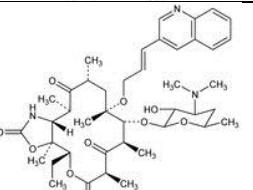
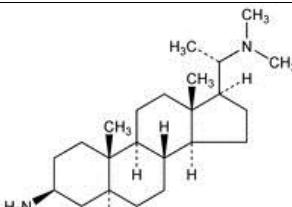
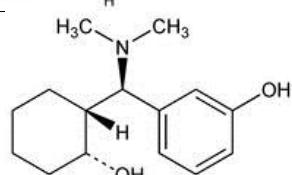
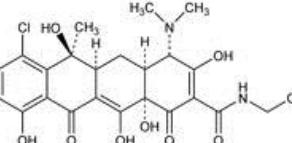
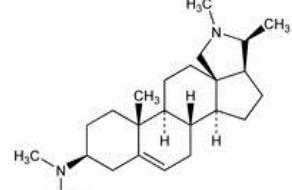
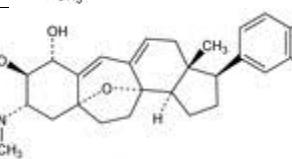
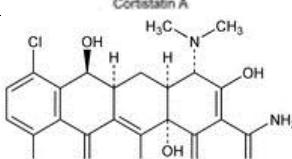
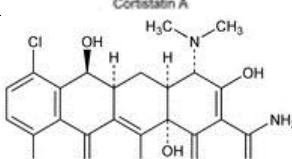
Trimipramine		M11164	1	Therapeutic
Tulathromycin		M11260	1	Veterinary therapeutic
Tylvalosin		M11759	1	Veterinary therapeutic
Ulipristal acetate		M11300	2	Therapeutic
Vamicamide		M519	1	Therapeutic
Venlafaxine		M11410	1	Therapeutic
Vetrebutine		M11438	1	Veterinary therapeutic
Zolmitriptan		M11660	1	Therapeutic

Table S5: Amines from the Merck index search with attributes to be reactive NDMA precursors, based on qualitative assessment of chemical functionality (n = 68)

Name	Structure	Merck Number	Category	Comments	Chemical class
Aclacinomycins		M1374	1	Therapeutic. Antitumour antibiotic, produced by <i>Streptomyces galilaeus</i> .	Macrolide
Adinazolam		M1418	1	Therapeutic	
Almotriptan		M1568	1	Therapeutic	
Amicetin		M1661	1	Antibiotic	Macrolide
Aminopentamide		M1725	1	Therapeutic. Veterinary therapeutic	

Aminopromazine		M1733	1	Therapeutic. Veterinary therapeutic.	Phenothiazine derivative
Azithromycin		M2177	1	Therapeutic (antibacterial). Veterinary therapeutic (antibacterial).	Macrolide
Bredereck's reagent		M2643	1	Chemical reagent	
Calyculin A		M2996	1	Chemical reagent	
Cartap		M3135	1	Insecticide	
Cethromycin		M3288	1	Therapeutic	Macrolide

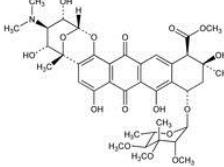
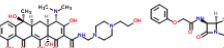
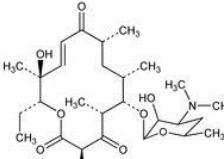
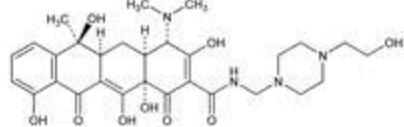
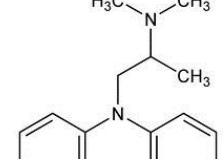
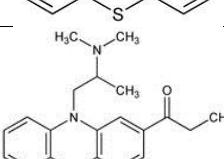
Chonemorphine		M114	1	Natural product (and antiparasitic agent).
Ciramadol		M653	1	Therapeutic
Clomocycline		M1081	1	Therapeutic
Conessine		M3750	1	Natural product
Cortistatins		M3796	1	Steroid alkaloid
Demeclacycline		M4160	1	Natural product
				Therapeutic. Veterinary therapeutic.
				Tetracycline

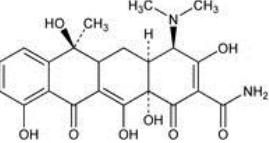
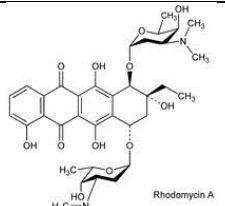
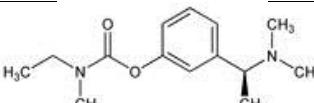
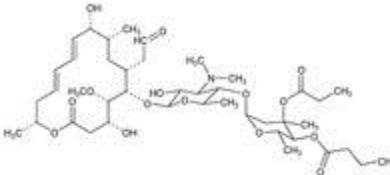
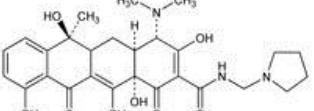
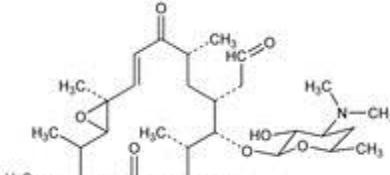
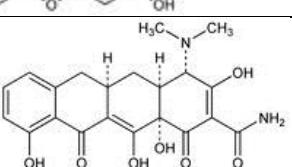
Desosamine		M4200	1	Natural product. Component of macrolide antibiotics (therapeutic).	Macrolide component.
Dimefline		M4497	1	Therapeutic	
Dimenhydrinate		M4500	5	Therapeutic	
Dimepheptanol		M695	1	Therapeutic and controlled substance (opioid).	Opioid
Dimethylthiambutene		M1119	1	Controlled substance and veterinary therapeutic.	
Dirithromycin		M4664	1	Therapeutic	Macrolide
Doxycycline		M4758	1	Therapeutic and veterinary therapeutic.	Tetracycline

Fonazine		M5528	1	Therapeutic	Phenothiazine derivative
Gamithromycin		M11761	1	Veterinary therapeutic	Macrolide
Guamecycline		M1182	1	Therapeutic	Tetracycline
Holarrhenine		M235	1	Natural product	Steroid alkaloid
Inosine pranobex		M6289	1	Therapeutic	
Isoaminile		M6425	1	Therapeutic	
Isothipendyl		M6543	1	Therapeutic	Phenothiazine derivative

Kurcholessine		M257	1	Natural product. Therapeutic	Steroid alkaloid
Levomethadyl acetate		M6789	1	Controlled substance (opiate). Therapeutic	Opiate
Lymecycline		M6959	1	Therapeutic	Tetracycline
Meclocycline		M7119	1	Therapeutic	Tetracycline
Menogaril		M813	1	Therapeutic activity, but never developed for clinical use.	Macrolide structure.
Metamfepramone		M321	1	Therapeutic, but never widely marketed.	
Methacycline		M7285	1	Therapeutic	Tetracycline

Methadyl acetate		M7287	1	Controlled substance (opiate).	Opiate
Methymycin		M7481	1	Natural product. Antibiotic.	Macrolide
Minocycline		M7553	1 and 2	Therapeutic. Veterinary therapeutic.	Tetracycline
Mycaminose		M7672	1	Component of carbomycin, a therapeutic (antibiotic) and natural product.	Macrolide component
N,N-1-Trimethyl-3,3-diphenylpropylamine		M507	1	Therapeutic	
Neomethymycin		M7808	1	Natural product. Antibiotic.	Macrolide
N-Methylephedrine		M7410	1	Therapeutic	

Nogalamycin		M8028	1	Natural product. Antibiotic therapeutic. No longer used clinically.	Macrolide
Penimepicycline		M868	1	Antibiotic therapeutic	
Picromycin		M8795	1	Natural product. Antibiotic.	Macrolide
Pipacycline		M8836	1	Therapeutic	Tetracycline
Promethazine		M9171	1	Therapeutic. Veterinary therapeutic	Phenothiazine derivative
Propiomazine		M9206	1	Therapeutic. Veterinary therapeutic.	Phenothiazine derivative

Quatrimycin		M9414	1	Antibiotic	Tetracycline
Rhodomycins		M9585	1	Natural product. Antibiotic.	Macrolide
Rivastigmine		M9639	1	Therapeutic	
Rokitamycin		M9649	1	Therapeutic	Macrolide
Rolitetracycline		M9651	1	Therapeutic	Tetracycline
Rosaramicin		M9662	1	Therapeutic	Macrolide
Sancycline		M922	1	Antibiotic	Tetracycline

Spinosyns		M10147	1	Insecticide. Veterinary therapeutic.	Macrolide
Taxine		M10485	1	Natural product. Poison found in yew tree.	
Telithromycin		M10531	1	Therapeutic	Macrolide
Tigecycline		M10858	1 and 2	Therapeutic	Tetracycline
Tildipirosin		M11772	1	Veterinary therapeutic	Macrolide
Tilidine		M10864	1	Controlled substance (opiate). Therapeutic	Opiate

Relative stereochemistry

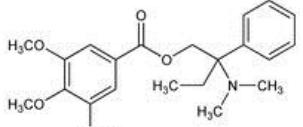
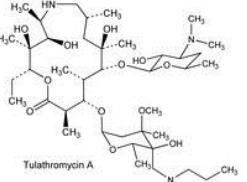
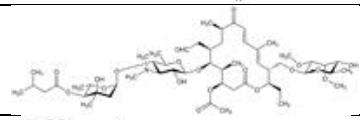
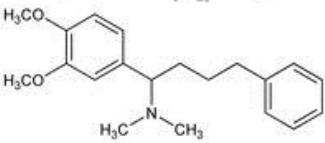
Trimebutine		M11138	1	Therapeutic
Tulathromycin		M11260	1	Veterinary therapeutic Macrolide
Tylvalosin		M11759	1	Veterinary therapeutic Macrolide
Vetرابutine		M11438	1	Veterinary therapeutic

Table S6: Molecular descriptors for the DMA group in the 25 selected potential NDMA precursors, with potentially the most potent shown in bold

Chemical	Partial charge (M062X)	Planarity (M062X) (°)	Bond length (M062X) (Å)	pK _a
Adinazolam	-0.358	127.8	1.46	6.8
Almotriptan	-0.481	121.6	1.457	8.8
Aminopentamide	-0.417	126.9	1.472	10.7
Calyculin A	-0.006	130.2	1.477	7.6
Cartap	-0.141	135.6	1.46	7
Chonemorphine	-0.498	128.2	1.475	9.9
Conessine	-0.552	121.7	1.472	9.6
Cortistatins	-0.461	131	1.464	8.1
Desosamine	-0.443	127.1	1.464	8.4
Dimefline	-0.31	122.1	1.465	8.1
Dimethylthiambutene	-0.555	122.1	1.471	8.8
Inosine Pranobex	-0.343	121.5	1.459	9
Isoaminile	-0.388	145.4	1.453	6.7
Isothipendyl	-0.553	128	1.467	8.4
Kurcholessine	-0.241	123.9	1.475	8.9
Mycaminose	-0.45	125.7	1.474	10.1
N,N-1-Trimethyl-3,3-diphenylpropylamine	-0.347	127.7	1.473	8.5
Neomethymycin	-0.467	122.3	1.471	8.7
N-Methylephedrine	-0.529	127.4	1.472	9.4
Promethazine	-0.539	127.7	1.469	8.3
Rivastigmine	-0.409	123.2	1.467	8.4
Spinosyns	-0.429	127.3	1.465	8.7
Taxine	-0.289	123	1.464	7.4
Tilidine	-0.629	127	1.472	9
Vetrabutine	-0.511	124.3	1.472	8.3

Table S7: Criteria for defining potentially reactive NDMA precursors, based on descriptors for seven most reactive precursors from Table S2

Descriptor	Min	Max
Partial charge	-0.522	-0.252
Planarity	121.3	127.7
Bond length (Å)	1.454	1.473
pK_a	8.3	10.1

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