COBALT AND COBALT COMPOUNDS

The agents considered herein include (a) metallic cobalt, (b) cobalt alloys (including cobalt-containing medical implants) and (c) cobalt compounds. Organic cobalt-containing agents (e.g., vitamin B_{12}) are not covered comprehensively in this monograph.

1. Chemical and Physical Data

1.1 Synonyms, trade names and molecular formulae

Synonyms, trade names and molecular formulae for cobalt, cobalt alloys and cobalt compounds are presented in Table 1. The cobalt alloys and compounds given in Table 1 are not an exhaustive list, nor are they necessarily the most commercially important cobalt-containing substances; the list indicates the range of cobalt alloys and compounds available.

Table 1. Synonyms (Chemical Abstracts Service names are given in bold type), trade names and atomic or molecular formulae of cobalt and cobalt compounds

Chemical name	Chem. Abstr. Services Reg. No.[a]	Synonyms and trade names	Formulae
Metallic cobalt			
Cobalt	7440-48-4	C.I. 77320; cobalt element; cobalt-59	Co
Cobalt alloys			
Cobalt-chromium alloy[b]	11114-92-4 (91700-55-9)	**Cobalt alloy (nonbase), Co, Cr; chromium alloy (nonbase), Co, Cr**	Co·Cr
Nickel-based cobalt alloy[b]	11068-91-0 (12604-26-1; 12616-60-3; 12616-61-4; 12624-82-7; 12630-37-4; 12636-02-1; 12672-01-4; 12774-12-8; 37323-85-6; 64941-39-5)	**Nickel alloy (base), Ni 47-59, Co 17-20, Cr 13-17, Mo 4.5-5.7, Al 3.7-4.7, Ti 3-4, Fe 0-1, C 0-0.1 (AISI 687)** APK 1; Astroloy; Cabot 700; NiCo18Cr15MoAlTi; Nimonic AP 1; NK17CADT; PM-ATS 380; PWA 1013; R 77; Rene 77; U 700; U 700m; U700PM; Udimet 700	C·Al·Co·Cr·Fe·Mo·Ni·Ti

Table 1 (contd)

Chemical name	Chem. Abstr. Services Reg. No.[a]	Synonyms and trade names	Formulae
***Metallic cobalt* (contd)**			
Cobalt-chromium-nickel-tungsten alloy	12638-07-2 (12618-75-6; 12748-86-6; 37329-48-9; 52827-91-5; 62449-84-7)	**Cobalt alloy (base), Co 48–58, Cr 24–26, Ni 9.5–12, W 7–8, Fe 2, Mn 0–1, Si 0–1, C 0.4–0.6 (ASTM A567-2)** AFNOR K-C25NW; AMS 5382; Co X-40; G-X 55; CoCrNiW 55 25; Haynes Stellite 31; HS 31; 31H114; K-C25NW; MAS 5382; PN 31H114; S-31; Stellite 31; Stellite 31 X 40; Stellite X40; 45VF; X 40	C·Co·Cr·Fe·Mn·Ni·Si·W
Cobalt-chromium-molybdenum alloy[b]	12629-02-6 (8064-15-1; 11068-92-1; 12618-69-8; 55345-18-1; 60382-64-1; 83272-15-5; 85131-98-2; 94076-26-3; 115201-64-4)	**Cobalt alloy (base), Co 56–68, Cr 25–29, Mo 5–6, Ni 1.8–3.8, Fe 0–3, Mn 0–1, Si 0–1, C 0.2–0.3 (AST A567-1)** Akrit CoMo35; AMS 5385D; Celsit 290; F 75; Haynes Stellite 21; HS 21; Protasul-2; Stellite 21; Vinertia; Vitallium; X25CoCrMo62 28 5; Zimaloy	C·Co·Cr·Fe·Mn·Mo·Ni·Si
Cobalt compounds			
Cobalt(II) acetate	71-48-7 (33327-32-1; 68279-06-1; 73005-84-2)	**Acetic acid, cobalt(2+) salt;** bis(acetato)cobalt; cobalt acetate; cobalt(2+) acetate; cobalt diacetate; cobaltous acetate; cobaltous diacetate	$Co(CH_3CO_2)_2$
Cobalt(II) acetate tetrahydrate	6147-53-1	**Bis(acetato)tetraquacobalt**	$Co(CH_3CO_2)_2 \cdot 4H_2O$
Cobalt(III) acetate	917-69-1	**Acetic acid, cobalt(3+) salt;** cobalt(3+) acetate; cobaltic acetate; cobalt triacetate	$Co(CH_3CO_2)_3$
Cobalt(II) carbonate	513-79-1	**Carbonic acid, cobalt(2+) salt (1:1);** C.I. 77353; cobalt carbonate (1:1); cobalt(2+) carbonate; cobalt monocarbonate; cobaltous carbonate	$CoCO_3$

Table 1 (contd)

Chemical name	Chem. Abstr. Services Reg. No.[a]	Synonyms and trade names	Formulae
Cobalt compounds **(contd)**			
Cobalt(II) carbonate hydroxide (1:1)	12069–68–0	Basic cobalt carbonate; carbonic acid, cobalt complex; cobalt carbonate hydroxide; cobalt, (carbonato)dihydroxydi–; **cobalt, [.mu.-[carbonato-(2-)-0:0']]dihydroxydi-**	$CoCO_3 \cdot Co(OH)_2$
Cobalt(II) carbonate hydroxide (2:3)	12602–23–2	**Cobalt, bis(carbonato(2-))-hexahydroxypenta-;** cobalt, bis(carbonato)hexahydroxypenta-; cobalt carbonate hydroxide; cobalt hydroxide carbonate	$2CoCO_3 \cdot 3Co(OH)_2$
Cobalt(II) carbonate hydroxide (2:3) monohydrate	51839–24–8	Basic cobalt carbonate; carbonic acid, cobalt(2+) salt, basic; **cobalt, bis(carbonato-(2-))hexahydroxypentamonohydrate;** cobaltous carbonate, basic	$2CoCO_3 \cdot 3Co(OH)_2 \cdot H_2O$
Cobalt(II) chloride	7646–79–9 (1332–82–7)	**Cobalt chloride ($CoCl_2$);** cobalt dichloride; cobaltous chloride	$CoCl_2$
Cobalt(II) chloride hexahydrate	7791–13–1	**Cobalt chloride, hexahydrate;** cobalt dichloride hexahydrate; cobaltous chloride hexahydrate	$CoCl_2 \cdot 6H_2O$
Cobalt(II) hydroxide	21041–93–0 (1307–85–3)	Cobalt dihydroxide; **cobalt hydroxide ($Co(OH)_2$);** cobalt(2+) hydroxide; cobaltous hydroxide	$Co(OH)_2$
Cobalt(III) hydroxide	1307–86–4	**Cobalt hydroxide ($Co(OH)_3$);** cobaltic hydroxide; cobalt trihydroxide	$Co(OH)_3$
Cobalt(II) naphthenate	61789–51–3	Cobalt naphthenates; naftolite; naphthenic acid, cobalt salt; **naphthenic acids, cobalt salts**	Unspecified
		Cobalt Nap–All; Naphthex Co; 8SN–Co	
Cobalt(II) nitrate	10141–05–6 (14216–74–1; 19154–72–4)	Cobalt bis(nitrate); cobalt(2+) nitrate; cobaltous nitrate; **nitric acid, cobalt(2+) salt**	$Co(NO_3)_2$

Table 1 (contd)

Chemical name	Chem. Abstr. Services Reg. No.[a]	Synonyms and trade names	Formulae
Cobalt compounds **(contd)**			
Cobalt(II) nitrate hexahydrate	10026-22-9 (13478-32-5)	Cobalt dinitrate hexahydrate; cobalt nitrate hexahydrate; cobalt(2+) nitrate hexahydrate; cobalt(II) nitrate hydrate; cobaltous nitrate hexahydrate; **nitric acid, cobalt(2+) salt, hexahydrate**	$Co(NO_3)_2 \cdot 6H_2O$
Cobalt(II) molybdenum(VI) oxide	13762-14-6 (12205-99-1; 14566-03-1; 63511-60-4)	Cobalt molybdate; cobalt molybdate(VI); cobalt(2+) molybdate; **cobalt molybdenum oxide ($CoMoO_4$);** cobaltous molybdate; cobalt monomolybdate; molybdenum cobaltate; molybdenum cobalt oxide; molybdic acid (H_2MoO_4), cobalt(2+) salt (1:1)	$CoMoO_4$
Cobalt(II) oxide	1307-96-6	C.I. 77322; C.I. Pigment Black 13; cobalt black; cobalt monoxide; cobalt monooxide; cobaltous oxide; **cobalt oxide (CoO);** cobalt(2+) oxide; monocobalt oxide	CoO
		Zaffre	
Cobalt(II,III) oxide	1308-06-1 (12314-25-9; 25729-03-7)	Cobaltic-cobaltous oxide; cobalto-cobaltic oxide; cobalto-cobaltic tetroxide; cobaltosic oxide; **cobalt oxide (Co_3O_4);** cobalt tetraoxide; tricobalt tetraoxide; tricobalt tetroxide	Co_3O_4
Cobalt(III) oxide	1308-04-9 (12314-25-9; 25729-03-7)	C.I. 77323; cobaltic oxide; **cobalt oxide (Co_2O_3);** cobalt(3+) oxide; cobalt peroxide; cobalt sesquioxide; cobalt trioxide;dicobalt oxide; dicobalt trioxide	Co_2O_3
Cobalt(III) oxide monohydrate	12016-80-7 (61864-72-0)	**Cobalt hydroxide oxide (Co(OH)O);** cobalt(III) hydroxide oxide; cobalt oxide hydroxide; cobalt oxyhydroxide	Co(OH)O or $Co_2O_3 \cdot H_2O$

Table 1 (contd)

Chemical name	Chem. Abstr. Services Reg. No.[a]	Synonyms and trade names	Formulae
***Cobalt compounds* (contd)**			
Cobalt(II) sulfate	10124-43-3 (10393-49-4)	Cobalt monosulfate; cobaltous sulfate; cobalt sulfate (1:1); cobalt(2+) sulfate; cobalt sulphate; **sulfuric acid, cobalt(2+) salt (1:1)**	$CoSO_4$
Cobalt(II) sulfide	1317-42-6	Cobalt monosulfide; cobaltous sulfide; cobalt(2+) sulfide	CoS
Dicobalt octacarbonyl	10210-68-1 (12553-61-6; 14525-26-9; 19998-88-0; 24917-04-2; 90043-99-5)	Cobalt, di-.mu.-carbonylhexacarbonyldi-; **cobalt tetracarbonyl dimer**	$[Co(CO)_4]_2$ or $Co_2(CO)_8$
Tetracobalt dodecacarbonyl	17786-31-1 (12083-62-9; 19212-11-4; 19478-05-8; 19495-98-8; 20623-64-7; 28963-39-5)	**Cobalt, tri-.mu.-carbonyl-nonacarbonyltetra-**	$[Co(CO)_3]_4$ or $Co_4(CO)_{12}$

[a]Replaced CAS Registry Numbers are given in parentheses.

[b]Approximately 5000 alloys of cobalt with other metals are listed by the Chemical Abstracts Registry Service, of which cobalt is the base metal for approximately 2000. Chromium is contained in approximately 1400 of these alloys and nickel in approximately 1500. An example of each is listed here.

1.2 Chemical and physical properties of the pure substances

Selected chemical and physical properties of cobalt and cobalt compounds covered in this monograph are presented in Table 2.

Metallic cobalt

Cobalt metal was isolated by the Swedish scientist G. Brandt in 1735; in 1780, T.O. Bergman established cobalt as an element (Donaldson, 1986).

Cobalt exists in two allotropic forms. The hexagonal close-packed form is more stable at temperatures below 417°C, and the face-centred cubic form at

Table 2. Physical properties of cobalt and cobalt compounds[a]

Chemical name	Atomic/ molecular weight	Melting-point (°C)	Typical physical description	Solubility
Metallic cobalt				
Cobalt	58.93	1495 (boiling-point, 2870)	Silver-grey, hard, magnetic, ductile, somewhat malleable metal	Practically insoluble in water Readily soluble in dilute nitric acid Readily soluble in hydrofluoric acid and readily in sulfuric and hydrochloric acids[b]
Cobalt compounds				
Cobalt(II) acetate	177.03	-	Light-pink crystals	Readily soluble in water
(tetrahydrate)	249.08	Loses four H_2O at 140	Red-violet monoclinic, deliquescent	Soluble in water, dilute acids, pentyl acetate and alcohols
Cobalt(III) acetate	236.07	100 (decomposes)	Dark-green, very hygroscopic powder or green crystals	Soluble in water, acetic acid, ethanol, *n*-butanol Aqueous solutions hydrolyse slowly at room temperature, rapidly at 60–70°C
Cobalt(II) carbonate	118.94	Decomposes	Red, trigonal	Practically insoluble in water, ammonium hydroxide, ethanol or methyl acetate Soluble in acids
Cobalt(II) carbonate hydroxide (2:3)	516.73	Decomposes[c]	Pale-red powder, usually containing some H_2O	Practically insoluble in water Soluble in dilute acids and ammonium carbonate solution
(monohydrate)	534.74	Decomposes[d]	Violet-red crystals	Insoluble in cold water Decomposes in hot water Soluble in acid and ammonium carbonate solution
Cobalt(II) chloride	129.84	724 (in HCl gas) decomposes at 400 on long heating in air	Pale-blue, hygroscopic leaflets; colourless in very thin layers; turns pink on exposure to moist air	Soluble in water (450 g/l at 7°C; 1050 g/l at 96°C), ethanol (544 g/l), acetone (86 g/l), methanol (385 g/l), glycerol and pyridine Slightly soluble in diethyl ether

Table 2 (contd)

Chemical name	Atomic/ molecular weight	Melting-point (°C)	Typical physical description	Solubility
(hexahydrate)	237.93	86; loses four H_2O at 52–56, an additional H_2O by 100 and another H_2O at 110	Pink to red, slightly deliquescent, monoclinic, prismatic; turns blue when heated or when hydrochloric or sulfuric acid is added; slight odour[e]	Soluble in ethanol and in water (767 g/l at 0°C; 1907 g/l at 100°C), acetone, diethyl ether (2.9 g/l) and glycerol
Cobalt(II) hydroxide	92.95	Decomposes	Blue-green or rose-red powder or microscopic crystals	Very slightly soluble in water (0.0032 g/l) Soluble in acid and ammonium salts Insoluble in aqueous hydroxide solutions
Cobalt(III) hydroxide (trihydrate)	219.91	Decomposes; loses H_2O at 100	Black-brown powder	Practically insoluble in water and ethanol Soluble in nitric acid[f], sulfuric acid and hydrochloric acid
Cobalt(II) molybdenum oxide	218.87	–	Grey-green powder	–
Cobalt naphthenate	–[g]	140[h]	Brown, amorphous powder or bluish-red solid[d]	Practically insoluble in water Soluble in ethanol, diethyl ether and oils
Cobalt(II) nitrate	182.96	100-105 (decomposes)	Pale-red powder	Soluble in water
(hexahydrate)	291.03	55–56; loses three H_2O at 55	Red, monoclinic; liquid becomes green and decomposes to the oxide above 74°C	Soluble in water (1338 g/l at 0°C; 2170 g/l at 80°C), ethanol (1000 g/l at 12.5°C), acetone and most organic solvents Slightly soluble in ammonium hydroxide

Table 2 (contd)

Chemical name	Atomic/ molecular weight	Melting-point (°C)	Typical physical description	Solubility
Cobalt(II) oxide	74.93	1795±20	Powder or crystals; colour varies from olive-green to red, depending on particle size, but the commercial material is usually dark-grey	Practically insoluble in water, ethanol and ammonium hydroxide Soluble in acids (hydrochloric, sulfuric, nitric[c])
Cobalt(II,III) oxide	240.80	895[c]; transition-point to CoO is 900–950	Black or grey crystals	Practically insoluble in water, aqua regia, hydrochloric or nitric acid Soluble in sulfuric acid and fused sodium hydroxide[d]
Cobalt(III) oxide	165.86	895 (decomposes)	Black-grey crystals	Insoluble in water and ethanol Soluble in acids
Cobalt(II) sulfate	154.99	735 (decomposes)	Dark-bluish crystals	Soluble in water (362 g/l at 20°C; 830 g/l at 100°C) and methanol (10.4 g/l at 18°C) Insoluble in ammonium hydroxide
(heptahydrate)	281.10	96.8; loses H_2O at 41.5, six H_2O at 71 and seven H_2O at 420	Pink-to-red monoclinic, prismatic	Soluble in water (604 g/l at 3°C; 670 g/l at 70°C), ethanol (25 g/l at 3°C) and methanol (545 g/l at 18°C)
Cobalt(II) sulfide	90.99		Exists in two forms: β-CoS—reddish, silver-white crystals or grey powder;	Practically insoluble in water (0.0038 g/l at 18°C) and soluble in acids
	>1116		α-CoS—black amorphous powder	Soluble in hydrochloric acid

Table 2 (contd)

Chemical name	Atomic/ molecular weight	Melting-point (°C)	Typical physical description	Solubility
Dicobalt octacarbonyl	341.95	Decomposes above 52	Orange crystals or dark-brown microcrystals	Practically insoluble in water Slightly soluble in ethanol Soluble in carbon disulfide and diethyl ether
Tetracobalt dodeca-carbonyl	571.86	–	Black crystals	Slightly soluble in cold water Soluble in benzene

[a]From Weast (1988); Budavari (1989), unless otherwise specified

[b]From Considine (1974)

[c]From CP Chemicals (1989a)

[d]From Sax & Lewis (1987)

[e]From Hall Chemical Co. (undated a)

[f]From Brauer (1965)

[g]The molecular weight of cobalt naphthenate varies, depending on the source of naphthenate and the method of preparation, ranging between 239–409 (6–10.5% cobalt) (US Environmental Protection Agency, 1983).

[h]From Bennett (1974)

[i]From Aldrich Chemical Co. (undated a)

higher temperatures (from 417°C to the melting-point; Considine, 1974). The free energy change is low, however, so that transformation from the face-centred cubic back to the hexagonal close-packed form is slow and may be inhibited by physical form (e.g., grain size or presence of other metals) (Donaldson, 1986).

The main oxidation states of cobalt are Co(2+) and Co(3+). Cobalt is stable to atmospheric oxygen, but when it is heated it is oxidized to the mixed oxide, Co(II,III) oxide (Co_3O_4); at temperatures above 900°C, Co(II) oxide (CoO) is the end-product. Cobalt metal does not combine directly with hydrogen or nitrogen but combines with sulfur, phosphorus and carbon when heated. Cobalt forms a protective layer of sulfide scale when reacted with sulfur at temperatures below 877°C or in an atmosphere of hydrogen sulfide. It forms a mixed oxide-sulfide scale in air containing sulfur dioxide (Donaldson *et al.*, 1986a).

Cobalt also has magnetic properties. Hexagonal cobalt is ferromagnetic. The cubic form is magnetically anisotropic up to about 1000°C and becomes paramagnetic at 1121°C. Single crystals show marked magnetic anisotropy up to about 250°C (Donaldson, 1986).

Cobalt compounds

With the exception of the mixed oxide (Co_3O_4), the major commercial cobalt chemicals are all compounds of cobalt in its stable +2 oxidation state. A few simple salts of cobalt in its +3 oxidation state have been used commercially (e.g., Co_2O_3), and many Co(III) complexes with ligands such as NH_3, CN^-, NO^{2-}, ethylenediaminetetraacetic acid, phthalocyanines and azo dyes have been studied extensively. These electron-donor ligands strongly stabilize Co^{3+} in solution, usually forming octahedral complexes, many of which can be isolated as stable salts. In acid solution, in the absence of such complexing ligands, Co^{2+} is the stable form and Co^{3+} is so unstable that it is reduced rapidly and spontaneously to Co^{2+}, oxidizing water to molecular oxygen. In contrast, in an alkaline solution containing ammonium hydroxide or cyanide, Co^{2+} is readily oxidized by air or hydrogen peroxide to the more stable Co^{3+} complex. The $Co^{2+} \leftrightarrows Co^{3+}$ interconversion is important in many applications of cobalt compounds, including their use as catalysts and as paint driers and in the reactions of vitamin B_{12} (National Research Council, 1977; Donaldson, 1986; Donaldson *et al.*, 1986a,b).

1.3 Technical products and impurities

(*a*) *Cobalt metal and cobalt alloys*

Cobalt metal is available for industrial use as 'broken' or 'cut' cathodes or electrolytic coarse powder. The cathodes measure 10-25 mm and weigh 20-50 g,

with a purity greater than 99.5%. The 'fine', 'extrafine' and 'superfine' cobalt powders manufactured from the cathodes have a submicrometre mean particle size and contain both allotropic crystal forms in varying proportions for different applications. Electrolytic coarse powder has a mean particle size of 4-10 μm (Cobalt Development Institute, 1989). Cobalt is also available as briquets, granules (99.5% cobalt), rondelles, powder (99.995% cobalt or 99.8% cobalt, < 2 μm), ductile strips (95% cobalt, 5% iron), high purity strips (99% cobalt), foil (99.95 or 99.99% cobalt, 0.1-1 mm), rods (99.998% cobalt, 5.0 mm) and wire (> 99.9% cobalt, 0.25-2 mm) (Sax & Lewis, 1987; American Chemical Society, 1988; Aldrich Chemical Co., 1990).

Cobalt alloys can be categorized into six broad types: superalloys (high-temperature alloys), magnetic alloys, hard-metal alloys, high-strength steels, electrodeposited alloys and alloys with special properties (Donaldson, 1986).

Elements used in cobalt alloys are classified in terms of their effect on the transition from the cubic to the hexagonal form. Enlarged-field components, which lower the transition temperature, include aluminium, boron, carbon, copper, iron, manganese, niobium, nickel, tin, titanium and zirconium. Restricted-field components, which raise the transition temperature, include antimony, arsenic, chromium, germanium, iridium, molybdenum, osmium, platinum, rhenium, rhodium, ruthenium, silicon, tantalum and tungsten (Donaldson, 1986).

Cobalt *superalloys*, a term generally applied to immensely strong, hard, wear- and corrosion-resistant alloys, were first introduced in the 1930s. They were developed for use at high temperatures where relatively severe mechanical stressing is encountered and where high surface stability is required. Their superior strength at high temperatures arises from a close-packed face-centred cubic, austentitic lattice system, which can maintain better tensile, rupture and creep properties at elevated temperatures than a body-centred cubic system (Donaldson & Clark, 1985; Donaldson, 1986).

Superalloys are usually either cobalt- or nickel-based. Cobalt-based superalloys typically consist of a cobalt-chromium face-centred cubic solid solution matrix with the following ranges of composition: chromium, 15-29.5%; nickel, ≤ 28%; tungsten, ≤ 15%; tantalum, ≤ 9%; molybdenum, ≤ 5.5%; aluminium, ≤ 4.3%; titanium, ≤ 4%; zirconium, ≤ 2.25%; carbon, 0.04-1%; and boron, ≤ 0.11%. Small quantities of niobium, yttrium, lanthanum, iron, manganese, silicon and rhenium are present; and the balance is cobalt. Chromium is added to improve resistance to hot corrosion and oxidation. Nickel is added to stabilize the face-centred cubic structure by offsetting the tendency of the refractory metals to initiate transformation to the hexagonal close-packed structure (Donaldson & Clark, 1985).

Nickel-based superalloys were developed from the nickel-chromium alloys that had been used for over 50 years for electrical resistance, which often contain cobalt. They consist of a face-centred cubic, solid solution matrix with the following ranges of composition: chromium, 1.6-28.5%; cobalt, 1.1-22%; tungsten, 0-12.5%; molybdenum, 0-10%; aluminium, 0-6%; titanium, 0-5%; boron, 0-0.62%; carbon, 0.04-0.35%; zirconium, 0-0.13%; small amounts of tantalum, hafnium, iron, manganese, silicon, vanadium, niobium, magnesium and rhenium; and the balance as nickel (Donaldson & Clark, 1985).

Vitallium (CAS No. 12629-02-6), a cobalt-chromium alloy containing 56-68% cobalt with additions of chromium (25-29%), molybdenum (5-6%) and nickel (1.8-3.8%) was developed in 1936 (ASTM A567-1; Planinsek & Newkirk, 1979; Donaldson *et al.*, 1986b; Johnston, 1988; Roskill Information Services, 1989).

Some representative analyses of cobalt-containing alloys are given in Table 3.

Magnetic alloys. Cobalt is the only element capable of increasing the saturation magnetization of iron and is an important constituent of permanent magnets, commercial magnet steel (35% cobalt) and soft-magnet alloys. Representative analyses of some Alnico magnetic alloys (cobalt added to alloys of aluminium, nickel and iron) are given in Table 4. Magnets combining cobalt with rare-earth minerals were developed in 1967. Rare-earth cobalt alloys contain 60-65% cobalt and have the composition RCo_5, where R represents a rare-earth metal (Donaldson, 1986). A samarium-cobalt magnet was commercially available in the early 1970s, and a series of magnets with the composition R_2Co_{17} was marketed in 1980.

In *'hard-metal' alloys* (cemented carbides), cobalt powder is used as a matrix or bonding agent. The most commonly used cemented carbide, tungsten carbide, contains 80-90% by weight of hard metal and 5-10% cobalt, although up to 30% cobalt may be used for certain purposes. The properties of cemented tungsten carbides are sometimes enhanced by addition of the carbides of niobium, tantalum or titanium (Donaldson, 1986).

Cobalt-containing high-strength steels. Although cobalt is not a common alloying element in steel, it can be an important component when high strength is required (Donaldson, 1986). Maraging steels, used in the fabrication of tools and other applications requiring high strength-to-weight ratios, typically contain 8-18% cobalt alloyed with iron, nickel (8-19%), molybdenum (1-14%) and small amounts of aluminium and titanium (Roskill Information Services, 1989).

Cobalt-containing martensitic stainless maraging steels, especially designed for corrosion resistance and high tensile strength, typically contain 5-20% cobalt, 10-15.5% chromium, 0-8.2% nickel, 2-5.5% molybdenum and small amounts of carbon and titanium (Roskill Information Services, 1989).

Table 3. Examples of superalloys containing cobalt (values in weight %)[a]

Trade name	Co	Cr	Ni	Fe	Mo	W	Ta	Nb	Al	Ti	Mn	Si	C	B	Zn
Nimocast alloy 263	20.0	20.0	55.0	0.5	5.8	–	–	–	0.5	2.2	0.5	–	0.06	0.008	0.04
Udimet 500	19.0	18.0	52.0	–	4.2	–	–	–	3.0	3.0	–	–	0.07	0.007	0.05
Hastelloy alloy X	1.5	22.0	47.0	18.5	9.0	0.6	–	–	–	–	0.5	0.5	0.10	–	–
Inconel alloy 617	12.5	22.0	54.0	–	9.0	–	–	–	1.0	–	–	–	0.07	–	–
Haynes alloy 1002	Balance	22.0	16.0	1.5	–	7.0	3.75	–	0.3	0.2	0.7	0.4	0.6	–	0.3
WI-52	63.0	21.0	–	2.0	–	11.0	–	2.0	–	–	0.25	0.25	0.45	–	–
Haynes alloy 188	39.0	22.0	22.0	3.0 max	–	14.0	–	–	–	–	1.25 max	0.4	0.1	–	–
Haynes alloy 556	20.0	22.0	20.0	29.0	3.0	2.5	0.9	0.1	0.3	–	1.5	0.4	0.1	–	–

[a]From Nickel Development Institute (1987)

Table 4. Composition and magnetic properties of Alnico alloys[a]

Composition (%)						Method of manufacture	Coercive force (kA/m)
Co	Ni	Al	Cu	Ti	Nb		
3–5	21–28	11–13	2–4	0–1	–	Cast	36–56
12–14	16–20	9–11	3–6	0–1	–	Cast	40–50
17–20	18–21	8–10	2–4	4–8	–	Cast	60–72
23–25	12–15	7.8–8.5	2–4	0–0.5	–	Field treated	46–52
32–36	14–16	7–8	4	4–6	–	Field treated	110–140
24–25	13–15	7.8–8.5	2–4	–	0–1	Columnar	56–62
32–36	14–16	7–8	4	4–6	0–1	Columnar	110–140

[a]From Donaldson (1986)

The uses and composition of *electrodeposited alloys* and *alloys with special properties* are described below. Typical specifications for one class of special purpose alloys, those used in surgical implants, are given in Table 5.

Table 5. Composition of some cobalt-containing alloys used for surgical implants (%)[a]

Element	Alloy			
	A	B	C	D
Cobalt	Balance	Balance	Balance	Balance
Chromium	27.0–30.0	19.0–21.0	18.0–22.0	26.0–30.0
Molybdenum	5.0–7.0	9.0–10.5	3.0–4.0	5.0–7.0
Nickel	1.0 max	33.0–37.0	15.0–25.0	1.0 max
Iron	0.75 max	1.0 max	4.0–6.0	0.75 max
Carbon	0.35 max	0.025 max	0.05 max	0.35 max
Silicon	1.0 max	0.15 max	0.50 max	1.0 max
Manganese	1.0 max	0.15 max	1.0 max	1.0 max
Nitrogen	NA	NA	NA	0.25 max
Phosphorus	NA	0.015 max	NA	NA
Sulfur	NA	0.010 max	0.010 max	NA
Titanium	NA	1.0 max	0.50–3.50	NA
Tungsten	NA	NA	3.0–4.0	NA

[a]From American Society for Testing and Materials (1984, 1987a,b, 1988)
NA, not applicable

(*b*) *Cobalt compounds*

Cobalt(II) acetate is sold by one company as a reddish-pink solution containing 6-9% cobalt and 2% acetic acid (Hall Chemical Co., undated b).

Cobalt(II) acetate tetrahydrate is available at purities up to 100% from several companies as pink to red-violet crystals (BDH Ltd, 1989a; CP Chemicals, 1989b; J.T. Baker, 1989a; Mallinckrodt, 1989a; Hall Chemical Co., undated c). Technical-grade cobalt(II) acetate tetrahydrate, offered by one US company as red crystals, contains a minimum of 23.5% cobalt and small amounts of impurities (iron, 0.005% max; copper, 0.005% max; chlorine, 0.01% max; sulfate ion, 0.05% max; insolubles in acetic acid, 0.03% max; Shepherd Chemical Co., 1987a, 1989a).

Cobalt carbonate is offered by one US company as a reddish-purple powder containing a minimum of 45.5% cobalt and small amounts of impurities (iron, 0.005% max; copper, 0.005% max; lead, 0.005% max; chlorine, 0.01% max; sodium, 0.6% max; insolubles in dilute hydrochloric acid, 0.05% max; cadmium, 0.005% max; sulfate ion, 0.2% max; Shepherd Chemical Co., 1987b, 1989b). Several companies offer cobalt carbonate as a pink powder or red crystals at 90-100% purity (CP Chemicals, 1989c; J.T. Baker, 1989b; Hall Chemical Co., undated d). Basic cobalt carbonate, the primary commercial product, typically contains 45-47% cobalt (Donaldson *et al.*, 1986a).

Cobalt chloride is sold commercially mainly as the hexahydrate or other hydrated form. Cobalt chloride hexahydrate is available from several companies as red crystals in purities up to approximately 100% (BDH Ltd, 1989b; CP Chemicals, 1989c; Mallinckrodt, 1989b; Aldrich Chemical Co., undated b,c; Hall Chemical Co., undated a). Technical-grade cobalt chloride hexahydrate, available from one US company as red crystals, contains a minimum of 24% cobalt and small amounts of impurities (iron, 0.02% max; copper, 0.02% max; sulfate ion, 0.1% max; water insolubles, 0.05% max; Shepherd Chemical Co., 1987c, 1989c). The hexahydrate is also available as a pink-to-red powder at 98-100% purity (J.T. Baker, 1989c) and as a clear reddish aqueous solution containing 14.5% cobalt (Hall Chemical Co., undated e). Cobalt chloride is also available commercially as a clear, purple aqueous solution containing approximately 6% cobalt chloride (Mallinckrodt, 1989c) and as essentially pure (99.999%) hydrated red-violet powder and chunks (Aldrich Chemical Co., undated d).

Anhydrous cobalt chloride is available from two companies as a blue powder at purities up to 97% (BDH Ltd, 1989c; Aldrich Chemical Co., undated e) and from another at a purity of 100% (Hall Chemical Co., undated f).

Cobalt(II) hydroxide is available commercially as a solid containing 62% cobalt and an antioxidant (Donaldson *et al.*, 1986a), as a blue-green, moist press cake (E grade) containing 68% cobalt hydroxide and less than 500 ppm ammonia (Hall Chemical Co., undated g), as a technical grade (95% cobalt hydroxide; Aldrich Chemical Co., 1990) and as a pink powder containing a minimum of 61% cobalt and small amounts of impurities (chlorine, 0.02% max; acetic acid insolubles, 0.2% max; copper, 0.01% max; iron, 0.01% max; manganese, 0.03% max; nickel, 0.3% max; sulfate ion, 0.3% max; Shepherd Chemical Co., 1988a, 1989d).

Cobalt molybdenum oxide is produced by one company in the USA (Chemical Information Services Ltd, 1988).

Commercial grade *cobalt naphthenate* is available as a solution of 65% cobalt naphthenate (6% cobalt) in white spirits (Nuodex, 1986; Hall Chemical Co., undated h). One US company offers 6 and 8% liquid grades; another offers liquid, flake and solid forms (American Chemical Society, 1988). One Canadian company and one US company offer 6% cobalt naphthenate in solution with white spirits and 10.5% flaked cobalt naphthenate (Dussek Campbell Ltd, 1989a,b; Shepherd Chemical Co., 1989e,f).

One US company offers *cobalt nitrate hexahydrate* as a red-brown crystalline powder at 99.999% purity or as red chips in reagent grade or at 99% purity. The reagent grade is 98% pure and contains small amounts of impurities (insolubles, $< 0.01\%$; chloride ion, $< 0.002\%$; copper, $< 0.002\%$; iron, $< 0.001\%$; ammonium, $\leq 0.2\%$; nickel, $\leq 0.15\%$; and sulfate ion, $\leq 0.005\%$) (Aldrich Chemical Co., 1990, undated f,g,h). The hexahydrate is available as pink-to-red crystals at 90-100% purity from three US companies and from one company in the UK (BDH Ltd, 1989d; J.T. Baker, 1989d; Mallinckrodt, 1989d; Hall Chemical Co., undated i). Technical-grade cobalt nitrate hexahydrate is available from one US company as small, red flakes with a slight odour of nitric acid and contains a minimum of 19.8% cobalt, with small amounts of impurities (iron, 0.002% max; copper, 0.005% max; lead, 0.005% max; zinc, 0.05% max; chlorine 0.005% max; sulfate ion, 0.01% max; water insolubles, 0.02% max; Shepherd Chemical Co., 1986a, 1989g). Aqueous cobalt nitrate ($Co(NO_3)_2 \cdot xH_2O$) is available from one US company as a dark-red solution containing approximately 14% cobalt (Hall Chemical Co., undated j).

Cobalt nitrate is also available in 1-2% aqueous nitric acid solution as a laboratory standard containing 1000 ppm cobalt (0.1% w/v; J.T. Baker, 1989e; Aldrich Chemical Co., 1990).

Cobalt(II) oxide is available as a laboratory reagent from one US company as a green, red, grey or black powder at 90-100% purity (70-74% as cobalt), with small amounts of impurities (chloride, 0.02% max; nitrogen compounds as nitrogen, 0.02% max; sulfur compounds as sulfate ion, 0.1% max; iron, 0.1% max; nickel, 0.2% max; insolubles in hydrochloric acid, 0.05%; J.T. Baker, 1989f,g). One

company in the UK offers cobalt oxide as a fine, black powder (BDH Ltd, 1989e). Cobalt(II) oxide is also available in ceramic grade (70-71% cobalt), metallurgical grade (76% cobalt) and high-purity powder grade (99.5%; may contain 10 ppm metallic impurities; American Chemical Society, 1988). Cobalt(II) oxide is produced by only a few companies (Chemical Information Services Ltd, 1988) and is not of major commercial importance.

Cobalt(II,III) oxide is available as a black powder at 99.995% purity (Aldrich Chemical Co., undated a), as a black powder with a cobalt content of 72-73% (Aldrich Chemical Co., 1990, undated i) and as a black-grey powder with 71-72% cobalt as cobalt oxide and less than 1% nickel as nickel monoxide (Hall Chemical Co., undated k). Another mixed oxide, containing a ratio of 3:1 cobalt(III) oxide:cobalt(II) oxide, is available at 99.999% purity (Chemical Dynamics Corp., 1989). It is produced by many companies throughout the world.

Cobalt(III) oxide is available in small quantities for laboratory use from one US company as a powder at 99.9996% purity (72.3% as cobalt) with small amounts of impurities (chloride, 80 μg/g; nitrate, 35 μg/g; silicon, 2 μg/g; aluminium, < 1 μg/g; copper, < 0.5 μg/g; iron, 1 μg/g; magnesium, 0.7 μg/g; nickel, 2 μg/g; J.T. Baker, 1989g).

Cobalt sulfide (form unspecified) is sold by one company in the USA (Chemical Information Services Ltd, 1988).

Cobalt sulfate heptahydrate is available from several companies as pink-to-dark-red crystals in purities of 90-100% (BDH Ltd, 1989f; J.T. Baker, 1989h; Mallinckrodt, 1989e; Aldrich Chemical Co., undated j,k; Hall Chemical Co., undated l). Technical-grade cobalt sulfate heptahydrate available from one US company as red-pink crystals contains a minimum of 20.8% cobalt and small amounts of impurities (iron, 0.005% max; copper, 0.002% max; water insolubles, 0.05% max; Shepherd Chemical Co., 1986b, 1989h). The monohydrate is available as pink-to-red crystals with a minimum of 33% cobalt and with small amounts of impurities (iron, 0.007% max; copper, 0.003% max; water insolubles, 0.1% max; Shepherd Chemical Co., 1987d, 1988b), and with a purity of 100% (Hall Chemical Co., undated m).

Cobalt sulfate is also available commercially as a rose-to-dark-red aqueous solution containing approximately 8% cobalt (CP Chemicals, 1989d; Hall Chemical Co., undated n).

2. Production, Use, Occurrence and Analysis

2.1 Production

(a) *Cobalt and cobalt alloys*

Cobalt, a major constituent of about 70 naturally occurring oxide, sulfide, arsenide and sulfoarsenide minerals, is produced primarily as a by-product of the mining and processing of copper and nickel ores and, to a lesser extent, of silver, zinc, iron, lead and gold ores.

Commercial cobalt production began in Canada in 1905. In 1924, a company in Zaire (then the Belgian Congo) started recovering cobalt during the mining of copper ores, and that country has been the world's largest producer since 1926 (Roskill Information Services, 1989). World mine production of cobalt peaked in the mid-1980s, but the production of refined cobalt metal has been decreasing since the early 1980s because beneficiation and extractive metallurgy are not designed for maximizing the recovery of cobalt (Roskill Information Services, 1989). World mine and metal production of cobalt in 1970-88 is presented in Table 6.

Table 6. World mine and metal production of cobalt, 1970-88 (tonnes)[a]

Year	Mine production	Metal production	Year	Mine production	Metal production
1970	28 985	25 909	1980	37 873	36 720
1971	26 405	27 203	1981	37 363	31 325
1972	30 177	24 645	1982	24 567	19 292
1973	35 746	28 113	1983	37 875	18 084
1974	39 453	30 745	1984	41 075	23 627
1975	37 479	25 275	1985	48 304	26 906
1976	26 024	22 827	1986	48 903	30 673
1977	26 303	25 227	1987	46 382	26 939
1978	32 817	24 780	1988	43 900[b]	25 286[c,d]
1979	36 148	34 317	1989	38 700[b,c]	NA

[a]From Roskill Information Services (1989), unless otherwise specified
[b]From Shedd (1990)
[c]Estimate
[d]From Shedd (1988)
NA, Not available

Between 1983 and 1987, cobalt was mined in amounts greater than 100 tonnes in 16 countries and was refined in 12. The cobalt-producing countries or regions in those years were Albania, Australia, Botswana, Brazil, Canada, China, Cuba, Finland, Morocco, New Caledonia, the Philippines, South Africa, the USSR, Zaire, Zambia and Zimbabwe. The countries that refined cobalt during this period were Belgium, Canada, China, Finland, France, Japan, Norway, South Africa, the USSR, Zaire, Zambia and Zimbabwe (Johnston, 1988; Shedd, 1988).

(i) *Cobalt mining, refining and/or production by country*

Australia: Cobalt is mined but not refined in Australia (Shedd, 1988). In 1986, one company ceased supplying nickel-cobalt sulfides to Japanese refineries and began to supply all of their by-products to a refinery in Finland (Kirk, 1986).

Belgium: Small quantities of partly processed materials containing cobalt have been imported, but information is inadequate to estimate the recovery of cobalt (Kirk, 1986). About one-third of the cobalt exported by Zaire is processed in Belgium, and about half of this production is exported to the USA (Kirk, 1985).

Botswana: One company in Botswana began mining for cobalt in 1973 (Kirk, 1985). The cobalt-containing nickel-copper matte is sent to Norway (74%) and Zimbabwe (26%) for refining (Shedd, 1988); previously, it was refined in the USA (Kirk, 1985).

Brazil: One company began production of electrolytic cobalt in late 1989 at a nickel plant with an initial production capacity of 300 tonnes. It produced a cobalt concentrate which was sent to a Norwegian refinery for processing. Previously, Brazil depended on imports from Canada, Norway, Zaire and Zambia (Kirk, 1987; Shedd, 1988, 1989).

Bulgaria: Bulgaria is known to produce ores that contain cobalt, but information is inadequate to estimate output (Kirk, 1985).

Canada: Cobalt production in Canada began in 1905 (Roskill Information Services, 1989). Three companies currently mine cobalt, and one of these refines it (Shedd, 1988). The intermediate metallurgical product cobalt oxide has been shipped to the UK for further processing, and a nickel-copper cobalt matte has been shipped to Norway (Kirk, 1986, 1987).

China: A primary cobalt deposit mine was equipped in 1986 and has a reported annual output of 45 thousand tonnes of ore (Kirk, 1986). Cobalt mine production in 1987 was estimated to be 270 tonnes (Johnston, 1988). A large deposit of nickel-copper-cobalt was discovered in China in 1988 (Shedd, 1988).

Czechoslovakia: Czechoslovakia is believed to recover cobalt from Cuban nickel-cobalt oxide and oxide sinter (Kirk, 1985; Shedd, 1988).

Finland: In 1986, a company in Finland began processing nickel-cobalt sulfide from Australian nickel oxide production into cobalt and nickel salts (Kirk, 1986). In

1987, a mining and metallurgical cobalt and nickel producing company in Finland suspended production of standard-grade cobalt powder and briquets to focus on producing extra-fine powder and cobalt chemicals. In 1988, the copper-cobalt mine was closed and cobalt concentrates were no longer produced (Kirk, 1987; Shedd, 1988).

Germany: Ores that contain cobalt are produced in Germany, but information is inadequate to estimate output (Kirk, 1985).

Greece: Ores that contain cobalt are produced in Greece, but information is inadequate to estimate output (Roskill Information Services, 1989).

India: A plant projected to open in 1990 can recover approximately 27 tonnes of cobalt per year from a lead-zinc ore mine in India. In addition, recovery of cobalt from lateritic overburden in chromite mines is being studied (Shedd, 1988).

Indonesia: One company in Indonesia produces ores that contain cobalt, but information is inadequate to estimate output (Shedd, 1988).

Japan: Mining of cobalt in Japan ceased in 1986. Two Japanese refiners have received nickel-matte from a Canadian facility in Indonesia and feedstock from Australia and the Philippines (Shedd, 1988).

Morocco: Mining of cobalt was begun in Morocco in the late 1930s (Roskill Information Services, 1989); mining of cobalt as a primary product ceased in 1982, but mining from cobalt-iron-nickel arsenides was resumed in 1988. Beginning in 1988, Morocco agreed to provide China with cobalt concentrate (Shedd, 1988).

New Caledonia: Ores and intermediate metallurgical products have been exported to France, Japan and the USA (Kirk, 1987; Shedd, 1988).

Norway: One company in Norway refines cobalt mostly from nickel-cobalt-copper matte imported from Canada (60%) and Botswana (30%) (Shedd, 1988).

Philippines: Cobalt was recovered as a by-product of nickel mining by a state-owned company in the Philippines until 1986, when the mine was closed. Production of cobalt from the mine peaked at about 1360 tonnes in 1979 (Kirk, 1987; Shedd, 1988).

Poland: Ores that contain cobalt are produced in Poland, but information is inadequate to estimate output (Kirk, 1985).

South Africa: Cobalt is mined and refined in South Africa (Shedd, 1988), and a foreign-owned company produced cobalt as a by-product of platinum mining operations (Kirk, 1987).

Spain: Ores that contain cobalt are produced in Spain, but information is inadequate to estimate output (Kirk, 1985).

Uganda: Construction of a cobalt refinery is planned in conjunction with the rehabilitation of copper mines, which ceased operation in 1979 (Shedd, 1988).

UK: Products of Canadian origin are processed in the UK (Kirk, 1986, 1987).

USA: The USA began mining cobalt in the late 1930s but ceased domestic mine production at the end of 1971. Refining of imported nickel-cobalt matte by the sole US cobalt refinery was discontinued in late 1985. In 1985-88, the USA imported 31% of its cobalt from Zaire, 21% from Zambia, 21% from Canada, 10% from Norway (originating in Canada and Botswana) and 17% from other countries (Shedd, 1990), which include Belgium, Finland, France, Germany, Japan, the Netherlands, South Africa and the UK (Kirk, 1987).

Two companies in the USA produce extra-fine cobalt powder: one is a foreign-owned company that uses imported primary metal; the other is a domestically controlled company that uses cobalt recovered from recycled materials. Seven companies produce cobalt compounds (Shedd, 1990).

USSR: Cobalt is mined and refined in the USSR (Shedd, 1988); in addition, nickel-cobalt sulfide concentrate from Cuba is refined (Kirk, 1985).

Zaire: Cobalt recovery from the mining of copper ores began in 1924, and since 1926 Zaire has been the world's largest producer of cobalt (Roskill Information Services, 1989). Sulfide and oxide concentrates are processed to cobalt metal in the form of cathodes and granules. About one-third of their exports go to Belgium for further processing (Kirk, 1985).

Zambia: Mining of cobalt began in Zambia in the late 1930s (Roskill Information Services, 1989). Cobalt is also mined and refined as a by-product of copper mining (Kirk, 1985; Shedd, 1988).

Zimbabwe: Cobalt is mined and refined in Zimbabwe and is also recovered from nickel-copper matte imported from Botswana (Shedd, 1988).

Mine and metal production of cobalt by country or region with reported outputs for 1984 to 1988 are presented in Tables 7 and 8.

(ii) *Metallurgy*

Cobalt-containing ores vary widely in composition but usually contain less than 1% cobalt. Although each type of ore (arsenide, sulfide or oxide) is processed differently, six general metallurgical processes can be distinguished; depending on the ore's composition, recovery of cobalt may require one or a combination of these techniques. It is important to note that in nearly all cases cobalt is a by-product of the refining of other metals (Roskill Information Services, 1989), especially copper and nickel. Refinery methods therefore are generally not designed to maximize cobalt recovery (Anon., 1990a).

The main sources of cobalt (in decreasing ease of recovery) are ores of copper-cobalt oxides (Zaire) and sulfides (Zaire and Zambia), copper-nickel sulfides (Canada), cobalt-iron-nickel arsenides (Morocco and China) and

Table 7. World mine production of cobalt by country or region, 1984-88[a]

Country	Mine output, metal content (tonnes)				
	1984	1985	1986	1987	1988[b]
Albania	590	590	590	590	590
Australia	938	1 136	1 218	1 200	1 100
Botswana	259	222	162	182	292[c]
Brazil	100	100	150	150	150
Canada	2 330	2 071	2 491	2 495	2 770
Cuba[d]	1 400	1 491	1 500	1 590	2 000
Finland	862	1 094	628	190	182
Morocco	NA	NA	NA	NA	253
New Caledonia[b]	500	677	700	750	800
Philippines	64	913	92	NA	NA
South Africa[b]	682	682	682	727	727
USSR[b]	2 590	2 725	2 815	2 815	2 860
Zaire	25 997	29 226	33 403	29 056[b]	25 425
Zambia	4 625	5 812[b]	5 770[b]	5 950[b]	6 675
Zimbabwe[b]	77	100	76	109	126
Total	41 014	46 838	50 277	45 804	43 950

[a]From Shedd (1988), unless otherwise specified
[b]Estimates
[c]Reported figure
[d]Estimates from reported nickel–cobalt content of granular and powder oxide, oxide sinter and sulfide production
NA, not available

nickel-cobalt oxides (lateritic nickel ore from most other sources) (Planinsek & Newkirk, 1979; Donaldson *et al.*, 1986a; Shedd, 1988).

After crushing and grinding, the first stage of cobalt recovery from ore involves the physical separation of cobalt-containing minerals from other nickel ores and gauge, usually by gravity (arsenide ores) or froth flotation (sulfoarsenide and sulfide ores). Flotation is also used for separating cobalt in oxide and mixed oxide-sulfide ores. Flotation is frequently aided by the addition of xanthates, oils or cyanide to depress cobalt flotation (Donaldson, 1986; Donaldson *et al.*, 1986a); the amount of cobalt in the concentrate is usually enhanced four to eight fold by these operations (Roskill Information Services, 1989).

Cobalt is extracted from ore and concentrated by pyrometallurgical, hydrometallurgical and electrolytic processes alone or in combination. Arsenic-free cobalt concentrates can be mixed with lime and coal and smelted in a reducing

Table 8. World metal production of cobalt by country, 1984-88 (tonnes)[a]

Country	1984	1985	1986	1987	1988[b]
Canada	2 218	2 027	1 994	2 205[b]	2 205
Finland	1 456	2 235	1 350	498	220
France	116	123	100[b]	109[b]	50
Japan	907	1 279	1 340	124	109
Norway	1 193	1 640	1 583	1 603	1 605
South Africa[b]	500	500	500	523	523
USSR[b]	4 725	4 815	5 315	5 315	5 315
Zaire	9 083	10 690	14 513	11 911	10 150
Zambia	3 475	4 365	4 348	4 483	4 995
Zimbabwe	78	92	76	110	126
Total	23 751	27 766	31 119	26 881	25 298

[a]From Shedd (1988)
[b]Estimates

environment to give copper-cobalt alloys. The alloy is further processed to separate copper and cobalt. The most commonly used hydrometallurgical processes involve roasting and leaching of ore concentrates (with acid or alkali solutions), fractional separation of cobalt from other metals in the leachate (by differential sulfide or hydroxide precipitation) and reduction of the cobalt ions to metal (by chemical or electrochemical means) (Donaldson, 1986; Donaldson *et al.*, 1986a; Roskill Information Services, 1989).

The three main processes for leaching cobalt from ores and concentrates are described below.

Acid sulfate leaching can be done by one of four methods: (a) treating oxide ore concentrates with sulfuric acid and reducing agents (SO_2); this is the primary process used in Zaire; (b) water extraction of cobalt sulfate from ores following an oxidizing roast; (c) cobalt sulfate extraction of sulfide ore concentrate following a sulfatizing roast; this method is used in Zaire, Zambia and Finland; or (d) pressure leaching with sulfuric acid, which has recently been introduced in Canada and is useful for arsenic-containing ores. The cobalt is separated from copper, iron, nickel and zinc (when present) by alkalinization and fractional dissolution with sulfide. Cobalt is precipitated as the hydroxide, redissolved and refined by electrolysis or hydrogen reduction to cobalt metal cathode or powder, respectively (Roskill Information Services, 1989).

Acid chloride leaching of ore mattes and recyclable materials is used as an alternative to acid sulfate leaching on oxides, sulfides, arsenides and alloys. This

method is usually followed by solvent extraction or ion exchange purification. The soluble chloride complexes are often formed by reaction with chlorine or hydrogen chloride gas or a metal chloride. This method is used in Japan.

Ammoniacal solution leaching gives rise to the hexammine cobalt complex $[Co(NH_3)_6]^{2+}$. This method has been used to treat alloy scrap and laterite or arsenide ores. It is used in Canada for processing lateritic nickel ores. The soluble extract is treated with hydrogen sulfide to produce mixed nickel-cobalt sulfides, which are redissolved in sulfuric acid. Cobalt powder is recovered after the introduction of ammonia and hydrogen under high pressure.

Metallic cobalt can also be recovered directly from purified leachate by electrolysis (electrowinning) after nickel has been removed as the carbonyl. Some cobalt salts can be formed by dissolution of the metal in the corresponding acid. Some refineries utilize cobalt hydroxide to form the oxide and other cobalt compounds directly (Donaldson, 1986; Donaldson *et al.*, 1986a; Roskill Information Services, 1989; Anon., 1990a).

(iii) *Production processes*

Refined *cobalt* is available to the industrial market primarily as broken or cut cathodes (92%) and to a lesser extent as electrolytic coarse powder (3%) and in other forms. The cathode form is further processed to alloys, chemicals and oxide or used in the manufacture of special cobalt powders for cemented carbide by chemical and pyrometallurgical processes. About 2000 tonnes of cobalt cathode are converted to a distinct allotropic mixture, called 'fine powder' or 'extrafine powder', by specialist producers for cemented carbide and diamond polishing. The process involved is a chemical reaction that results in a submicrometre powder with a high proportion of face-centred cubic crystal retained in the mixture. This special material differs from electrolytic coarse powder and from cobalt powders generated during industrial attritive operations, which are predominantly hexagonal crystals (Cobalt Development Institute, 1989).

Cobalt alloys are usually manufactured from broken or cut cathodes by electric arc or by induction melting techniques, although vacuum induction melting is required for some alloys containing metals such as aluminium, titanium, zirconium, boron, yttrium and lanthanum. The resultant master alloy is then remelted and cast into moulds (Donaldson & Clark, 1985; Donaldson, 1986).

An important use of cobalt is in the production of cemented tungsten carbide, also called 'hard metal'. Hard metals are used to tip the edges of drills and cutting tools and for dies, tyre studs and stamping machines (Kipling, 1980). Hard metal is made by a process in which precise weights of tungsten carbide (80-90% by weight) and cobalt metal powder (5-10%) and, in some grades, small amounts of other carbides (titanium, tantalum, niobium and molybdenum) are added and thoroughly

mixed in mills. The cobalt thus acts as a matrix; nickel is also used with cobalt as a matrix in some grades. Organic solvents, such as acetone and *n*-hexane, are added for mixing; the mixture is dried, and the organic solvents are evaporated off. The powder is put into frames made of steel or rubber and then pressed into the desired shapes; the pieces are placed on graphite plates and embedded in nitrous aluminium powder; and the pressed material is presintered in hydrogen furnaces at 500-800°C. After presintering, the material has the consistency of chalk, and it is cut, ground, drilled or shaped into the configurations required. The shaped material is finally sintered at temperatures of 1550°C. After sintering, the product approaches the hardness of diamond. Hard-metal products are sand blasted or shot blasted, brazed into holders made of iron using fluoride-based fluxes and then ground with diamond or carborundum wheels. These processes are illustrated in Figure 1 (Kusaka *et al.*, 1986).

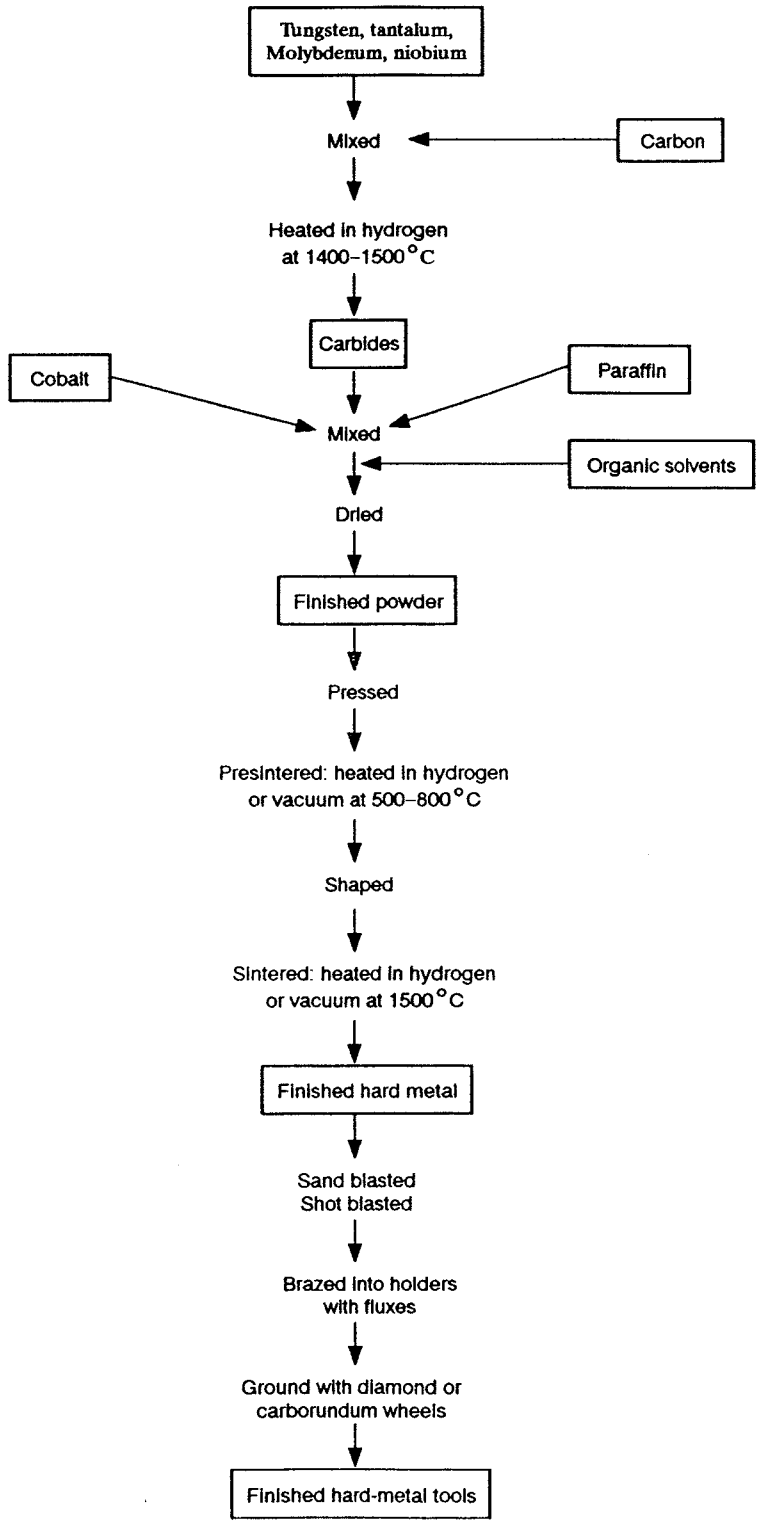
The manufacture of some alloys containing cobalt and their further fabrication into engineering parts can be assumed to take place to some extent in almost all industrialized countries. Manufacture specifically of superalloys for aircraft engines is concentrated in the USA, the UK, France, Germany and Japan, but small volumes of manufacture and specialist manufacture occur in several other regions. Use of cobalt in magnetic applications occurs mainly in Japan, but the USA and European countries (particularly Germany, France and the UK) also have large production capacities (Johnston, 1988).

(*b*) *Cobalt compounds*

Europe produces 50% of the global amount of cobalt chemicals and 70% of fine cobalt powders (Johnston, 1988). Most cobalt chemicals (75-80%) are produced by six companies in Belgium, Germany, Finland and the USA. A further 6-8% is made by three Japanese companies; minor quantities are made directly from concentrates in France and South Africa; and the balance is shared by a number of small manufacturers serving local markets or specializing in perhaps one group of cobalt products, such as naphthenates for the paint (Sisco *et al.*, 1982) and ink industries.

Most countries—industrialized or not—have a ceramics industry of some kind or size, many of them very ancient, and in each there is some use of cobalt oxide or some manufacture of cobalt pigment. The major world suppliers of cobalt pigments are, however, located in Germany, the USA, the Netherlands and the UK.

Fig. 1. Steps in the manufacture of hard-metal tools[a]



[a]From Kusake *et al.* (1986)

Cobalt(II) acetate is prepared commercially (a) by concentrating solutions of cobalt powder in acetic acid in the presence of oxygen or (b) from cobaltous hydroxide or carbonate and an excess of dilute acetic acid. Preparation of the tetrahydrate involves treatment of cobalt powder in acetic acid solution with hydrogen peroxide (Donaldson *et al.*, 1986a; Budavari, 1989).

Cobalt(III) acetate can be prepared by electrolytic oxidation of cobalt(II) acetate tetrahydrate in glacial acetic acid containing 2% (v/v) water. Another method is oxidation of solutions of cobaltous salts by alkaline persulfates in the presence of acetic acid (Budavari, 1989).

Cobalt(II) chloride can be produced by several processes: (a) from cobalt powder and chlorine, (b) from the acetate and acetyl chloride, (c) by dehydration of the hexahydrate with thionyl chloride and (d) by dissolving cobalt metal, oxide, hydroxide or carbonate in hydrochloric acid (Considine, 1974; Donaldson *et al.*, 1986a; Budavari, 1989). The hexahydrate is prepared by treating an aqueous solution of a cobaltous salt with hydrochloric acid (Budavari, 1989). Solutions of high-purity cobalt chloride and its hexahydrate can be manufactured by dissolving high-purity cobalt metal electrolytically using a dilute hydrochloric acid electrolyte at about 60°C (Donaldson *et al.*, 1986a).

Cobalt(II) carbonate is prepared by heating cobalt sulfate with a solution of sodium bicarbonate. Basic cobalt carbonate (cobalt(II) carbonate hydroxide (2:3) monohydrate) is prepared by adding sodium carbonate to a solution of cobaltous acetate followed by filtration and drying (Sax & Lewis, 1987).

Cobalt(II) hydroxide is prepared commercially as a pink solid by precipitation from a cobalt(II) salt solution with sodium hydroxide. Precipitation at higher temperatures (55-70°C) causes partial oxidation of cobalt(II) to cobalt(III) and yields the pink form, whereas precipitation at lower temperatures yields the blue form. Cobalt(II) hydroxide is prepared *in situ* during the manufacture of secondary batteries: typically, a spongy nickel foam plate is impregnated with an acidic solution of cobalt chloride, nitrate or sulfate, and cobalt(II) hydroxide is precipitated by alkali treatment (Donaldson *et al.*, 1986a).

Cobalt(III) hydroxide can be produced by several methods, e.g., addition of sodium hydroxide to a solution of cobaltic salt, action of chlorine on a suspension of cobaltous hydroxide, or action of sodium hypochlorite ion on a cobaltous salt (Brauer, 1965; Sax & Lewis, 1987).

Cobalt(II) molybdenum(VI) oxide is obtained by raising the pH to 6.4 to coprecipitate the hydroxides of cobalt and molybdenum from mixed solutions of cobalt nitrate and ammonium molybdate. The product is dried at 120°C and calcined at 400°C to give the mixed metal oxide (Donaldson *et al.*, 1986a). This is invariably also mixed with aluminium oxide in commercial manufacture and use.

Cobalt(II) naphthenate is prepared by treating cobalt hydroxide or cobalt acetate with naphthenic acid (Sax & Lewis, 1987), which is recovered as a by-product of petroleum refining. Commercial naphthenic acids used in the production of cobalt naphthenate differ widely in properties and impurities, depending upon the crude oil source and refining processes. All contain 5-25 wt % hydrocarbons, the composition of which corresponds to the petroleum fraction from which the naphthenic acids are derived; and all contain impurities (e.g., phenols, mercaptans and thiophenols) in small quantities (Sisco *et al.*, 1982).

Cobalt(II) nitrate hexahydrate is produced by dissolving cobalt metal, the oxide, hydroxide or carbonate in dilute nitric acid and concentrating the solution (Considine, 1974; Donaldson *et al.*, 1986a).

Cobalt(II) oxide (CoO) containing 78.7% cobalt is usually manufactured by controlled oxidation of the metal at above 900°C, followed by cooling in a protective atmosphere to prevent partial oxidation to cobalt(II,III) oxide (Donaldson *et al.*, 1986a).

Cobalt(II) oxide can also be prepared by additional processing of the white alloy formed during the processing of arsenic-free cobalt-copper ores to remove copper and iron as sulfates and calcining cobalt as the carbonate (Morral, 1979) or by calcination of cobalt carbonate or its oxides at high temperatures in a neutral or slightly reducing atmosphere (Sax & Lewis, 1987).

Another method for preparing cobalt(II) oxide is dissolution of a cobalt salt that is unstable at high temperatures (e.g., cobalt sulfate) in molten sodium sulfate or potassium fluoride. The cobalt salt decomposes, leaving the cobalt(II) oxide, which crystallizes out at high temperatures. The water-soluble salts are then dissolved, leaving cobalt(II) oxide crystals (Wilke, 1964).

Cobalt(II,III) oxide (Co_3O_4) containing 73.44% cobalt can prepared by the controlled oxidation of cobalt metal or cobalt(II) oxide or by thermal decomposition of cobalt(II) salts at temperatures below 900°C. It absorbs oxygen at room temperature but is not transformed to cobalt(III) oxide (Co_2O_3) (Donaldson *et al.*, 1986a).

Pyrohydrolysis of cobalt chloride has also been used to manufacture cobalt(II,III) oxide. The reaction is performed in a spray roaster by heating a fine spray of aqueous solution of cobalt(II) chloride in a countercurrent heating gas stream. The hydrogen chloride gas produced is removed with the exhaust gases, and the cobalt(II,III) oxide falls to the bottom of the furnace (Donaldson *et al.*, 1986a).

Cobalt(III) oxide (Co_2O_3) is derived by heating cobalt compounds (e.g., hydroxides) at low temperature with an excess of air (Sax & Lewis, 1987).

Cobalt(II) sulfate heptahydrate is prepared commercially by dissolving cobalt metal in sulfuric acid (Donaldson *et al.*, 1986a).

α-*Cobalt(II) sulfide* can be precipitated from cobalt nitrate hexahydrate by reaction with hydrogen sulfide and dried for 90 h, the temperature being raised slowly from 100 to 540°C (Brauer, 1965). β-*Cobalt(II) sulfide* can be synthesized by heating fine cobalt powder mixed with fine sulfur powder at 650°C for two to three days. It can also be derived by treating a solution of cobalt chloride with acetic acid, precipitating with hydrogen sulfide and drying for 90 h, the temperature being raised slowly from 100 to 540°C (Brauer, 1965). Cobalt sulfides are normally produced *in situ* as needed, as mixed metal catalysts with molybdenum (Roskill Information Services, 1989).

Dicobalt octacarbonyl is prepared commercially by heating cobalt metal with carbon monoxide at high pressure (200-300 atm) [20.2-30.3 × 10^3 kPa] or by heating a mixture of cobalt(II) acetate with cyclohexane at about 160°C and 300 atm (30.3 × 10^3 kPa) in the presence of a 1:1 mixture of carbon monoxide:hydrogen (Donaldson *et al.*, 1986a). Dicobalt octacarbonyl is frequently prepared *in situ* as needed.

2.2 Use

Cobalt compounds have been used as blue colouring agents in ceramic and glass for thousands of years, although most of the blue colour of ancient glasses and glazes has been found to be due to copper. Cobalt has been found in Egyptian pottery dated at about 2600 BC, in Persian glass beads dating from 2250 BC, in Greek vases and in pottery of Persia and Syria from the Christian era, in Chinese pottery from the Tang (600-900 AD) and Ming (1350-1650 AD) dynasties and in Venetian glass from the early fifteenth century. Leonardo Da Vinci was one of the first artists to use cobalt as a brilliant blue pigment in oil paints. The pigment was probably produced by fusing an ore containing cobalt oxide with potash and silica to produce a glass-like material (a smalt), which was then reduced to the powdered pigment. In the sixteenth century, a blue pigment called zaffre was produced from silver-cobalt-bismuth-nickel-arsenate ores in Saxony (Young, 1960; Donaldson, 1986).

It was not until the twentieth century, however, that cobalt was used for industrial purposes. In 1907, a US scientist, E. Haynes, patented a series of cobalt-chromium alloys known as stellites that were very resistant to corrosion and wear at high temperatures (Kirk, 1985). Cobalt was added to tungsten carbide in 1923 to produce cemented carbides (Anon., 1989) and to permanent magnet alloys known as Alnicos (cobalt added to alloys of aluminium, nickel and iron) in 1933 (Johnston, 1988).

(i) *Cobalt*

Cobalt has many important uses in industry today, and in some major applications there is no suitable replacement. The most important use of metallic cobalt is as an alloying element in superalloys, magnetic and hard-metal alloys, such as stellite and cemented carbides, cobalt-containing high-strength steels, electrodeposited alloys and alloys with special properties. Cobalt salts and oxides are used as pigments in the glass and ceramics industries, as catalysts in the oil and chemical industries, as paint and printing ink driers and as trace metal additives for agricultural and medical uses (Donaldson, 1986).

Most cobalt is used industrially in the form of cobalt metal as an alloying component and in the preparation of cobalt salts. Estimated consumption as primary raw materials, such as cobalt metal, cobalt oxide and cobalt salts, in selected countries in 1979-87, is presented in Table 9. These countries represented approximately 59% of total consumption in the western world in 1979, 71.5% in 1980, 65% in 1981, 65.5% in 1982, 59.4% in 1983, 53% in 1984, 53.6% in 1985 and 62.5% in 1986. Consumption of cobalt in the western world represented approximately 85% of total world consumption from 1983 to 1988 (Roskill Information Services, 1989).

Table 9. Consumption of cobalt in selected countries, 1979-87 (thousand tonnes)[a]

Country	1979	1980	1981	1982	1983	1984	1985	1986	1987[b]
USA	7.9	6.9	5.3	4.3	5.1	5.4	6.1	6.6	6.9
Japan	2.2	1.9	1.5	1.4	1.5	1.8	1.7	1.7	1.8
UK	2.5	2.3	2.00	1.1	1.2	0.91	0.96	1.6	1.33
France	0.95	1.0	0.75	1.5	0.51	0.62	0.48	0.74	NA
Italy	0.23	0.23	0.19	0.23	0.30	0.38	0.36	0.57	0.56
Sweden	0.29	0.39	0.21	0.21	0.17	0.31	0.36	0.36	0.26
Canada	0.12	0.11	0.10	0.09	0.10	0.11	0.16	0.1[c]	NA

[a]From Roskill Information Services (1989)
[b]Preliminary
[c]Estimated

Industrial consumption of cobalt in the western world averaged 4000 tonnes in 1936-46, 7000 in 1947-52, 10 000 in 1953-62, 16 800 in 1963-72, 19 500 in 1973-78, 21 000 in 1979-81 and 17 500 in 1982-84. Recently, less cobalt has been used in alloys and more in chemical applications. Table 10 presents overall estimates of cobalt consumption in western economies by end use.

Table 10. Evolution of cobalt consumption in selected countries (thousand tonnes)[a]

End product	1950	1960	1970	1981	1987
Alloys	2.85	5.95	6.98	8.74	6.83
Hard metals	0.30	0.73	0.78	1.43	2.02
Magnets	2.10	3.77	3.41	2.47	2.15
Ceramics	0.90	1.60	1.55	1.81	2.04
Chemicals	1.35	2.46	2.79	4.56	6.77
Total	7.50	14.50	15.5	19.01	19.81

[a]From Johnston (1988)

(ii) *Cobalt alloys*

Superalloys are used primarily in the manufacture of components for gas turbine and jet engines. Their combined properties of resistance to hot corrosion and high strength at elevated temperatures contribute to their great commercial and strategic importance. They are used in turbine components that operate at temperatures above 540°C, including ducts, cases and liners, as well as the major turbine blade, vane, disc and combustion-can components. Nickel-based superalloys are usually used for gas turbine components such as discs because they are more workable than cobalt-based superalloys; the latter have excellent resistance to thermal shock and hot corrosion and are used for combustor tubes, stator vanes and diaphragms. Superalloys designed to operate for long periods at temperatures above 900°C sacrifice some of their resistance to oxidation and hot corrosion for increased strength. The nickel-based superalloys are more resistant to oxidation than the cobalt-based superalloys because they have a higher aluminium content and form a better aluminium oxide coating on the alloy. The cobalt-based superalloys primarily form a chromium oxide coating which is not as stable, and when they are used in components subject to extremely high operating temperatures, such as turbine blades and nozzle guide vanes, oxidation-resistant protective coatings are required. Two types of coating can be used: intermetallic and overlay coatings. Intermetallic coatings are applied by heat treatment of the surface of the alloy with cement powders containing aluminides or, less often, silicides. Overlay coatings, which are applied by hot vapour deposition methods, are alloys containing aluminium, chromium and yttrium together with nickel, cobalt or iron. Other applications of the superalloys include airframes, chemical reactors, natural gas transmission pipelines, marine equipment and hazardous waste incineration equipment (Donaldson & Clark, 1985; Donaldson, 1986; Kirk, 1987; Cobalt Development Institute, 1989).

Magnetic alloys. Cobalt is used in a wide variety of magnetic applications, including telecommunication systems, magnetic couplings, electromagnets, meters, loudspeakers, permanent magnet motors and repulsion devices. Alnico magnets, invented in the mid-1930s, are used for heavy-duty applications such as automobile anti-skid braking systems. Consumption of Alnicos declined through the 1960s and 1970s due to the introduction in the 1960s of the less powerful but cheaper and smaller ferrite-ceramic combinations of barium and strontium with iron (Kirk, 1985; Donaldson, 1986; Cobalt Development Institute, 1989; Anon., 1990b).

Magnets combining cobalt with rare-earth minerals were developed in 1967 (Johnston, 1988). The first such magnets were samarium-cobalt alloys, but limited supplies of samarium led to the development of competitive neodymium-iron-boron magnets, which became available commercially in 1983. Rare-earth cobalt magnets have remained important because of their power/size advantages in certain applications. In the 1980s, they contributed to the miniaturization of electrical and electronic equipment. They are used as focusing magnets in travelling wave tubes, as magnetic bearings in ultra-high-speed centrifugal separators and inertia wheels, and in actuators, motors, and generators of various sizes, from watches to 100-hp [74.6-kw] motors (Kirk, 1985; Donaldson, 1986; Anon., 1990b).

Magnetic alloys are also used in medicine to provide an external attractive force. For instance, Alnicos have been used to operate a reed switch in implanted heart pacemakers; samarium-cobalt magnets have been used to hold dental plates in mouth reconstruction, to correct funnel chest and to remove magnetic fragments from the posterior portion of the eye. Magnetic cobalt alloys attached to flexible tubes have also been used to remove iron-containing material from the intestinal and bronchial tubes. Platinum-cobalt and samarium-cobalt magnetic alloys are also used as prostheses, to provide a mechanical closing device in situations where muscle function is impaired. They have been used in the treatment of urinary incontinence in women, to close eyelids in patients with facial paralysis and as colostomy closure devices. In addition, rare-earth-cobalt magnets are used in hearing aids (Donaldson *et al.*, 1986b).

Use of cobalt in magnetic alloys in western countries declined from 28% in 1950, 26% in 1960, 22% in 1970 and 13% in 1981 to 10.8% in 1987 (Johnston, 1988).

Hard-metal alloys (cemented carbides) have essential applications in wear-related engineering because of their high strength, corrosion resistance and ability to retain hardness at elevated temperature. 'Fine', 'extrafine' and 'superfine' special cobalt powders are used as the metal matrix or bonding agent in cemented carbides used in cutting, grinding and drilling tools destined for use on hard materials, such as metals and rocks, and in diamond polishing. Annual industrial consumption of these special powders is approximately 2000 tonnes. Applications of cemented carbides include grinding wheels, moulds, seal rings, dies, valves,

nozzles, pump liners, wear parts subject to severe shock, hot mill rolls, extrusion and can tooling, cutters and slitters, mining, drilling and tunnelling (Kirk, 1985; Donaldson, 1986; Anon., 1989; Cobalt Development Institute, 1989).

Consumption of cobalt for hard-metal alloys in the western world rose from 4% in 1950 to 10.2% in 1987. The tungsten carbide industry accounted for the majority of use in 1987 and diamond polishing for the rest (Johnston, 1988).

Cobalt-containing high-strength steels (maraging steels) are used in the aerospace industry for the manufacture of helicopter drive shafts, aircraft landing gear components and hinges for swing-wing aircraft. Machine component uses include timing mechanisms in fuel injection pumps, index plates for machine tools, bolts and fasteners, barrels for rapid-firing guns and components for cryogenic applications. They also find use in marine equipment, such as deep-submergence vehicles and foil assemblies on hydrofoil ships. In addition, they are used in the manufacture of tools, especially hot forging and stamping dies, close tolerance plastic moulds and die holders (Roskill Information Services, 1989).

Cobalt-containing martensitic stainless maraging steels have been developed for a variety of applications, including in machine construction, the aerospace industry, the chemical industry and naval engineering (Roskill Information Services, 1989).

Electrodeposited nickel-cobalt alloys have good corrosion resistance in many environments and have been used as protective coatings in the production of mirrors and decorative coatings and for electroforming. Electrodeposited cobalt-tungsten alloys retain their hardness at high temperature and are used to improve the wear resistance of hot forging dies. Electrodeposited cobalt alloys containing iron, nickel, platinum or phosphorus have magnetic properties suitable for use in recording systems and computer applications (Donaldson, 1986).

Alloys with special properties. Some cobalt-containing alloys have special applications as dental material, surgical implants, low expansion alloys and springs. Properties that are suitable for dentistry include ease of casting, resistance to tarnish, compatibility with mouth tissues, high strength and stiffness, and low density. Vitallium, a cobalt-chromium alloy, was used for cast denture bases, complex partial dentures and some types of bridgework. A modified alloy is used to fuse porcelain coatings to crowns *via* a metal bridge.

Cobalt-chromium surgical implant alloys were first used in the 1940s for femoral head cups because of their resistance to corrosion by body fluids; they were subsequently developed for use in bone replacement and bone repair (Donaldson, 1986). The use of metallic implants has played an increasingly important role in orthopaedy: about 500 000 knee, hip and other joint replacements were manufactured in the 1970s (Donaldson *et al.*, 1986b). Total joint arthroplasty using artificial prostheses has become a common surgical technique in the treatment of

severely injured or diseased hip joints; other applications include plates, screws and nails. The implantation of each metallic device is associated with the release of metal, either by corrosion, dissolution or wear or some combination of these processes. Although different materials have been used in the fabrication of prostheses, the preferred material for clinically acceptable knee or hip prostheses is the cobalt-chromium-molybdenum alloy (Donaldson *et al.*, 1986b; Cobalt Development Institute, 1989).

A range of iron-nickel-cobalt alloys is used by the electronics industry for sealing metals in glasses (Donaldson, 1986).

A new chemical use of cobalt is in the manufacture of video tapes. Cobalt is used to coat the basic ferric oxide particles to increase coercivity and reconcile opposing properties of erasability and control of stray magnetic effects. Manufacturers of high-quality audio tapes have also applied this development. Thin films containing cobalt phosphate and cobalt-nickel alloy particles are the most important metallic recording materials. The introduction of cobalt-chromium film for perpendicular recording is a potentially very important use of cobalt. Normally, magnetic particles are orientated horizontally on the tape surface; but by getting them to orientate vertically, much closer packing of information is allowed. Magnetic optical recording (using gadolinium-cobalt and terbium-cobalt alloys) and, to a much smaller extent, bubble memory applications also involve cobalt. Another use of cobalt is as an additive in dry electric cells (Donaldson *et al.*, 1988).

(iii) *Cobalt compounds*

Table 11 summarizes the uses of a number of compounds of cobalt. The commercially significant compounds are the oxides, hydroxide, chloride, sulfate, nitrate, phosphate, carbonate, acetate, oxalate and other carboxylic acid derivatives (Donaldson, 1986).

The compounds of cobalt have a variety of end uses. Cobalt oxides and organic compounds are used in paints, ceramics and allied products as decolorizers, dyes, dryers, pigments and oxidizers. Cobalt oxide, used as a ground-coat frit, promotes the adherence of enamel to steel. In the rubber industry, organic cobalt compounds are used to promote the adherence of metal to rubber in steel-belted radial tyres. Cobalt is also used in chemical processes. It is used in the petroleum industry principally as a catalyst for hydrodesulfurization, oxidation, reduction and synthesis of hydrocarbons. The artificial isotope cobalt-60 provides a controllable source of gamma-radiation and is used in physical, chemical and biological research, the treatment of cancer, and in industrial radiography for the investigation of physical strains and imperfections in metals (Kirk, 1985).

Table 11. Industrial uses of cobalt compounds[a]

Compound	Formula	Uses
Acetate(III)	$Co(C_2H_2O_2)_3$	Catalyst
Acetate(II)	$Co(C_2H_2O_2)_2 \cdot 4H_2O$	Driers for lacquers and varnishes, sympathetic inks, catalysts, pigment for oil-cloth, mineral supplement, anodizer, stabilizer for malt beverages
Acetylacetonate	$Co(C_5H_7O_2)_3$	Vapour plating of cobalt
Aluminate	$CoAl_2O_4$	Pigment, catalysts, grain refining
Ammonium sulfate	$CoSO_4(NH_4)_2SO_4 \cdot 6H_2O$	Catalysts, plating solutions
Arsenate	$Co_3(AsO_4)_2 \cdot 8H_2O$	Pigment for paint, glass and porcelain
Bromide	$CoBr_2$	Catalyst, hydrometers
Carbonate	$CoCO_3$	Pigment, ceramics, feed supplements, catalyst
Carbonate (basic)	$2CoCO_3 \cdot Co(OH)_2 \cdot H_2O$	Chemicals
Carbonyl	$Co_2(CO)_8$	Catalyst
Chloride	$CoCl_2 \cdot 6H_2O$	Chemicals, sympathetic inks, hydrometers, plating baths, metal refining, pigment, catalyst
Chromate	$CoCrO_4$	Pigment
Citrate	$Co_3(C_6H_5O_7)_2 \cdot 2H_2O$	Therapeutic agents, vitamin preparations
Dicobalt manganese tetroxide	$MnCo_2O_4$	Catalyst
Dicobalt nickel tetroxide	$NiCo_2O_4$	Catalyst, anode
Dilanthanum tetroxide	La_2CoO_4	Catalyst, anode
2-Ethylhexanoate	$Co(C_8H_{15}O_2)_2$	Paint and varnish drier
Ferrate	$CoFe_2O_4$	Catalyst, pigment
Fluoride(II)	CoF_2	Fluorinating agent
Fluoride(III)	CoF_3	Fluorinating agent
Fluoride	$CoF_2 \cdot 4H_2O$	Catalyst
Fluorosilicate	$CoSiF_6 \cdot 6H_2O$	Ceramics
Formate	$Co(CHO_2)_2 \cdot 2H_2O$	Catalyst
Hydroxide	$Co(OH)_2$	Paints, chemicals, catalysts, printing inks
Iodide	CoI_2	Moisture indicator
Lanthanum trioxide	$LaCoO_3$	Electrode
Linoleate	$Co(C_{18}H_{31}O_2)_2$	Paint and varnish drier
Lithium oxide	$LiCoO_2$	Battery electrode
Manganate	$CoMn_2O_4$	Catalyst; electrocatalyst

Table 11 (contd)

Compound	Formula	Uses
Naphthenate	$Co(C_{11}H_{10}O_2)_2$	Catalyst, paint and varnish drier
Nitrate	$Co(NO_3)_2 \cdot 6H_2O$	Pigments, chemicals, ceramics, feed supplements, catalyst
Oleate	$Co(C_{18}H_{33}O_2)_2$	Paint and varnish drier
Oxalate	CoC_2O_4	Catalysts, cobalt powders
Oxide(II)	CoO	Chemicals, catalysts, pigments
Oxide(II,III)	Co_3O_4	Enamels, semiconductors
Oxides	Mixed metal	Pigments
Phosphate	$Co_3(PO_4)_2 \cdot 8H_2O$	Glazes, enamels, pigments, steel pretreatment
Potassium nitrite	$K_3Co(NO_2)_6 \cdot 1.5H_2O$	Pigment
Resinate	$Co(C_{44}H_{62}O_4)_2$	Paint and varnish drier, catalyst
Sodium oxide	$NaCoO_2$	Battery electrode
Stearate	$Co(C_{18}H_{35}O_2)_2$	Paint and varnish drier, tyre cord adhesives
Succinate	$Co(C_4H_4O_4) \cdot 4H_2O$	Therapeutic agents, vitamin preparations
Sulfamate	$Co(NH_2SO_3) \cdot 3H_2O$	Plating baths
Sulfate	$CoSO_4 \cdot xH_2O$	Chemicals, ceramics, pigments
Sulfide	CoS	Catalysts
Tricobalt tetralanthanum decaoxide	$La_4Co_3O_{10}$	Catalyst
Tungstate	$CoWO_4$	Drier for paints and varnishes

[a]From Donaldson (1986); Donaldson *et al.* (1986a)

Cobalt is an effective catalyst for many organic reactions. Its major use in this way is in hydrotreating catalysts, the active components of which are molybdenum and cobalt sulfides. This type of catalyst is used in the synthesis of fuels (Fischer-Tropsch process). The reactions catalysed by cobalt also include the oxo synthesis, in which olefins and carbon monoxide are combined to form aldehydes. The basic catalyst is cobalt carbonyl ($CO_2(CO)_8$), although other cobalt carbonyls can be used. In both the Fischer-Tropsch and the oxo process, the catalysts are normally generated *in situ* in the reactor. Cobalt catalysts are also used in hydrogenation reactions, such as the hydrogenation of nitriles to amines. Cobalt salts are valuable oxidation catalysts, e.g., for the production of terephthalic acid by the oxidation of *para*-xylene, and the manufacture of phenol by the oxidation of toluene. Cobalt-containing catalysts have also been used for polymerization

reactions, e.g., polyethylene production by the Amoco process (Morral, 1979; Donaldson, 1986; Donaldson *et al.*, 1986a; Johnston, 1988; Schrauzer, 1989).

Combinations of the oxides of cobalt and those of aluminium, magnesium, zinc and silicon are constituents of blue and green ceramic glazes and pigments (Donaldson, 1986). Cobalt zinc silicate is used in a blue underglaze paint for porcelain articles; the pigment is specially developed to withstand intense heat (Raffn *et al.*, 1988). Cobalt is also used in the glass industry to impart blue colours and to mask the greenish tinge in glass or porcelain caused by iron impurities (Donaldson, 1986).

Spinels are mixed metal oxides with a special crystal structure, based on magnesium and aluminium oxides ($MgAl_2O_4$). These two metals may be partially replaced in the crystal structures by other metals, such as cobalt(II) and chromium(III). Spinels occur naturally and are also produced synthetically. Some cobalt spinels, such as the cobalt-magnesium-aluminium and cobalt-aluminium oxide spinels, are used as pigments (Donaldson *et al.*, 1986a; Sax & Lewis, 1987).

An important use of cobalt is as a drying agent for paints, varnishes, lacquers and printing inks. In these processes, cobalt oleate, resinate and linoleate have been used, but cobalt naphthenate is the more common ingredient (Buono & Feldman, 1979). Cobalt naphthenate is also added to polyester and silicone resins to promote hardening (Bedello *et al.*, 1984).

Consumption in ceramics was relatively stable from 1950 to 1987, ranging from a low of 9.5% to a high of 12% of the total annual cobalt consumption. Use of cobalt in chemicals in 1987 was almost equal to the amount used in alloys. Consumption in chemicals was 17-18% during 1950-70, 24% in 1981 and 34.2% in 1987; use in chemicals during 1987 represented 42.6% of consumption in Europe and 34.4% in the USA. In 1987, applications were: chemicals, catalysts, paint, ink and rubber additives, 24.9%; unspecified, 3.7%; electronics and magnetic tape, 2.8%; medical and veterinary, 1.5%; and plating and anodizing, 1.3% of total cobalt consumption (see Table 10; Johnston, 1988).

Cobalt(III) acetate has been used as a catalyst in cumene hydroperoxide decomposition (Budavari, 1989). *Cobalt(II) acetate* is used much more commonly, in the manufacture of drying agents for inks and varnishes, as dressings for fabrics, as catalysts and pigments, and in anodizing and agricultural applications. Mixed metal acetates such as cobalt-tin acetate can also be prepared (Donaldson, 1986; Donaldson *et al.*, 1986a; Budavari, 1989). During the 1960s, cobalt(II) acetate, cobalt chloride and cobalt sulfate (see below) were used as foam stabilizers in malt beverages in Canada, Belgium and the USA. In 1964-66, US breweries reportedly added up to 1.5 μg/ml of cobalt in 20-25% of all beer sold (Morral, 1979; Budavari, 1989; Cobalt Development Institute, 1989).

Cobalt(II) carbonate is used in ceramics, as a trace element added to soils and animal feed, as a temperature indicator, as a catalyst and in pigments (Morral, 1979; Sax & Lewis, 1987). Basic cobalt carbonate is often used as a starting material in the manufacture of other chemicals, such as cobalt oxide, cobalt pigments and cobalt salts. It is also used in ceramics and in agriculture (Donaldson, 1986; Donaldson *et al.*, 1986a; Budavari, 1989).

The main use of *cobalt(II) chloride* hexahydrate is as an intermediate in the manufacture of other cobalt salts. It has been used in invisible inks because, when it is heated, the crystal water is liberated and the almost invisible colour changes to dark blue (Suvorov & Cekunova, 1983). Because of its hygroscopic nature, anhydrous cobalt chloride has been used in barometers and as a humidity indicator in hygrometers; the anhydrous form turns from blue to pink when hydrated. Other uses include the absorption of military poison gas and ammonia, as electroplating flux for magnesium refining, as a solid lubricant and dye mordant, in the preparation of catalysts, for painting on glass and porcelain, as a temperature indicator in grinding, as a fertilizer additive, as a trace mineral supplement in animal feed and in magnetic recording materials (Morral, 1979; Donaldson *et al.*, 1986a; Budavari, 1989). The hexahydrate is used to prepare a standard solution of cobalt for analytical purposes (National Library of Medicine, 1989).

Cobalt chloride is also used in the ceramic and glass industries, in pharmaceuticals for the manufacture of vitamin B_{12} and as catalysts for the oxidation in air of toxic waste solutions containing sulfites and antioxidants (Considine, 1974). It was used as a foam stabilizer in malt beverages in the 1960s (see under cobalt acetate above). Cobalt chloride has been used as an adjunct to iron therapy (if cobalt deficiency is suspected) in patients with refractory anaemia to improve haematocrit, haemoglobin and erythrocyte values. Although cobalt stimulates erythropoietin production, it also blocks certain enzymes involved in iron transport and may stimulate erythrocyte production by causing intracellular hypoxia. Therapeutic doses of 20-300 mg per day orally have been used (Goodman & Gilman, 1975; Goodman-Gilman *et al.*, 1985; Berkow, 1987). According to Reynolds (1989), its general therapeutic use is unjustified.

Cobalt(II) hydroxide is used in the manufacture of other cobalt compounds, as a starting material to make driers for paints and printing inks, as a catalyst or starting material for catalysts and in solutions for impregnating electrodes in storage batteries (Morral, 1979; Donaldson *et al.*, 1986a; Budavari, 1989).

Cobalt(III) hydroxide is used as an oxidation catalyst (Sax & Lewis, 1987; Budavari, 1989).

Cobalt molybdenum oxide is used with aluminium oxide as a desulfurization and reforming catalyst in oil refining (Considine, 1974; Donaldson, 1986; Sax & Lewis, 1987).

Cobalt(II) naphthenate is used primarily as a drying agent in paints, inks and varnishes. Additionally, it is used to enhance the adhesion of sulfur-vulcanized rubber to steel and other metals (i.e., in tyres), as a dressing for fabrics, as a catalyst and as an antistatic adhesive (Buono & Feldman, 1979; Donaldson *et al.*, 1986a; Sax & Lewis, 1987).

Cobalt(II) nitrate hexahydrate is used mostly in the preparation of catalysts, in pigments, chemicals, ceramics, feed supplements, battery materials, invisible inks, hair dyes and vitamin B_{12} preparations. It serves as an important source of high-purity cobalt for use in the electronics industry (Considine, 1974; Morral, 1979; Donaldson, 1986; Donaldson *et al.*, 1986a; Budavari, 1989).

Cobalt(II) oxide (CoO) is used as a starting material for the manufacture of other chemicals and catalysts, in pigments such as colour reagents and in ceramics, gas sensors and thermistors (Donaldson *et al.*, 1986a).

Cobalt(II,III) oxide (Co_3O_4) is used in ceramics and enamels as a colorizer and decolorizer, in semiconductors, as a catalyst, in solar collectors, in grinding wheel coolants and as an implant into the oesophagus of cobalt-deficient ruminants (Morral, 1979; Donaldson, 1986; Donaldson *et al.*, 1986a; Sax & Lewis, 1987).

Lilac pigments containing 22-33 wt % *cobalt(III) oxide* (Co_2O_3) and blue-green pigments containing 8-20 wt % cobalt(III) oxide are used in ceramics. A prime enamel has been prepared that contains 0.8 wt % cobalt(III) oxide (Donaldson *et al.*, 1986a). Cobalt(III) oxide monohydrate is used as an oxidation catalyst (Budavari, 1989).

Cobalt(II) sulfate is the preferred source of water-soluble cobalt salts used in the manufacture of other cobalt chemicals and in electroplating, because it has less tendency to deliquesce or dehydrate than the chloride or nitrate. The monohydrate and heptahydrate are used in plating, feed supplements, to make catalysts, magnetic recording materials, anodizing agents and corrosion protection agents (Morral, 1979; Donaldson *et al.*, 1986a; Budavari, 1989). Cobalt sulfate is also used in the manufacture of vitamin B_{12} during the biological fermentation of molasses by *Pseudoneras denitrificans* (Cobalt Development Institute, 1989). Treating cobalt-deficient soil with 100-150 g/acre [247-371 g/ha] of cobalt sulfate prevents cobalt deficiency in ruminant animals (Jones *et al.*, 1977); injection of cobalt sulfate solution through rumenal fistulas and subcutaneous implantation of slow-release cobalt glasses have been used as alternative methods of supplying cobalt (Donaldson *et al.*, 1986b). In the 1960s, cobalt sulfate was used in various countries as a foam stabilizer in beer (see under cobalt acetate above).

Both α- *and* β-*cobalt sulfides* are used as catalysts for hydrodesulfurization of organic compounds in petroleum refining. The sulfide is generated as needed by passing hydrogen sulfide over mixed cobalt-molybdenum-aluminium oxides in refinery reactors to form catalytic cobalt sulfide *in situ* (Brauer, 1965; Donaldson *et al.*, 1986a; Budavari, 1989).

2.3 Occurrence

(*a*) *Geological occurrence*

Cobalt is widely distributed throughout the environment. It is thirty-third in abundance among the elements in the earth's crust, accounting for 0.001-0.002%. The largest concentrations of cobalt are found in mafic (igneous rocks rich in magnesium and iron and comparatively low in silica) and ultramafic rocks; the average cobalt content in ultramafic rocks is 270 mg/kg, with a nickel:cobalt ratio of 7. Sedimentary rocks contain varying amounts of cobalt; average values are 4 mg/kg for sandstone, 6 mg/kg for carbonate rocks and 40 mg/kg for clays or shales. Levels of cobalt in metamorphic rock depend on the amount of the element in the original igneous or sedimentary source. Cobalt has also been found in meteorites (Donaldson, 1986; Donaldson *et al.*, 1986b; Weast, 1988; Budavari, 1989).

Cobalt minerals occur in nature as a small percentage of other metal deposits (particularly copper), generally as sulfides, oxides or arsenides, which are the largest mineral sources. Smaltite ($CoAs_2$) has a cobalt content of 25% and is the most important arsenide found in the USA, Canada and Morocco; other arsenides include safflorite $(CoFe)As_2$, skutterudite ($(Co,Fe)As_3$) and the arsenosulfide (CoAsS; cobaltite), which contains up to 35% cobalt and is found in Cobalt City, Australia, and in Burma. Carrollite ($(Co,Ni)_2CuS_4$) and linnaeite (Co_3S_4) are sulfides which contain 40-50% cobalt and are found in the African copper belt; siegenite ($(Co,Ni)_3S_4$), which contains 25% cobalt, is found in the mines of Missouri, USA. The supplies of oxides that have the greatest economic importance are heterogenite (CoO(OH)) and sphaerocobaltite (containing 50% cobalt) from Katanga, Zaire, and asbolite (obtained from manganese copper) from New Caledonia (Kipling, 1980; Merian, 1985; Donaldson, 1986; Budavari, 1989; Schrauzer, 1989).

(*b*) *Occupational exposure*

The main route of absorption during occupational exposure to cobalt is *via* the respiratory tract, due to inhalation of dusts, fumes or mists containing cobalt or inhalation of gaseous cobalt carbonyl. Occupational exposures occur during the production of cobalt powder, in hard-metal production, processing and use, and in the use of cobalt-containing pigments and driers. Workers who regenerate spent catalysts may also be exposed to cobalt sulfides.

Occupational exposure to cobalt can be measured by analysis of ambient air levels and by biological monitoring, i.e., analyses of cobalt concentrations in blood or urine (for reviews see Ferioli *et al.*, 1987; Alessio & Dell'Orto, 1988; Angerer, 1989; Angerer *et al.*, 1989). (See also Table 19 and p. 419).

Data on exposure to cobalt measured by air and biological monitoring in various industries and occupations are summarized in Table 12. Where possible, the correlations between the concentrations of cobalt in air and biological body fluids are given. Information available to date on blood and urinary concentrations of cobalt indicates that these tests are suitable for assessing exposure on a group basis. The determination of urinary levels of cobalt seems to offer more advantages than that of blood levels. The biological indicator levels are influenced by the chemical and physical properties of the cobalt compound studied and by the time of sampling. It should be noted that the type of compound, the timing of collection of biological samples (normally at the end of a shift) and the analytical methods differ among the studies.

Using biological indicators, the concentration of cobalt in air was related to that in biological fluids; an exposure to 50 μg/m^3 cobalt in air was found to be equivalent to a level of 2.5 μg/l cobalt in blood and 30 μg/l cobalt in urine (Angerer, 1989).

Lehmann *et al.* (1985) took stationary and personal air samples at workplaces during dry grinding (with exhaust facilities) in the mechanical processing of cobalt alloys containing 5-67% cobalt. They found the following airborne concentrations: stationary sampling—total dust, 0.1-0.85 mg/m^3 (median, 0.55 mg/m^3; 13 samples); cobalt in total dust, 0.06-23.3 μg/m^3 (median, 0.4 μg/m^3; 13 samples); personal sampling—total dust, 0.42-2.05 mg/m^3 (median, 0.55 mg/m^3; six samples); cobalt in total dust, 0.2-69.1 μg/m^3 (median, 3.2 μg/m^3; seven samples).

In dental laboratories, concentrations of cobalt were measured during the preparation and polishing of cobalt-chromium alloys and ranged from 30 to 190 μg/m^3 (Kempf & Pfeiffer, 1987).

Kusaka *et al.* (1986) carried out extensive personal air monitoring at different stages of hard-metal (cemented carbide) manufacturing and processing; the results, by group of workers, are given in Table 13. A similar study was performed by Lehmann *et al.* (1985), who took stationary and personal air samples during various grinding operations involving hard metal (Table 14). The airborne concentrations of cobalt were mainly below 100 μg/m3; higher concentrations were observed mainly during dry and wet grinding operations without ventilation or exhaust facilities. Exposure to cobalt during wet grinding presumably originates not only in the workplace but also from cobalt dissolved in coolants. After one week of use,

Table 12. Occupational exposures to cobalt in various industries and activities[a]

Industry/activity	No. of samples	Sex	Concentration of cobalt in ambient air	Concentration of cobalt in blood and urine	Comments	References
Hard-metal production (two subgroups)	10	M	a. Mean, 0.09 mg/m^3 b. Mean, 0.01 mg/m^3 (personal samples)	Blood: a. Mean, 10.5 μg/l b. Mean, 0.7 μg/l Urine: a. Mean, [106] μg/l b. Mean, [~3] μg/l Sampling on Friday pm	Significant correlations: air:urine (r = 0.79); air:blood (r = 0.87); blood:urine (r = 0.82)	Alexandersson & Lidums (1979); Alexandersson (1988)
Hard-metal grinding (seven subgroups)	153	–	Up to 61 μg/m^3 (stationary samples)	Median values for all subgroups: serum, 2.1 μg/l; urine, 18 μg/l	Significant correlation: serum (x)/urine (y) y = 2.69x + 14.68	Hartung & Schaller (1985)
Hard-metal tool production (11 subgroups)	170 5	M F	Mean, 28-367 μg/m^3 (personal samples)	Blood: mean, 3.3-18.7 μg/l; urine, 10-235 μg/l Sampling on Wednesday or Thursday at end of shift	Significant correlations (based on mean values): air (x)/urine (y): y = 0.67x + 0.9; air (x)/blood (y): y = 0.004x + 0.23; urine (x)/blood (y): y = 0.0065x + 0.23	Ichikawa *et al.* (1985)
Hard-metal production (six subgroups)	27	–	Breathable dust range, 0.3-15 mg/m^3 with 4-17% cobalt	Serum: mean, 2.0-18.3 μg/l; urine, 6.4-64.3 μg/g creatinine	Significant correlation: serum/urine, r = 0.93	Posma & Dijstelberger (1985)
Hard-metal production	26	M	Range, approx. 0.002–0.1 mg/m^3; median, approx. 0.01 mg/m^3 (personal samples)	Urine: Monday at end of shift (a) up to 36 μg/l ; Friday at end of shift (b) up to 63 μg/l	Significant correlations: air (x)/urine (y): (a) y = 0.29x + 0.83; (b) y = 0.70x + 0.80	Scansetti *et al.* (1985)
Cobalt powder production Presintered tungsten carbide production Hard-metal use	6 15 7	– – –	a. Range, 0.675-10 mg/m^3 b. Range, 0.120-0.284 mg/m^3 c. Range, 0.180-0.193 mg/m^3	Urine: a. mean, 35.1 μg/l b. mean, 9.6 μg/l c. mean, 11.7 μg/l Sampling on Sunday (24 h)	Times of sampling: Monday am for basic exposure level; Friday evening for cumulative exposure level	Pellet *et al.* (1984)

Table 12 (contd)

Industry/activity	No. of samples	Sex	Concentration of cobalt in ambient air	Concentration of cobalt in blood and urine	Comments	References
Cobalt powder and cobalt salt production (seven subgroups)	40	M	Mean, 46-1046 μg/m^3 (stationary samples)	Blood: mean, 5-48 μg/l; urine: mean, 19-438 μg/l Post-shift sampling	Significant correlations: air/urine; air/blood; blood (x)/urine (y): $y = 7.5x + 11.2$	Angerer *et al.* (1985)
Cobalt oxide processing and cobalt salt manufacture	49	M	Median, 0.52 mg/m^3; range, 0.1-3.0 mg/m^3 (personal samples)	Urine: mean, 0.34 mg/l; range, 0.1-0.9 mg/l	Poor correlation air:urine	Morgan (1983)
Painting porcelain with soluble cobalt salts	46	F	a. Range, 0.07-8.61 mg/m^3	Blood: a. Mean, 2.16 μg/l; b. Mean, 0.63 μg/l; Urine: a. Mean, 8.35 μg/mmol creatinine; b. Mean, 0.13 μg/mmol creatinine	Significant correlation: blood/urine ($r = 0.88$)	Christensen & Mikkelsen (1986)
Painting porcelain with slightly soluble cobalt salts	15	F	b. Range, 0.05-0.25 mg/m^3 (personal samples)			

[a]From Angerer & Heinrich (1988)

Table 13. Airborne concentrations of cobalt at various stages in the manufacture and processing of hard metals[a]

Activity	No. of workers	No. of samples	Concentration of cobalt ($\mu g/m^3$)	
			Mean ± SD	Range
Powder	12	38	688 ± 1075	6–6388
Press				
Rubber	4	19	473 ± 654	48–2905
Machine	25	27	85 ± 95	4–407
Sintering	21	38	28 ± 26	2–145
Shaping	47	129	126 ± 191	6–1155
Grinding				
Wet	131	205	53 ± 106	11–1247
Dry	1	2	1292 ± 179	1113–1471
Electron discharging	5	5	4 ± 1	1–5
Blasting	2	5	3 ± 1	1–4

[a]From Kusaka *et al.* (1986)

Table 14. Concentrations of cobalt in total dust during hard-metal grinding[a]

Type of grinding/ type of sample	No. of workplaces	No. of companies	Sampling time (h)	Concentration of cobalt ($\mu g/m^3$)	
				Median	Range
Dry grinding with exhaust facilities					
Stationary	16	6	2	3.1	0.1–203.5
Personal	16	5	2	12.3	0.5–223.8
Wet grinding without exhaust facilities					
Stationary	9	5	2	12.8	2.4–90.4
Personal	14	5	2	42.5	7.9–208.0
Wet grinding with exhaust facilities					
Stationary	8	1	2	6.9	1.1–11.8
Personal	7	1	2	13.7	1.3–29.9

[a]From Lehmann *et al.* (1985)

levels of up to 118 mg/kg were found in the coolant; after four weeks, up to 182 mg/kg were observed (Lehmann *et al.*, 1985). This finding was confirmed by Hartung (1986). Einarsson *et al.* (1979) studied the dissolution of cobalt in nine commercial cutting fluids one to five days after use in the grinding of hard-metal alloys. After one day, most of the cobalt liberated by grinding was found in solution; this percentage decreased when grinding was continued using the same coolant fluid. Only a small fraction of the cobalt was found as particles in the circulating fluid. The authors concluded that the bulk probably remains in the sediment in the storage tank.

The concentration of cobalt dust was measured in the air of a Danish porcelain factory in 1981. In personal air samples taken for 19 female plate painters, the levels were 0.07-8.61 mg/m3. The cobalt levels in blood and urine were measured in 1982 in 46 female plate underglaze painters exposed to soluble cobalt silicate and in 51 female plate overglaze painters with no exposure to cobalt. The mean levels in the blood of exposed persons (longer than four weeks) were 2.16 µg/l (range, 0.2-24; median, 1.0) compared with 0.24 µg/l in the controls (range, 0.05-0.6; median, 0.2). Mean levels in urine were: 77 µg/l (median, 26; range, 2.2-848) in exposed workers and 0.94 µg/l (median, 0.3; range, 0.05-13.8) in unexposed workers (Mikkelsen *et al.*, 1984; Christensen & Mikkelsen, 1986). In 1984, after conditions in the workplace had been improved, the concentration of cobalt in air had decreased to about 0.05 mg/m3. The mean urinary level of cobalt in 38 of the 46 workers investigated originally who were selected for urine analysis was 2.6 µg/mmol creatinine (range, 0.16-16.1) compared to 4.2 µg/mmol creatinine (range, 0.24-29.1) in 1982. A significant correlation was observed between blood cobalt and creatinine-corrected urinary cobalt levels ($p < 0.001$). In 1982, in a factory using a slightly soluble cobalt silicate, the mean cobalt levels in blood and urine from 15 female plate painters were 0.63 µg/l (median, 0.60; range, 0.37-1.58) and 0.13 µg/mmol creatinine (median, 0.11; range 0.02-0.37), respectively (Christensen & Mikkelsen, 1986; see also Table 12).

(*c*) *Air*

Levels of cobalt in the ambient air are a function of the extent to which particles of soil are dispersed by the wind. They are higher near factories in which cobalt is used, and atmospheric concentrations of cobalt in remote areas are very low: less than 1 ng/m3 in the Antarctic. In other areas, ambient air concentrations are usually around 1 ng/m3. Levels exceeding 10 ng/m3 have been reported in heavily industrialized cities (Elinder & Friberg, 1986). Combustion of organic materials containing cobalt is reported to be an additional source of emission (Lange, 1983; Angerer & Heinrich, 1988). Coal contains up to 40 mg/kg (average, 1 mg/kg) cobalt (Angerer & Heinrich, 1988), and hard coal contains about 8 mg/kg

(Schrauzer, 1989). Merian (1985) estimated a global annual generation of about 5000 tonnes of cobalt from the burning of coal.

A survey of atmospheric trace elements in the UK in 1977 showed ambient concentrations of cobalt in the range of 0.04-6.5 ng/kg at seven stations sampled. Around 57% of the cobalt content was in a soluble form (Cawse, 1978).

(d) Tobacco smoke

The content of cobalt in cigarettes has been studied by means of neutron activation; different brands of tobacco were found to contain < 0.01-2.3 mg/kg dry weight (Wyttenbach *et al.*, 1976; Iskander, 1986; Iskander *et al.*, 1986). When cigarettes were smoked in a standard smoking machine, 0.5% of the cobalt content of the cigarette was transferred into smoke condensate (Nadkarmi & Ehmann, 1970).

(e) Water and sediments

Uncontaminated samples of fresh water generally contain low concentrations of cobalt, ranging from 0.1 to 10 μg/l (Schrauzer, 1989). Concentrations of 0.1-5 μg/l have been found in drinking-water (Elinder & Friberg, 1986).

Approximately 20 000 tonnes of cobalt are transported annually by rivers to oceans, where they are precipitated (Merian, 1985). A cobalt content of 74 mg/kg has been measured in sediments (Schrauzer, 1989). Natural transport is not significantly affected by mining activities or industrial use. The concentration of cobalt in seawater is normally quite low, at 0.002-0.007 μg/l, the level decreasing with increased depth (Knauer *et al.*, 1982).

(f) Foods and beverages

Human dietary intake of cobalt is highly variable; Table 15 summarizes estimated total intake of cobalt from food in various countries. Most of the cobalt ingested is inorganic: vitamin B_{12}, which occurs almost entirely in food of animal origin, accounts for only a very small fraction. Vegetables contain inorganic cobalt but little or no vitamin B_{12} (Friedrich, 1984; Donaldson *et al.*, 1986b).

Values for the cobalt content of foods vary widely between reports, even among analyses of the same foods, probably owing as much to differences in environmental cobalt levels as to analytical difficulties or inadequate analytical techniques. Green leafy vegetables and fresh cereals are the richest and most variable sources of cobalt (0.2-0.6 μg/g dry mass), while dairy products, refined cereals and sugar contain the least cobalt (0.01-0.03 μg/g dry mass; Donaldson *et al.*, 1986b). Plant products have been estimated to contribute up to 88% of the total cobalt in the Japanese diet (Yamagata *et al.*, 1963). Normal cows' milk contains very little cobalt (average,

Table 15. Total daily intake of cobalt from food *per caput*

Country	Daily intake *per caput* (μg)	Reference
Canada	45–55	Kirkpatrick & Coffin (1974)
Finland	13	Varo & Koivistoinen (1980)
Germany	17	Pfannhauser (1988)
	15	Pfannhauser (1988)
	5–10 (vitamin B_{12} only)	Schormüller (1974)
Hungary	100	Lindner-Szotyori & Gergely (1980)
Italy	9	Pfannhauser (1988)
Japan	19.5	Yamagata *et al.* (1963)
Netherlands	5–7	Pfannhauser (1988)
Spain	25	Barberá & Farré (1986)
UK (vitamin B_{12} only)	7.0	Spring *et al.* (1979)
USA	5–6	Harp & Scoular (1952)
USSR	1.7	Reshetkina (1965)
	31	Nodiya (1972)

about 0.5 μg/l); shelled eggs have been reported to contain 0.03 μg/g (Donaldson *et al.*, 1986b). Varo and Koivistoinen (1980) found concentrations of 30-50 μg/kg dry weight in fish and vegetables; that in meat and dairy products was 10 μg/kg. The daily diet of the 70-kg 'reference man' contains cobalt at 0.01-0.02 mg/kg fresh weight (based on 20-40 μg/day intake) (Donaldson *et al.*, 1986b).

In 15 commercial beers analysed in 1965 using a colorimetric method, the levels of cobalt were well below 0.1 mg/l. When cobalt salts had been added during processing, values of up to 1.1 mg/l were recorded (Elinder & Friberg, 1986).

The cobalt content of five brewed teas averaged 0.2 μg/g (range, 0.16-0.34) and that of seven brewed coffees, 0.75 μg/g (range, 0.42-2.0 μg/g; Horwitz & Van der Linden, 1974).

(*g*) *Soils and plants*

In one study, the cobalt content of soils ranged from 1 to 40 mg/kg (Merian, 1985) with an average of 8 mg/kg (Schrauzer, 1989). In general, cobalt tends to be deficient in areas where there is granite, sand or limestone and in volcanic and peaty soils. Good drainage may reduce cobalt content (Kipling, 1980). The solubilities of cobalt compounds are pH-dependent, and cobalt is more mobile in acid soils than in alkaline soils (Schrauzer, 1989).

In industrialized areas, up to 75 mg/kg cobalt have been found in the soil around factories using cobalt powders, and higher concentrations may occur in waste-metal dumps (Kipling, 1980).

The uptake of cobalt by plants is species-dependent: cobalt is hardly detectable in green beans and the level is exceedingly low in radishes (Schrauzer, 1989). Leafy plants, such as lettuce, cabbage and spinach, have a relatively high cobalt content, whereas the content is low in grasses and cereals (Kipling, 1980). It is as yet unknown whether cobalt is essential for plants. In some cases, small amounts of cobalt produce positive growth effects, but these are dose-dependent and may be indirect (Schrauzer, 1989). It has been suggested that the element is necessary for the fixation of nitrogen in vegetables that are relatively rich in cobalt. Cobalt concentrations in pastures vary according to season and the presence of fertilizers (Kipling, 1980).

(*h*) *Human tissues and body fluids*

Over the years, there has been a progressive downward adjustment in the reported normal levels of cobalt in human tissues and body fluids as a result of improvements in analytical methodology. Concentrations of cobalt observed in the blood and urine of the general population are summarized in Table 16. The concentrations in body fluids are well below the microgram per litre level; mean concentrations reported in serum range from 0.1 to 0.3 μg/l.

Alexandersson (1988) found that smokers with no occupational exposure had a significantly higher mean cobalt concentration in urine (0.6 μg/l; SD, 0.6) than nonsmokers (0.3 μg/l; SD, 0.1). There was no difference between smokers and nonsmokers in the cobalt levels in blood.

Patients in various stages of renal failure showed a significantly higher serum concentration of cobalt than a control group, but there was no correlation to the degree of renal insufficiency. Haemodialysis did not influence the levels, whereas kidney transplantation reduced them (Lins & Pehrsson, 1984). Values for whole blood were a little higher than serum concentrations but were not well documented (Iyengar & Woittiez, 1988). In urine samples obtained from normal adults, the concentrations of cobalt were reported to be approximately 0.1-2 μg/l (see Table 16). Greatly increased urinary levels have been reported for persons taking multivitamin pills containing cobalt (Reynolds, 1989).

Considerable differences have been found in the levels of cobalt in hair, ranging from 0.4 to 500 μg/kg (Iyengar & Woittiez, 1988).

In autopsy studies, the liver has been shown to contain the highest concentration of cobalt, with individual values ranging from 6 to 151 μg/kg (median, 30 μg/kg) in seven studies. This may be attributed, at least in part, to differences in

Table 16. Concentrations of cobalt in urine, serum and whole blood of persons not exposed occupationally to cobalt

Urine		Serum (or plasma) (μg/l)	Whole blood (μg/l)[a]	Reference
Mean	Range			
–	–	0.108 ± 0.06	–	Versieck *et al.* (1978)
–	–	–	0.5 ± 0.1	Alexandersson & Swensson (1979)
0.4 μg/l	0.2–1.2	–	0.5	Alexandersson & Lidums (1979)
–	–	0.195 ± 0.015 (plasma)	–	Kasperek *et al.* (1981)
0.18 μg/creatinine	–	–	–	Kennedy *et al.* (1981)
0.38 μg/l	0.1–0.75 μg/l	–	–	Schumacher-Wittkopf & Angerer (1981)
1.3 μg/l	–	–	–	Hartung *et al.* (1982)
–	–	0.01–1.9	–	Masiak *et al.* (1982)
–	–	–	0.09 ± 0.02	Ostapczuk *et al.* (1983)
–	–	0.15 ± 0.07 (plasma)	–	Andersen & Høgetveit (1984)
0.94 μg/l	0.05–13.8 μg/l	–	–	Mikkelsen *et al.* (1984)
–	4.6 μg/g creatinine	–	–	Posma & Dijstelberger (1985)
0.41 μg/l or 0.28 μg/g creatinine	–	–	–	Scansetti *et al.* (1985)
2.0 μg/l	–	–	1.9 ± 1.1	Ichikawa *et al.* (1985)
–	–	0.28	–	Lewis *et al.* (1985)
0.09 μg/mmol creatinine	0.004–1.21 μg/mmol creatinine	–	0.24 (0.05–0.6)	Christensen & Mikkelsen (1986)
–	–	0.1	–	Hartung (1986)
–	–	0.73 ± 0.10 (plasma)	–	Collecchi *et al.* (1986)
0.4 μg/l	0.1–2.2 μg/l	–	0.5 (0.1–1.2)	Alexandersson (1988)
0.01 μg/l	–	–	0.2–1.3	Angerer *et al.* (1989)

[a]Range, or mean ± standard deviation

–, not given

food intake, since this organ stores vitamin B_{12} (Iyengar & Woittiez, 1988). In New Zealand, 96 human liver samples showed a mean concentration of 120 μg/kg wet weight cobalt, with no significant difference between sex, age or regional district (Pickston *et al.*, 1983). Levels of cobalt were lower in liver carcinoma tissue than in normal hepatocytes from the same liver samples (Kostić *et al.*, 1982). The total cobalt content of a 70-kg, unexposed man was estimated to be about 1.5 mg. The total amount of vitamin B_{12} in the body of an adult is about 5 mg, corresponding to 0.25 mg cobalt, of which 50-90% is localized in the liver (Schrauzer, 1989).

Cobalt concentrations in the hearts of patients dying from myocardiopathy associated with the consumption of beer containing cobaltous salts were found to be 10 times higher than in normal cardiac muscle (Sullivan *et al.*, 1968).

(*i*) *Iatrogenic exposure*

Cobalt is the major constituent (approximately 62%) of porous-coated cobalt-chromium alloys used in surgical implants; therefore, body levels of cobalt (urine, serum) have been used as an index of the wear rate of the prostheses. Table 17 summarizes the results of several investigations on trace metal concentrations in the body fluids of patients with total knee and hip arthroplasty with metal prostheses. Cobalt-containing particles have also been identified by microscopic examination of tissues adjacent to prostheses (Hildebrand *et al.*, 1988; Sunderman *et al.*, 1989).

Certain authors observed significant increases in mean concentrations of cobalt in the serum or urine from patients with various metal implants (especially those with metal-to-metal contact), while others found that the concentrations of this metal were only sporadically elevated. These discordant results may reflect greater rates of release of metals from implants with metal-to-metal *versus* metal-to-polyethylene articular surfaces, as well as differences among the cobalt-containing alloys used (e.g., porous-coated *versus* non-porous surfaces and cemented *versus* cementless implants). Analytical limitations may also play a major role, since the concentrations of cobalt in the serum and urine specimens from control subjects far exceeded the currently accepted ranges. Analytical inaccuracies in previous studies probably resulted from metal contamination during specimen collection, inattention to quality assurance techniques and/or inadequate instrumental sensitivity and specificity (Sunderman *et al.*, 1989).

Raithel *et al.* (1989) investigated the cobalt content in tissues surrounding hip arthroplasties and in distant muscle samples. From 10 patients with loosening of prostheses, tissue samples were taken from the implanted cup (polyethylene surface to avoid metal-to-metal friction), from the implanted shaft and from the musculus vastus lateralis, and the patients received new hip prostheses. The old cobalt-chromium-molybdenum types (ASTM F 75-74) were replaced after 5-15.5 years

Table 17. Cobalt concentrations in body fluids of patients with total hip or knee arthroplasty[a]

Study	No. of patients	Period of observation	Type of implant	Observations	Concentrations of cobalt		
					Urine	Blood	Synovial fluid
Coleman *et al.* (1973)	12	3 weeks to 32 months	Hip, cobalt-molybdenum-chromium alloy, cemented, nonporous, with or without polyethylene component (C cast alloy)	Increased cobalt and chromium in blood and urine, only with metal-to-metal contact (no polyethylene)	15-73 µg/l after 1 year	4.5-16 µg/l after 1 year	
Jones *et al.* (1975)	4	Not given	Hip, cobalt-chromium-molybdenum alloy, cemented, nonporous, with metal-to-metal contact (C cast alloy)	Increased cobalt in urine and (in one case) in synovial fluid and liver, bone and brain tissues	22-55 µg/l	–	250 µg/l 0.5-3 mg/kg
Miehlke *et al.* (1981)	30	6 months to 10 years	Knee, cobalt-chromium alloy, cemented, nonporous, with or without polyethylene component	Increased cobalt and chromium in synovial fluid and serum, especially with metal-to-metal contact	–	0.16-79 µg/l	0.36-7200 µg/l
Jorgensen *et al.* (1983)	10	Not given	Hip, cobalt-chromium-molybdenum alloy, porous-coated or nonporous, cementless	Increased cobalt in urine, especially in patients with porous-coated implants	Porous: mean, 14.2 µg/l; nonporous: mean, 8.4 µg/l		
Black *et al.* (1983)	15	1 day to 6 months	Hip, cobalt-chromium-nickel alloy, cemented, nonporous, polyethylene cup (cobalt-chromium/UMHWPE THRs[a]	Increase in serum chromium (peak at 15 days), serum nickel (peak at 6 months); normal serum cobalt	–	–	–
Bartolozzi & Black (1985)	14	1 to >30 days	Hip, cobalt-chromium alloy, cemented, nonporous, polyethylene cup	Increase in chromium (serum peak at 10 days, urine peak at 15 days)	Peak, 26.2 ng/mg creatinine	Peak, 39.9 pg/mg protein	
Pazzaglia *et al.* (1986)	17	7-15 years	Hip, cobalt-chromium-molybdenum alloy, cemented, nonporous, with or without polyethylene cup	Increased cobalt and chromium in urine and chromium in plasma	0.9-1.05 µg/l		–
Jones & Hungerford (1987)	14	1 week to 1 year	Hip, cobalt-chromium alloy, cementless, porous-coated, polyethylene cup (PCA®)	Increased urinary nickel in 2 of 14 patients at 6 months; increased urinary nickel and cobalt in 3 of 4 measured at 1 year	–	–	–

Table 17 (contd)

Study	No. of patients	Period of observation	Type of implant	Observations	Concentrations of cobalt		
					Urine	Blood	Synovial fluid
Braun *et al.* (1986)	22	5 months to 3 years	Hip, cobalt-chromium-molybdenum alloy, cementless, porous-coated, polyethylene cup, fixed	Increased urinary chromium	–	–	–
Raithel *et al.* (1989)	15	2 years	Fixed hip, cobalt-chromium-nickel-molybdenum alloy, cemented, nonporous with polyethylene cup	Increased serum cobalt	–	1.8 µg/l	
	10	5-15.5 years (mean, 12.5)	Loose hip, cobalt-chromium-nickel molybdenum alloy, cemented, nonporous with polyethylene cup; old hip replaced	Increased urinary chromium, nickel and cobalt, increased serum nickel	3.8 µg/l	–	
Sunderman *et al.* (1989)	28	1 day to 2.5 years	Knee or hip, cobalt-chromium alloy (ASTM F-75-82), porous-coated, 10 cemented, 18 cementless with polyethylene	Slight increase in serum and urinary cobalt in knee prostheses. 2 patients, substantially elevated levels (7 weeks and 22 months post-arthroplasty, with loosening of prostheses); serum and urinary chromium levels also elevated in one patient	1 µg/g creatinine (6-120 weeks) 7.7 µg/g creatinine and 5.6 µg/l in the 2 patients	0.15 µg/l (6-120 weeks) 1 and 1.15 µg/l in the 2 patients	

[a]Ultrahigh molecular weight polyethylene (total hip replacements)

(median, 12.5 years). The concentrations of cobalt in the tissues surrounding the shaft ranged from 367 to 6510 μg/kg (median, 868 μg/kg), and those in tissues surrounding the cup, from 98 to 16 293 μg/kg (median, 1080 μg/kg). Muscle tissue contained 24-151 μg/kg (median, 124 μg/kg) cobalt.

Hildebrand *et al.* (1988) also found extremely high concentrations of cobalt, up to three orders of magnitude (140 μg/g dry weight) above the normal values, in connective tissue taken on a Vitallium plate.

(j) Others

The total concentration of cobalt in cement made in Asia ranged from 8.1 to 14.2 μg/g. The metal existed mainly as insoluble salts; the concentration of water-soluble cobalt was 0.39-0.65 μg/g (Goh *et al.*, 1986). The cobalt content in 42 US cement samples was < 0.5 μg/g (Perone *et al.*, 1974).

The cobalt content of 30 household cleaning products sold in Spain in 1985 ranged from 0.1 to 14 mg/l; the highest levels were found in two bleaches, containing 1.1 and 1.4 mg/l (Vilaplana *et al.*, 1987).

2.4 Regulatory status and guidelines

Occupational exposure limits and guidelines established in different parts of the world are given in Table 18.

Table 18. Occupational exposure limit values for cobalt[a]

Country or region	Year	Concentration (mg/m^3)	Interpretation[b]
Australia	1985	0.1 cobalt, metal fumes and dust	TWA
Belgium	1989	0.05 cobalt, metal dust and fumes (as Co)	TWA
Bulgaria	1985	0.5 cobalt and compounds (as Co); cobalt, metal dust and fumes (as Co)	TWA
Canada	1980	0.1 cobalt as metal dust and fume	TWA
Czechoslovakia	1985	0.05 cobalt and compounds (as Co)	TWA
		0.1 cobalt and compounds (as Co)	max
Denmark	1988	0.1 cobalt carbonyl (as Co); cobalt hydrocarbonyl (as Co)	TWA
		0.05 cobalt in the form of powder, dust and fumes and inorganic compounds (as Co)	TWA
Finland	1987	0.05 cobalt and inorganic compounds (as Co)	TWA

Table 18 (contd)

Country or region	Year	Concentration (mg/m^3)	Interpretation[b]
Hungary	1987	0.1 cobalt and compounds (as Co) 0.2 cobalt and compounds (as Co)	TWA STEL
Indonesia	1987	0.1 cobalt and compounds (as Co)	TWA
Italy	1987	0.1 cobalt, metal dust and fumes (as Co)	TWA
Mexico	1987	0.1 cobalt, metal dust and fumes (as Co)	TWA
Netherlands	1986	0.1 cobalt, metal dust and fume (as Co)	TWA
Norway	1981	0.05 cobalt and compounds (as Co)	TWA
Poland	1985	0.5 cobalt and compounds (as Co); cobalt, metal dust and fumes (as Co)	TWA
Romania	1985	0.2 cobalt and cobalt oxide and cobalt, metal dust and fumes (as Co) 0.5 cobalt and cobalt oxide and cobalt, metal dust and fumes (as Co)	TWA max
Sweden	1988	0.05 cobalt and inorganic compounds (as Co)	TWA
Switzerland	1987	0.1 cobalt dust and compounds (as Co)	TWA
Taiwan	1987	0.1 cobalt, metal dust and fumes (as Co)	TWA
UK	1987	0.1 cobalt and compounds (as Co)	TWA
USA			
ACGIH	1989	0.05 cobalt (as Co) metal dust and fumes 0.1 cobalt carbonyl (as Co); cobalt hydrocarbonyl (as Co)	TWA Guide-lines
OSHA	1988	0.1 cobalt (as Co) metal dust and fume	TWA
USSR	1987	0.5 cobalt and compounds (as Co); cobalt, metal dust and fumes (as Co) 0.01 cobalt hydrocarbonyl and decomposition products (as Co)	max
Venezuela	1987	0.1 cobalt, metal dust and fumes (as Co)	TWA
Yugoslavia	1985	0.1 cobalt and compounds (as Co); cobalt, metal dust and fumes (as Co)	TWA

[a]From Direktoratet for Arbeidstilsynet (1981); Arbeidsinspectie (1986); Cook (1987); Health and Safety Executive (1987); National Swedish Board of Occupational Health (1987); Arbejdstilsynet (1988); National Institute for Occupational Safety and Health (1988); American Conference of Governmental Industrial Hygienists (ACGIH) (1989); US Occupational Safety and Health Administration (OSHA) (1989); United Nations Environment Programme (1990). Guidelines and standards are generally prepared by scientific bodies and sometimes become official standards, or they are recognized and applied in practice on a voluntary basis as a guide for monitoring the working environment or for technical prevention.

[b]TWA, 8-h time-weighted average; STEL, 10–15-min short-term exposure limit

2.5 Analysis

Typical methods for the analysis of cobalt in air, water, various working materials, food and biological materials are summarized in Table 19.

Table 19. Methods for the analysis of cobalt

Sample matrix	Sample preparation	Assay procedure[a]	Limit of detection	Reference
Urine	Digestion with nitric/sulfuric acid; ion-exchange separation	GF/AAS	0.1 µg/l	Lidums (1979)
	Chelatization, extraction	GF–AAS	0.1 µg/l	Schumacher-Wittkopf & Angerer (1981)
	Dilution with nitric acid	GF–AAS	Not given	Hartung *et al.* (1983)
	Dilution with nitric acid	GF–AAS	2 µg/l	Pellet *et al.* (1984)
	Digestion with sulfuric, nitric, perchloric acid; chelation, extraction	F–AAS	1 µg/l	Ichikawa *et al.* (1985)
	Direct analysis	GF–AAS	6 µg/l	Bouman *et al.* (1986)
	N,N–Hexamethyleneammonium-hexamethylenedithiocarbamic acid/xylene extraction	GF–AAS (Z)	1 µg/l (0.2 µg/l for 6 ml urine)	Bouman *et al.* (1986)
	Magnesium nitrate modifier	GF–AAS (Z)	2.6 µg/l	Kimberley *et al.* (1987)
Blood, urine	Dilution with nitric acid	GF–AAS (Z)	0.1 µg/l	Christensen *et al.* (1983)
	Protein precipitation; dilution with nitric acid	GF–AAS (Z)	0.1 µg/l	Christensen & Mikkelsen (1986)
Blood	Digestion with nitric, sulfuric acid	GF–AAS	0.1 µg/l	Lidums (1979)
	Dilution and matrix modification	GF–AAS	0.2 µg/l	Delves *et al.* (1983)
	Freeze-dried, low-temperature ashing; resolved in nitric acid	GF–AAS (Z)	0.8 µg/l	Ichikawa *et al.* (1985)
Blood, tissues	Digestion with nitric, sulfuric, perchloric acid	ICP	10 µg/kg blood 0.2 µg/kg tissue	National Institute for Occupational Safety and Health (1985)
Blood, serum	Wet digestion with nitric, sulfuric, perchloric acid; chelation, extraction	GF–AAS	0.1 µg/l	Barfoot & Pritchard (1980)
Serum	Dry ashing at 450°C	NAA	Not given	Versieck *et al.* (1978)

Table 19 (contd)

Sample matrix	Sample preparation	Assay procedure[a]	Limit of detection	Reference
Plasma, urine	Palladium matrix modification	GF-AAS (Z)	0.15 µg/l	Sampson (1988)
Biological materials	Wet digestion with nitric, sulfuric acid	ADPV	1 ng/l in the analyte solution	Ostapczuk *et al.* (1983)
Air	Digestion with nitric acid	GF-AAS	Not given	Hartung *et al.* (1983)
	Digestion with nitric, perchloric acid	ICP	1 µg/sample	National Institute for Occupational Safety and Health (1984a)
	Digestion with aqua regia	F-AAS	0.6 µg/sample	National Institute for Occupational Safety and Health (1984b)
	Digestion with hydrochloric, nitric acid	GF-AAS	1 µg/m^3	Ichikawa *et al.* (1985)
	Digestion with nitric acid	GF-AAS	20 ng/m^3 (sample volume 1.5 m^3)	Kettrup & Angerer (1988)
Seawater	Direct analysis	DPCSV	6 pmol (0.4 ng)	Donat & Bruland (1988)
Water	Chelation with ammonium pyrrolidinedithiocarbamate; preconcentration on activated charcoal	F-AAS, ICP	< 1 µg/l	Berndt *et al.* (1985)
Food	Dry digestion; triethanolamine electrolyte	Adsorption voltammetry	Not given	Meyer & Neeb (1985)
	Dry digestion; chelation with sodium di(trifluoroethyl)dithiocarbamate	GC	50 ng/sample	Meyer & Neeb (1985)
	Digestion with nitric acid; extraction with cupferron, chloroform	F-AAS	1.4 ng/ml	Barberá *et al.* (1986)
Milk	Ashing in muffle furnace	GF-AAS (Z)	Not given	Gunshin *et al.* (1985)

[a]Abbreviations: GF-AAS, graphite furnace-atomic absorption spectrometry; F-AAS, flame atomic absorption spectrometry; Z, background correction for Zeeman effect; ICP, inductively coupled plasma emission spectrometry; NAA, neutron activation analysis; ADPV, adsorption differential pulse voltammetry; DPCSV, differential pulse cathodic stripping voltammetry; GC, gas chromatography

Methods for quantitative analysis include graphite furnace-atomic absorption spectrometry (GF-AAS), inductively coupled plasma emission spectrometry (ICP), neutron activation analysis and electrochemical methods such as differential pulse anodic stripping voltammetry (DPASV). ICP and X-ray fluorescence appear to be too insensitive for the determination of cobalt in environmental and biological matrices; this is also true of the older photometric methods, which also showed lack of specificity.

With NAA, cobalt can be determined at the nanogram per kilogram level. This method offers the advantage that it requires little sample preparation, but its application is restricted to a few highly specialized laboratories. Voltammetry and, in particular, GF-AAS are much more common and permit determination of cobalt at the nanogram per kilogram level. GF-AAS, in comparison to voltammetry, does not usually require complete digestion of the sample, which makes the technique more practicable.

Air samples are collected on cellulose ester membrane filters, wet-digested with nitric and perchloric acids or aqua regia and analysed by AAS or ICP (National Institute for Occupational Safety and Health, 1984a,b; Kettrup & Angerer, 1988). The routine procedures do not permit identification of individual cobalt compounds.

Analysis of cobalt in soil, food, industrial samples and human tissues also requires complete digestion of the matrices. The US Environmental Protection Agency (1983) established standard methods using ICP and GF-AAS for the chemical analysis of water and wastes. An extremely low detection limit of 1.2 ng/l natural water was obtained using cation-exchange liquid chromatography with luminol chemiluminescence (Boyle *et al.*, 1987). A similarly high sensitivity, 0.64 ng/kg, is obtained by photoacoustic spectroscopy after extraction with 2-nitroso-1-naphthol/*meta*-xylene (Kitamori *et al.*, 1986).

Determination of cobalt in whole blood, plasma, serum and urine is used as a biological indicator of exposure to cobalt (Ichikawa *et al.*, 1985; Ferioli *et al.*, 1987; Angerer *et al.*, 1989). Choice of specimen, sampling strategies, specimen collection, transport, storage and contamination control, as well as quality control and quality assurance procedures (Schaller *et al.*, 1987), are of fundamental importance for an adequate monitoring programme. GF-AAS and DPASV are practical and reliable techniques that furnish the requisite sensitivity for measuring cobalt concentrations in biological samples. The detection limits for cobalt determination by GF-AAS analysis with Zeeman background collection are below 0.6 µg/l of body fluids, depending on the type of sample preparation.

Greater sensitivity in DPASV analysis can be achieved by using a dimethylglyoxime-sensitized mercury electrode, which provides detection limits down to 1 ng/l for cobalt in biological media (Ostapczuk *et al.*, 1983, 1984).

Koponen *et al.* (1982) analysed cobalt-containing airborne dusts from hard-metal manufacturing and grinding processes by AAS and instrumental NAA. The structure of the dusts was studied by scanning electron microscopy with an energy dispersive X-ray. Cobalt was found to exist as separate particles in the dust from the mixing of raw material powders only. In the dusts from the pressing, forming and grinding of hard metal, cobalt appeared mainly in contact with tungsten carbide particles.

3. Biological Data Relevant to the Evaluation of Carcinogenic Risk to Humans

3.1 Carcinogenicity studies in animals

(*a*) *Inhalation exposure*[1]

Hamster: As part of a larger study, groups of 51 male Syrian golden hamsters (ENG:ELA strain), two months of age, were exposed by inhalation to 0 or 10 mg/m^3 *cobalt[II] oxide* dust (with a mass median diameter of 0.45 μm) for 7 h per day on five days per week for life. Median survival was 16.6 months in treated hamsters compared to 15.3 months in controls. No difference in the incidence of any tumour was observed between the cobalt oxide-treated and untreated hamsters (Wehner *et al.*, 1977). [The Working Group noted the poor survival of the treated and control animals.]

(*b*) *Intratracheal instillation*

Rat: Groups of 50 male and 50 female Sprague-Dawley rats, ten weeks of age, received intratracheal instillations of 2 or 10 mg/kg bw *cobalt[II] oxide* powder (derived from thermal decomposition of cobalt[II] nitrate; approximately 80% of particles 5-40 μm [purity unspecified]) or 10 mg/kg bw of a *cobalt-aluminium-chromium spinel* (a blue powder [purity unspecified], with the empirical formula Co[II] 0.66, Al 0.7, Cr[III] 0.3, O 3.66, made of a mixture of CoO, $Al(OH)_3$ and Cr_2O_3 ignited at 1250°C; 80% of particles < 1.5 μm) in saline every two weeks (then

[1]The Working Group was aware that an inhalation study of cobalt sulfate heptahydrate was planned in mice and rats (IARC, 1990)

every four weeks from the nineteenth to the thirtieth treatment) for two years (total doses, 78 and 390 mg/kg bw cobalt oxide and 390 mg/kg bw cobalt spinel). Control groups of 50 males and 50 females received instillations of saline only or remained untreated. Animals were allowed to live until natural death or were sacrificed when moribund. No appreciable difference in body weights or survival times was observed between the treated and control groups [exact survival data not given]. Bronchoalveolar proliferation was observed in 0/100 untreated controls, 0/100 saline controls, 51/100 low-dose cobalt oxide-treated rats and 70/100 high-dose cobalt oxide-treated rats, and in 61/100 rats treated with the spinel. [The Working Group noted that the nature of the bronchoalveolar proliferation or possible association with inflammation was not described.] No pulmonary tumour was observed in 100 untreated or 100 saline controls. In the groups treated with the low dose of cobalt oxide, one male and one female developed benign lung tumours; in the groups treated with the high dose of cobalt oxide, one bronchoalveolar carcinoma occurred in a female and three adenocarcinomas and two bronchoalveolar adenomas were observed in males; in the groups receiving the spinel, one squamous-cell carcinoma was observed in males and two squamous-cell carcinomas were observed in females (Steinhoff & Mohr, 1991).

In a smaller experiment by the same authors, groups of 20 female Sprague-Dawley rats, 10 weeks of age, received weekly intratracheal instillations of 10 mg/kg bw *cobalt[II] oxide* for seven weeks and 20 mg/kg bw once every two weeks for 20 treatments (total dose, 470 mg/kg bw), and 20 mg/kg bw benzo[*a*]pyrene following the same dose regimen (total dose, 200 mg/kg bw), with a four-day interval between the two treatments. A further group of 20 females received treatment with benzo[*a*]pyrene alone. Animals were allowed to live their natural lifespan or were sacrificed when moribund [exact survival not stated]. Eight rats treated with cobalt oxide and benzo[*a*]pyrene had squamous-cell carcinomas and one had an adenocarcinoma of the lung. One animal given benzo[*a*]pyrene had a squamous-cell carcinoma of the lung (Steinhoff & Mohr, 1991).

Hamster: In a large experiment to study the effects of particulates on *N*-nitrosodiethylamine (NDEA)-induced respiratory tract carcinogenesis, groups of 25 male and 25 female hamsters [strain unspecified], seven weeks old, were given subcutaneous injections of 0.5 mg NDEA in saline or saline alone once a week for 12 weeks. One week later and once a week thereafter for 30 weeks, 4 mg *cobalt[II,III] oxide* powder (particle size, 0.5-1.0 μm [purity unspecified]) suspended in a gelatin and saline vehicle were administered by intratracheal instillation. Groups of 25 male and 25 female hamsters receiving subcutaneous injections of NDEA or saline and intratracheal instillations of the gelatin-saline vehicle served as controls. At the end of treatment (42 weeks), 39, 43, 33 and 43 animals were still alive in the four groups, respectively. Animals were observed for an additional 43-68 weeks

following the last intratracheal instillation. Two of 50 hamsters receiving injections of saline and cobalt oxide by intratracheal instillation developed pulmonary alveolar tumours; 1/50 hamsters receiving injections of saline and gelatin-saline intratracheally developed a tracheal tumour. The incidences of tumours at various sites in hamsters given NDEA with cobalt oxide in gelatin-saline were similar to those in animals receiving NDEA and gelatin-saline alone (Farrell & Davis, 1974).

(*c*) *Subcutaneous injection*

Rat: In a study designed to monitor cobalt-induced hyperlipidaemia, 20 male Wistar rats, about four weeks of age, received two courses, separated by a nine-day interval, of five daily subcutaneous injections of 40 mg/kg bw *cobalt[II] chloride* [purity unspecified] dissolved in saline, and were observed for 12 months. A control group of 20 males received injections of saline alone. At the end of the observation period, 8/11 surviving treated rats had developed subcutaneous fibrosarcomas (four of which were reported to be distant from the injection site), whereas none of the 19 surviving controls developed a tumour [$p < 0.001$, Fisher's exact test]. Post-mortem examinations were not made on the nine rats that died during the experiment. In a second experiment, 20 male Wistar rats received the same treatment but were observed for eight months. No control group was provided. At the end of this observation period, six of the 16 survivors had subcutaneous fibrosarcomas, including one tumour distant from the site of injection. Four rats that died during the observation period were not autopsied (Shabaan *et al.*, 1977).

Groups of 10 male Sprague-Dawley rats, 10 weeks of age, received subcutaneous injections of saline (two groups) or 2 mg/kg bw *cobalt[II] oxide* [purity unspecified] suspended in saline, five times a week, or subcutaneous injections of 10 mg/kg bw cobalt[II] oxide in saline once a week over a period of two years (total dose, 1000 mg/kg bw). Animals were allowed to live their natural lifespan or were sacrificed when moribund [survival data not given]. Malignant tumours (histiocytomas or sarcomas) developed at the injection site in 0/10, 0/10, 5/10 and 4/10 rats in the four groups, respectively (Steinhoff & Mohr, 1991).

(*d*) *Subcutaneous implantation*

Rat: Groups of five male and five female Wistar rats, four to six weeks of age, received subcutaneous implants of four pellets (approximately 2 mm in diameter) of either a *cobalt-chromium-molybdenum* (and lesser amounts of nickel) alloy (Vitallium; see p. 374 of this monograph), nickel metal, copper metal, nickel-gallium alloy (60% nickel, 40% gallium) or one of seven other implant materials not known to contain nickel, chromium or cobalt. Animals were observed for up to 27 months [survival of animals receiving cobalt-chromium-molybdenum alloy not given]. Sarcomas (mostly fibrosarcomas and rhabdomyosarcomas) developed around the

implants in 5/10 rats that received nickel pellets and in 9/10 rats that received nickel-gallium alloy pellets; no sarcoma developed in rats that received the cobalt-chromium-molybdenum pellets or in any of the other groups (Mitchell *et al.*, 1960).

(*e*) *Intramuscular injection*

Mouse: A group of 50 female Swiss mice, two to three months of age, received single intramuscular injections of 10 mg/site of unwashed powdered *cobalt[II] oxide* (particle size, ≤ 5 μm [purity unspecified]) in 10% aqueous penicillin G procaine in each thigh. Within two to six days, 25 mice had died. A further group of 25 females received similar injections of the powdered cobalt oxide that had been washed repeatedly in distilled water; this washed cobalt oxide did not induce acute mortality. The 25 survivors of the first group and the 25 mice from the second group were combined, and 46 were still alive 13 weeks after injection. A control group of 51 female mice similarly received intramuscular injections of penicillin G procaine vehicle (60 000 IU/site) into each thigh; 48 survived 13 weeks after injection. Animals were observed for up to 110 weeks [survival unspecified]. No tumour developed at the injection site in any of the cobalt oxide-treated or control mice. Incidences of tumours at other sites were similar in the treated and control groups (Gilman & Ruckerbauer, 1962).

A group of 30 mice [sex, strain and age unspecified] received intramuscular injections of 0.2 mg cobalt as *cobalt naphthenate* [purity, dosage, schedule, vehicle and duration unspecified] into the right hind limb. Tumours of the muscle in the hind leg developed in eight of the mice (Nowak, 1966). [The Working Group noted the incomplete reporting.]

Rat: A group of 10 male and 10 female hooded rats, two to three months old, received a single intramuscular injection of 28 mg *cobalt metal powder* (spectrographically pure, 400 mesh; 3.5 μm × 3.5 μm to 17 μm × 12 μm with large numbers of long narrow particles of the order of 10 μm × 4 μm) in 0.4 ml fowl serum into the thigh; a control group of ten males and ten females received fowl serum only. Average survival times were 71 weeks in treated males and 61 weeks in treated females; survival of controls was not specified. During the observation period of up to 122 weeks, 4/10 male and 5/10 female treated rats developed sarcomas (mostly rhabdomyosarcomas) at the injection site compared to 0/20 controls. A further group of ten female rats received a single intramuscular injection of 28 mg *cobalt metal powder* in 0.4 ml fowl serum; others received injections of 28 mg zinc powder (five rats) or 28 mg tungsten powder (five rats). Average survival time for cobalt-treated rats was 43 weeks. During the observation period of up to 105 weeks, sarcomas (mostly rhabdomyosarcomas) developed in 8/10 cobalt powder-treated rats; none occurred in the zinc powder- or tungsten powder-treated rats. No other

tumour occurred in any of the cobalt-treated or other rats, except for one malignant lymphoma in a zinc-treated rat (Heath, 1954a, 1956).

In a supplementary study, a group of 30 male hooded rats, two to three months of age, received a single intramuscular injection of 28 mg *cobalt metal powder* (spectrographically pure [particle size unspecified]) in 0.4 ml fowl serum into the right thigh; a control group of 15 males received a single injection of fowl serum only. The rats were killed at intervals of one to four weeks after injection or at fortnightly intervals up to 20 weeks after injection, when the first tumour appeared. The author described leukocyte infiltration, muscle fibre necrosis and regeneration and the development of a tumour nodule in one rat (Heath, 1960).

Groups of 10 male and female Wistar rats [sex ratio unspecified], two to three months old, received a single intramuscular injection of 30 mg/site of powdered, reagent-grade *cobalt[II] oxide* (particles ground to ≤ 5 μm and washed repeatedly in distilled water) suspended in 10% aqueous penicillin G procaine or penicillin G procaine (90 000 IU/site) alone into the thigh muscle and were observed for 74 weeks [number of survivors unspecified]. No tumour occurred at the site of injection in the 10 control rats during the study, whereas rhabdomyosarcomas developed at the injection site in 5/10 cobalt oxide-treated rats. Metastases were seen in four of the five tumour-bearing rats. No other neoplasm was noted in control or treated rats (Gilman & Ruckerbauer, 1962).

A group of 30 male and female Wistar rats [sex ratio unspecified], two to three months of age, received simultaneous intramuscular injections of 20 mg/site of powdered *cobalt[II] sulfide* [purity unspecified] (ground to ≤ 5 μm diameter and washed repeatedly in water) suspended in penicillin G procaine into each thigh. A total of 35 sarcomas were observed at the 58 injection sites in the 29 rats that survived 13 weeks after treatment, with a mean latency of 28 weeks. Metastases were noted in 16/29 rats with tumours; no other neoplasm was seen. No control was reported (Gilman, 1962).

Groups of male and female Wistar rats [sex ratio unspecified], two to three months of age, received two simultaneous intramuscular injections (five rats) in each thigh or single injections (19 rats) of *cobalt[II] oxide* (20 mg/site; particle size ≤ 5 μm; washed repeatedly in water) suspended in aqueous procaine G penicillin. No control group was reported. A total of 13 sarcomas (mostly rhabdomyosarcomas) were noted at the 29 injection sites of the 24 rats that survived 13 weeks of treatment (mean latency, 25 weeks). Metastases were noted in 3/12 rats with tumours (Gilman, 1962).

In a series of three experiments, a total of 80 female hooded rats, seven to nine weeks of age, received an intramuscular injection of 28 mg/rat of wear particles, obtained by working in Ringer's solution *in vitro* of artificial hip or knee prostheses

made from *cobalt-chromium-molybdenum* alloy (66.5% cobalt, 26.0% chromium, 6.65% molybdenum, 1.12% manganese; particle diameter, down to 0.1 μm [mostly 0.1-1 μm]), in 0.4 ml horse serum and were observed for up to 29 months [survival not specified]. No control group was reported. Sarcomas developed at the injection site in 3/16, 4/14 and 16/50 rats in the three series, respectively. Approximately half of the tumours were rhabdomyosarcomas; the remainder were mostly fibrosarcomas (Heath *et al.*, 1971; Swanson *et al.*, 1973).

(f) Intramuscular implantation

Rat: As a follow-up to the studies by Heath and Swanson (see above), groups of female Wistar and hooded rats, weighing 190-310 and 175-220 g, respectively, received intramuscular implants of 28 mg of coarse (100-250 μm diameter; 51 Wistar rats) or fine (0.5-50 μm diameter, 85% 0.5-5 μm; 61 Wistar and 53 hooded rats) particles as a dry powder, obtained by grinding a *cobalt-chromium-molybdenum* alloy (68% cobalt, 28% chromium, 4% molybdenum), and were observed for life. A sham-operated control group of 50 female Wistar rats was available. Survival at two years was 11/51 rats receiving the coarse particles, 7/61 Wistar rats receiving the fine particles, 0/53 hooded rats receiving the fine particles and 5/50 Wistar controls. No tumour was noted at the implantation site of rats treated with either of the alloy particles or in sham-operated control animals (Meachim *et al.*, 1982).

Groups of 15 male and 15 female Sprague-Dawley rats, aged 20-30 days, received intramuscular implants of polished rods (1.6 mm diameter, 8 mm length) of one of three *alloys* (wrought Vitallium: 19-20% chromium, 14-16% tungsten, 9-11% nickel, < 0.15% carbon, < 2% [manganese], < 1% silicium, < 3% iron, balance cobalt; cast Vitallium: 27-30% chromium, 5-7% molybdenum, < 2.5% nickel, < 0.3% carbon, < 1% [manganese], < 1% silicium, < 0.75% iron, balance cobalt; $MP_{35}N$ alloy: 19-21% chromium, 33-37% nickel, < 0.025% carbon, < 1% iron, < 0.15% manganese, 9.5-10.5% molybdenum, < 0.15% silicium, 0.65-1% titanium; balance cobalt) and were observed for up to two years [survival unspecified]. Groups of 15 male and 15 female untreated and sham-operated control animals were available. No benign or malignant tumour developed at the implant site in any of the groups receiving metal implants or in either control group. The incidences of malignant tumours at distant sites did not differ significantly among the treated and control groups (Gaechter *et al.*, 1977).

Guinea-pig: A group of 46 female Dunkin-Hartley guinea-pigs, weighing 550-930 g, received intramuscular implants of 28 mg of a powdered *cobalt-chromium-molybdenum* alloy (68% cobalt, 28% chromium, 4% molybdenum; particle diameter, 0.5-50 μm) and were observed for life; 12/46 animals were alive at three years. No control group was reported. No tumour was

observed at the implantation site of any guinea-pig; nodular fibroblastic hyperplasia was observed at the implantation site in eight animals (Meachim *et al.*, 1982).

(*g*) *Intra-osseous implantation*

Rat: Groups of 10-17 male and 8-15 female Sprague-Dawley rats, 30-43 days of age, received implants of one of seven test materials containing *cobalt alloyed with chromium and nickel, molybdenum, tungsten and/or zirconium*, with traces of other elements (as small rods, 1.6 mm diameter and 4 mm length, powders or porous compacted wire), in the femoral bone and were observed for up to 30 months. Groups of 13 male and 13 female untreated and sham-operated controls were available. Average survival was longer than 22 months. Sarcomas at the implant site were observed in 1/18 rats (males and females given cobalt-based alloy powder containing 41% Co), 3/26 rats (males and females given $MP_{35}N$ powder containing 33% Co) and 3/32 rats (males and females given porous compacted wire containing 51% Co). No tumour was observed in two groups of 25 rats given rods containing 69 or 47% cobalt, in two groups of 26 rats given rods containing 0.11 or 33% cobalt, in two groups of 25 and 26 untreated rats, or in a group of 26 sham-treated control rats (Memoli *et al.*, 1986).

(*h*) *Intraperitoneal injection*

Mouse: In a screening study based on the enhanced induction of lung tumours, groups of 10 male and 10 female strain A mice, six to eight weeks of age, received intraperitoneal injections of *cobalt[III] acetate* (> 97% pure) in saline three times per week for eight weeks (total doses, 95, 237 and 475 mg/kg bw). After 30 weeks, lung tumours were found in 8/20, 8/20 and 10/17 mice in the respective treatment groups, and in 7/19 saline-treated controls (not significant) (Stoner *et al.*, 1976).

Rat: Groups of 10 male and 10 female Sprague-Dawley rats, 10 weeks of age, received three intraperitoneal injections at two-month intervals of saline or 200 mg/kg bw *cobalt[II] oxide* [purity unspecified] or *cobalt-aluminium-chromium spinel powder* (see above) in saline (total dose, 600 mg/kg bw). Animals were allowed to live their natural lifespan or were sacrificed when moribund [survival not given]. Malignant peritoneal tumours occurred in 1/20 controls (histiocytoma), 14/20 cobalt oxide-treated rats (10 histiocytomas, three sarcomas, one mesothelioma) and 2/20 spinel-treated animals (one histiocytoma, one sarcoma) (Steinhoff & Mohr, 1991).

(*i*) *Intrarenal administration*

Rat: Two groups of 20 and 18 female Sprague-Dawley rats, weighing 120-140 g, received a single injection of 5 mg *cobalt[II] sulfide* [reagent grade; purity and

particle size unspecified] or 5 mg *metallic cobalt powder* [purity unspecified] suspended in 0.05 ml glycerine into each pole of the right kidney. A group of 16 female rats receiving injections of 0.05 ml glycerine into each pole of the kidney served as controls. After 12 months, all rats were necropsied; no tumour was observed in the kidneys of treated or control rats (Jasmin & Riopelle, 1976). [The Working Group noted the short duration and inadequate reporting of the experiment.]

(j) Other

Rat: Two groups of 10 female hooded rats, two to three months of age, received *intrathoracic injections* of 28 mg *cobalt metal powder* (spectrographically pure; particle size, < 400 mesh; 3.5 μm × 3.5 μm to 17 μm × 12 μm, with many long narrow particles of the order of 10 μm × 4 μm) in serum [species unspecified] through the right dome of the diaphragm (first group) or through the fourth left intercostal space (second group) and were observed for up to 28 months. Death occurred within three days of the treatment in 6/10 rats injected through the diaphragm and in 2/10 rats injected through the intercostal space. The remaining rats in the first group (diaphragm) survived 11-28 months and in the second group (intercostal space), 7.5-17.5 months. Of the 12 rats that survived the injection, four developed intrathoracic sarcomas (three of mixed origin, including rhabdomyosarcomatous elements, one rhabdomyosarcoma arising in the intercostal muscles) (Heath & Daniel, 1962).

Rabbit: Twelve male rabbits [strain unspecified], weighing 2-2.5 kg, were given intramuscular, intravenous, intrapleural or intrahepatic injections of *cobalt naphthenate* [purity and dose unspecified]. Within two to six months, tumours developed at the site of injection in eight rabbits, including one pleural mesothelioma, one haemangioendothelioma of the liver, one osteochondroma of the ear and five skeletal muscle tumours (Nowak, 1961). [The Working Group noted the lack of controls, the small number of animals and the incomplete reporting of the experiment.]

A summary of most of these studies is given in Table 20.

3.2 Other relevant data

The metabolism and toxicity of cobalt have been reviewed (Taylor & Marks, 1978; Elinder & Friberg, 1986). Recent interest has centred on the biological monitoring of cobalt, i.e., the determination of cobalt in human biological materials such as blood and urine, and how such data may be used to assess absorption, exposure and possible health risks (Alessio & Dell'Orto, 1988).

Table 20. Summary of animal carcinogenicity studies by form of cobalt

Reference	Species/ strain	Sex	Dose schedule	Experimental parameter/ observation	Group				Comments
					0	1	2	3	
Cobalt metal powder									
Heath (1954, 1956)	Rat Hooded	M	i.m., single inj., fowl serum	Dose (mg) Survival (122 weeks) Local sarcoma	0 Not given 0/10	28 4/10			
		F		Dose (mg) Survival (122 weeks) Local sarcoma	0 Not given 0/10	28 5/10	28 8/10		
Heath & Daniel (1962)	Rat Hooded	F	intrathoracic in serum	Dose (mg) Survival (3 days) Thoracic tumour	0	28 12/20 4/12			
Jasmin & Riopelle (1976)	Rat Sprague-Dawley	F	intrarenal	Dose (mg) Survival (12 months) Kidney tumour	0 Not given 0/16	5 0/18			Inadequate
Cobalt alloys									
Heath *et al.* (1971); Swanson *et al.* (1973)	Rat Hooded	F	i.m., single inj., wear particles from Co/Cr/Mo, in horse serum	Dose (mg) Survival (29 months) Local sarcoma	0 Not given	28 23/80			
Gaechter *et al.* (1977)	Rat Sprague-Dawley	M+F	i.m. impl. Co/Cr/W/Ni/C/Mn/Si/Fe (1.6 x 8 mm)	Dose (polished rod) Survival (2 years) Local tumour	0[a] Not given 0/30	0[a] 0/30	1 0/90		No significant difference in distant tumours
Memoli *et al.* (1986)	Rat Sprague-Dawley	M+F	intraoss. impl., Co/Cr/Ni/Mo/W/Zr	Dose (powder, wire, rod) Survival (30 months) Local sarcoma	0[a] Not given 0/51	0[a] 0/26	1 7/76[b]		
Mitchell *et al.* (1960)	Rat Wistar	M+F	s.c. impl. Co/Cr/Mo/Ni	Dose (pellets ~ 2-mm diam) Survival (27 months) Local tumour	Not given	 0/10			
Meachim *et al.* (1982)	Rat Wistar and hooded	F	i.m. impl. Co/Cr/Mo fine and coarse particles	Dose (mg) Survival (2 years) Local tumour	0 5/50 0	28 11/51 0	28 7/61 0	28 0/53 0	

Table 20 (contd)

Reference	Species/ strain	Sex	Dose schedule	Experimental parameter/ observation	Group				Comments
					0	1	2	3	
Cobalt alloys (contd)									
Steinhoff & Mohr (1991)	Rat Sprague-Dawley	M+F	3 i.p. inj., Co/Al/Cr spinel powder	Dose (mg/kg/bw) Survival (2 years) Local tumour	0 Not given 1/20	200 2/20			
Steinhoff & Mohr (1991)	Rat Sprague-Dawley	M+F	Intratracheal inst. 1 x 2 weeks Co/Al/Cr spinel 2 years	Dose (mg/kg bw) Survival (2 years) Squamous-cell tumour of the lung	0 Not given 0/200	10 3/100			
Meachim *et al.* (1982)	Gunea-pig	F	i.m. impl. Co/Cr/Mo powder	Dose (mg) Survival (3 years) Local tumour Local fibroblastic hyperplasia		28 12/46 0/46 8/46			
Cobalt[II] oxide									
Gilman & Ruckerbauer (1962)	Mouse Swiss	F	i.m. inj. in each thigh	Dose (mg/site) Survival (13 weeks) Local sarcoma	0 48/51 0/48	10 46/75 0/46			
Steinhoff & Mohr (1991)	Rat Sprague-Dawley	M	Intratracheal inst. 1 x 2 weeks 2 years	Dose (mg/kg bw) Survival (2 years) Benign squamous pulmonary tumour Bronchioalveolar adenoma Pulmonary adenocarcinoma Bronchoalveolar adenocarcinoma	0 Not given 0/100 0/100 0/100 0/100	2 1/50 0/50 0/50 0/50	10 0/50 2/50 2/50 1/50		
		F		Dose (mg/kg bw) Survival Bronchoalveolar adenoma Bronchoalveolar carcinoma	0 Not given 0/100 0/100	2 1/50 0/50	10 0/50 1/50		

Table 20 (contd)

Reference	Species/ strain	Sex	Dose schedule	Experimental parameter/ observation	Group				Comments
					0	1	2	3	
Cobalt[II] oxide (contd)									
Gilman & Ruckerbauer (1962)	Rat Wistar	M+F	i.m. inj.	Dose (mg/site) Survival (90 days) Local sarcoma	0 10/10 0/10	30 10/10 5/10			
Gilman (1962)	Rat Wistar	M+F	i.m. inj.	Dose (mg/site) Survival (13 weeks) Local sarcoma		20 24/32 13/29 sites			
Steinhoff & Mohr (1991)	Rat Sprague-Dawley	M	s.c. inj. 2 mg/kg bw 5/week or 10 mg/kg bw 1/week for 2 years	Dose (mg/kg bw) Survival (2 years) Local malignant tumour	0 Not given 0/20	2 5/10	10 4/10		
Steinhoff & Mohr (1991)	Rat Sprague-Dawley	M/F	3 i.p. inj. at 2-month intervals	Total dose (mg/kg bw) Survival (2 years) Local malignant tumour	0 Not given 1/20	200 14/20			
Wehner *et al.* (1977)	Hamster ENG:ELA	M	Inhalation 7 h/day, 5 d/week for life	Dose (mg/m^3) Survival (18 months) Reticulum-cell sarcoma Carcinoma Lymphosarcoma Leukaemia Plasma-cell tumour	0 7/51 0/51 0/51 0/51 0/51 1/51	10 9/51 1/51 1/51 0/51 0/51 0/51			No statistical difference
Cobalt[II] sulfide									
Gilman (1962)	Rat Wistar	M+F	i.m. inj.	Dose (mg/site) Survival (13 weeks) Local sarcoma		20 29/30 35/58 sites			
Jasmin & Riopelle (1976)	Rat Sprague-Dawley	F	intrarenal	Dose (mg) Survival (12 months) Kidney tumours	0 Not given 0/16	5 0/20			Inadequate

Table 20 (contd)

Reference	Species/ strain	Sex	Dose schedule	Experimental parameter/ observation	Group				Comments
					0	1	2	3	
Cobalt[II] chloride									
Shabaan *et al.* (1977)	Rat Wistar	M	s.c. inj. 2 x 5 d, 9–d interval	Dose (mg/kg bw) Survival[c] Subcutaneous sarcoma	0 19/20 0/19	40 11/20 8/11	40 16/20 6/16		$p < 0.001$ (Fisher exact test)
Cobalt naphthenate									
Nowak (1966)	Mouse NS	NS	i.m. inj. NS	Dose (mg) Survival Tumour of the striated muscle	0	0.2 8/30			Inadequate
Nowak (1961)	Rabbit	M	i.m. i.v. i. pleural i. hepatic	Dose unspecified	0	5 1 1 1			Inadequate
Cobalt[III] acetate									
Stoner *et al.* (1976)	Mouse Strain A	M+F	i.p. inj. 3/week, 24 doses	Total dose (mg/kg bw) Survival (30 weeks) Pulmonary tumour	0 19/20 7/19	95 20/20 8/20	237 20/20 8/20	475 17/20 10/17	Not significant

[a]Group 0, untreated; group 1, sham-treated

[b]Powder, 1/18 sarcoma; $MP_{35}N$, 3/26 sarcomas; compacted wire, 3/32 sarcomas

[c]12 months for groups 0 and 1; at 8 months for group 2

NS, not specified

(*a*) *Experimental systems*

(i) *Absorption, distribution, metabolism and excretion*

Cobalt compounds

The gastrointestinal absorption of radiolabelled cobalt chloride in rats was found to vary between 11 and 34%, depending on the administered dose (0.01-1000 μg/rat). The relative absorption decreased with increasing dose (Taylor, 1962). However, less than 0.5% of cobalt oxide given at an oral dose of 5 mg was absorbed by hamsters (Wehner & Craig, 1972).

The pulmonary absorption of inhaled cobalt(II) oxide (particle size, 1.0-2.5 μm) by hamsters was both rapid and high: about 25% was recovered in the carcass, lung, liver and kidney 24 h after inhalation of 0.8 mg cobalt oxide; essentially all of the cobalt oxide was eliminated by the sixth day after exposure (Wehner & Craig, 1972). Intratracheally instilled cobalt(II) oxide (1.5 μg) was cleared slowly from the rat lung (half-time, 15 days), and only very low concentrations were found in extrapulmonary tissues (Rhoads & Sanders, 1985). After inhalation or instillation of cobalt oxides in dogs and rats, the highest concentrations of cobalt were found in the lungs (Barnes *et al.*, 1976; Rhoads & Sanders, 1985). After rapid initial elimination (half-time, 0.7 days), the half-time of cobalt oxides deposited in the lungs of dogs was 36-86 days (Barnes *et al.*, 1976).

Kreyling *et al.* (1986) exposed beagle dogs by inhalation to radioactive cobalt[II,III] oxide particles of different size (0.3-2.7 μm) and found that small particles were cleared more rapidly from the lungs. Brune *et al.* (1980) exposed rats by inhalation to chromium-cobalt-containing abrasive dust obtained from dental laboratories. The concentration of cobalt in the lung increased with the length of exposure, indicating slow elimination of deposited metal. Histological examination revealed macrophages containing metal particles. The concentration of cobalt was also elevated in liver and kidney, showing that some systemic uptake of cobalt had taken place. Animals given cobalt chloride orally or by injection showed highest concentrations in the liver, with lower concentrations in kidney, pancreas and spleen (Taylor & Marks, 1978; Stenberg, 1983). Relatively high concentrations were also found in myocardium (Stenberg, 1983; Clyne *et al.*, 1988) and in cartilage and bone (Söremark *et al.*, 1979).

The major proportion of parenterally administered cobalt is cleared rapidly from the body, mainly *via* urine: 63% of radioactive cobalt chloride was recovered in the urine of rats within 24 h (Taylor, 1962). After a single intravenous injection of cobalt chloride to rats, about 70 and 7% were recovered in the urine and faeces, respectively, during the first three days (Onkelinx, 1976). Similarly, 73 and 15% of an intravenous dose of cobalt chloride (0.3 mg/kg bw) to rats was eliminated *via* urine and faeces, respectively, within four days (Gregus & Klaassen, 1986). Dogs

injected intravenously with 20 μg/kg bw radioactive cobalt sulfate eliminated 40-70% of the label in urine and bile (90% in urine) over a period of 7-13 h (Lee & Wolterink, 1955). In rats, only 2-7% of intravenously injected cobalt chloride was eliminated in the bile (Cikrt & Tichy, 1981; Gregus & Klaassen, 1986).

Autoradiographic examination of pregnant mice injected intravenously with radioactive cobalt chloride revealed high activity in maternal liver, kidney, pancreas and cartilage and in the fetal skeleton and other tissues (Flodh, 1968; Söremark *et al.*, 1979).

Metal alloy implants

In an experiment *in vitro* simulating mechanical stress on four different types of metallic hip prostheses, three of which contained cobalt, more than 1 mg/l cobalt was found in solution, and metal particles with a size down to 0.1 μm were formed as a result of frictional movement (Swanson *et al.*, 1973).

(ii) *Toxic effects*

Cobalt compounds

The oral LD_{50}s for different inorganic cobalt(II) compounds (cobalt fluoride, oxide, phosphate, bromide, chloride, sulfate, nitrate and acetate) in rats ranged from 150 to 500 mg/kg bw anhydrous compound (Speijers *et al.*, 1982). When the amounts were expressed in moles, the variability in toxicity between different compounds ranged from 1.5 to 3 mmol/kg cobalt. Acute effects recorded in the animals included sedation, diarrhoea and decrease in body temperature. All hamsters died after 6-h exposures by inhalation to 100 mg/m^3 cobalt oxide (Wehner & Craig, 1972). Pulmonary haemorrhagia and oedema and death were observed in guinea-pigs exposed by inhalation to cobalt chloride [dose unclear] (Höbel *et al.*, 1972).

Life-time exposure of hamsters to cobalt oxide by inhalation (10 mg/m^3, 7 h per day, five days a week) resulted in emphysema and in hyperplastic and hypertrophic changes in the alveolar epithelium and distal bronchi (Wehner *et al.*, 1977). Exposure of rabbits by inhalation to concentrations of 0.4 or 2 mg/m^3 cobalt chloride for 6 h per day on five days a week for 14-16 weeks produced nodular aggregation of alveolar type II cells, abnormal accumulation of enlarged, vacuolated alveolar macrophages and interstitial inflammation (Johansson *et al.*, 1987).

Daily doses of 2.5-10 mg/kg bw cobalt(II) salts given orally or parenterally caused polycythaemia in rats (Orten & Bucciero, 1948; Hopps *et al.*, 1954; Oskarsson *et al.*, 1981); reduced weight gain was seen as an early sign of general toxicity in some of these studies. Parenteral administration of 10-60 mg/kg bw cobalt chloride caused hyperlipidaemia in rabbits (Caplan & Block, 1963), induction of hepatic haemoxygenase and a decrease in activity of δ-aminolaevulinic

synthase and certain cytochrome P450-dependent drug metabolizing enzymes in rats (Maines & Kappas, 1975; Maines *et al.*, 1976; Numazawa *et al.*, 1989).

Myocardial toxicity of cobalt salts has been reported in rats (Grice *et al.*, 1969; Lin & Duffy, 1970; Rona, 1971), guinea-pigs (Mohiuddin *et al.*, 1970; Desselberger & Wegener, 1971), rabbits (Hall & Smith, 1968) and dogs (Sandusky *et al.*, 1981) following long-term dietary (10-100 mg/kg bw) or parenteral (5-30 mg/kg bw) administration. Observed toxic effects included noninflammatory myocardial degeneration, alterations in mitochondria and myofibrils and abnormal electrocardiographic traces.

Metallic cobalt

Intratracheal instillation of metallic cobalt (50 mg/animal; sterile suspension [particle size not given]) caused pulmonary haemorrhage and oedema and death in rats (Harding, 1950).

In miniature swine exposed to 0.1-1 mg/m^3 metallic cobalt particles (0.4-3.6 μm) for 6 h per day on five days per week for three months by inhalation, a progressive decrease in lung compliance was observed. In addition collagenization of alveolar septa in lung biopsies and electrocardiographic changes indicative of cardiomyopathy were observed (Kerfoot *et al.*, 1975).

In contrast to findings with cobalt chloride, exposure of rabbits by inhalation to metallic cobalt dust (0.2-1.3 mg/m^3, 6 h per day, five days per week for four weeks) had no profound effect on alveolar macrophages (Johansson *et al.*, 1980, 1986).

Cobalt released from cobalt metal, alloys or dissolved salts was cytotoxic to chick primary cultures and rodent fibroblast cell lines, inducing cell death, growth inhibition and mitotic abnormalities at concentrations greater than 7.5 μg/ml (Heath, 1954b; Daniel *et al.*, 1963; Bearden, 1976; Bearden & Cooke, 1980; Takahashi & Koshi, 1981).

(iii) *Effects on reproduction and prenatal toxicity*

Reproductive effects: Ingested cobalt chloride (265 mg/kg diet for 98 days, providing an initial dose of 20 mg/kg bw cobalt) induced degenerative and necrotic changes in the seminiferous tubules of rats. Cyanosis and vascular engorgement of the testes were seen on day 35 of treatment, and necrosis, degenerative and necrotic changes in the germinal epithelium and Sertoli cells by day 70. Damaged tubules were present side by side with normal ones. Multinucleated giant cells containing cellular debris were observed in the damaged tubules. Loss of sperm-tail filaments and degeneration of sperm mitochondria were also observed (Corrier *et al.* 1985a; Mollenhauer *et al.*, 1985). The same group of investigators did not find the lesion in sheep treated with 3.0-15.0 mg/kg bw cobalt for 109 days (Corrier *et al.* 1985b).

Intraperitoneal injection of cobalt chloride (1 mg/kg bw cobalt) 16 and 6 days before sacrifice stimulated spermiogenesis and spermatogenesis in the mouse testis (Niebrój, 1967). Intraperitoneal administration of 200 μmol [47.6 mg]/kg bw cobalt chloride for three days to male mice resulted in small but significant decreases in fertility two to three weeks later in an acute study. Similarly, in a chronic study, 100, 200 and 400 mg/l cobalt chloride given in drinking-water *ad libitum* for 7-13 weeks decreased fertility, sperm concentration, sperm mobility and testicular weight in a time-dose-dependent manner (Pedigo *et al.*, 1988). [The Working Group noted that the apparent differences in the results described above may be due to differences in dose and duration of observation.]

Developmental toxicity: Embryonic death was reported following administration to rats of cobalt chloride in the drinking-water either before and during pregnancy (0.05-5 mg/l) or during pregnancy only (0.005-0.05 mg/l) (Nadeenko *et al.*, 1980). In contrast, no developmental toxicity was observed in the offspring of rats given daily doses of 0, 25, 50 or 100 mg/kg bw cobalt chloride by gavage on days 6-15 of gestation, except for a nonsignificant increase in the incidence of stunted fetuses in the groups given 50 and 100 mg/kg (Paternain *et al.* 1988).

Numbers of litters as well as growth and survival of the offspring were reduced in rats that received 12, 24 and 48 mg/kg bw per day cobalt chloride by gavage from day 14 of gestation through day 21 of lactation (Domingo *et al.*, 1985).

Delay in ossification of the skeleton during embryonic and fetal development was observed at gestation day 17 in the offspring of six- to eight-week-old female mice (24-26 g) administered cobalt chloride (0.1 ml of a 5 mM solution [4.8 mg/kg bw]) intravenously on day 8; the effect was not seen when the cobalt was administered on day 3 of pregnancy. There was no change in fetal body weight on day 17 of pregnancy, and no increase in the frequency of resorption or implantation sites compared with controls (Wide, 1984).

In CF-1 mice, cobalt chloride was reported to protect against cleft lip and palate induced by cortisone (Kasirsky *et al.*, 1967).

As reported in an abstract, fetal damage was detected on gestation day 15 in hamsters administered cobalt acetate (40, 60, 80, 100 or 160 mg/kg bw) subcutaneously on day 8 of pregnancy. The resorption rate ranged from 6% at the low dose to 100% at the high dose. Central nervous system defects were reported at the median doses. Similarly, resorptions and central nervous system defects were observed after intraperitoneal injections of 40-70 mg/kg (Gale, 1980). [The Working Group noted that no information on maternal toxicity was reported.]

Studies on the effects of cobalt salts on chick embryos have produced conflicting results, perhaps due to differences in dose and routes of administration. Degeneration of the brain (Ridgway & Karnofsky, 1952), neural tube

malformations (Adhikari, 1967), lethality, eye abnormalities and structural defects (Kury & Crosby, 1968; Gilani & Alibai, 1985, abstract) have been reported.

(iv) *Genetic and related effects*

The results of tests for genetic and related effects of cobalt and cobalt compounds, with references, are given in Table 21. Other studies are described in the text.

The genetic toxicology of cobalt and cobalt compounds has been reviewed (Léonard & Lauwerys, 1990). With few exceptions, only soluble cobalt[II] salts have been tested. Only two reports were available on genetic effects of insoluble cobalt sulfide, and no data have been reported on genetic effects of metallic cobalt.

Like other metallic compounds, cobalt compounds are known to be relatively inactive in prokaryotic systems (Rossman, 1981; Swierenga *et al.*, 1987). The precipitation of metal as phosphates in bacterial culture media may contribute to this inactivity (Rossman, 1981; Arlauskas *et al.*, 1985). However, four of 15 cobalt[III] complexes with aromatic ligands were active in a DNA repair assay and were mutagenic to *Salmonella typhimurium* (Schultz *et al.*, 1982). Several other studies of cobalt salts with positive results have been reported in prokaryotes.

Cobalt[II] chloride was inactive in the λ prophage induction assay, and it gave conflicting results in the *Bacillus subtilis rec*$^{+/-}$ growth inhibition assay. In the study with positive results, a preincubation procedure was used. Cobalt[II] chloride was inactive in all but one bacterial mutagenicity test. One study gave positive results in the absence but not in the presence of an exogenous metabolic system.

In bacteria, cobalt[II] chloride was reported to reduce the incidence of spontaneous mutations and to inhibit mutations induced by *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine and Trp-P-1 (Kada & Kanematsu, 1978; Inoue *et al.*, 1981; Mochizuki & Kada, 1982). It was comutagenic with several heteroaromatic compounds (Ogawa *et al.*, 1986, 1987, 1988).

In *Saccharomyces cerevisiae*, cobalt[II] chloride induced gene conversion and mitochondrial but not other types of mutation. Cobalt[II] salts induced chlorophyll mutations, chromosomal aberrations and aneuploidy in plant cells.

In cultured mammalian cells *in vitro*, predominantly positive results were obtained, with induction of DNA-protein cross-linkage, DNA strand breakage and sister chromatid exchange. Chromosomal aberrations were not observed in cultured human cells. [The Working Group noted the low concentrations employed.] Cobalt[II] chloride induced aneuploidy in cultured human lymphocytes. It also induced mutations at the *hprt* locus in Chinese hamster V79 cells, but not, in a single study, at the *tk* locus in mouse lymphoma L5178Y cells.

Cobalt[II] acetate enhanced viral transformation in Syrian hamster embryo cells, and cobalt sulfide induced morphological transformation in Syrian hamster

embryo cells; the crystalline form of cobalt sulfide was more active than the amorphous form.

Cobalt[II] chloride administered *in vivo* to Syrian hamsters by intraperitoneal injection induced aneuploidy in bone marrow and testes. In an assay for dominant lethal mutation in mice, reported as an abstract, significant increases in early embryonic losses were observed (Pedigo, 1988).

A mechanism for the genetic effects of soluble Co[II] salts may involve decreased fidelity of DNA polymerase (Sirover & Loeb, 1976). Cobalt[II] chloride caused extensive cleavage of isolated DNA in the presence of hydrogen peroxide; this effect was attributed to the generation of reactive oxygen species at those sites of DNA bound to cobalt ions (Yamamoto *et al.*, 1989).

(*b*) *Humans*

(i) *Absorption, distribution, excretion and metabolism*

The normal concentrations of cobalt in blood and urine from non-occupationally exposed persons are about 0.1-2 μg/l. The levels of cobalt in blood, and particularly in urine, increase in proportion to the level of occupational exposure and can be used for biological monitoring in order to assess individual exposure (Elinder *et al.*, 1988). Increased levels of cobalt have also been found in blood (serum) from uraemic patients (Curtis *et al.*, 1976; Lins & Pehrsson, 1984).

In a patient who died three months after treatment with cobalt[II] chloride (50 mg per day for three months), the myocardial concentration of cobalt was 1.65 mg/kg wet weight, which was 25-80 times higher than that in control samples (0.01-0.06 mg/kg) (Curtis *et al.*, 1976). Increased levels of cobalt were also reported in lung and mediastinal lymph nodes from hard-metal workers with lung disease; concentrations of cobalt were about 100-1000 μg/kg in two lung tissue samples compared to 5 μg/kg wet weight in controls, and 3280 μg/kg in mediastinal lymph nodes compared to > 2 μg/kg in controls (Hillerdal & Hartung, 1983).

The mean urinary excretion within 24 h of radioactive cobalt chloride given orally at 20 μM was estimated to be about 18% (Sorbie *et al.*, 1971). When healthy persons and uraemic patients were given 50 mg cobalt chloride orally, the two healthy volunteers eliminated between 5.7 and 8.3% of the dose *via* the urine within one week; elimination was considerably slower in uraemic patients, confirming the importance of renal clearance (Curtis *et al.*, 1976). High concentrations of radiolabelled cobalt were found in the liver shortly after parenteral administration of cobalt chloride to humans. After eight days, 28-56% and 2-12% of the dose were eliminated *via* the urine and faeces, respectively. A significant component (9-16% of the administered dose) was cleared very slowly, with a biological half-time of about two years (Smith *et al.*, 1972). Similar results, suggesting that a small

Table 21. Summary of studies on genetic and related effects of cobalt

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
Cobalt(II) salts				
PRB, Prophage induction in *Escherichia coli*	–	0	4.0000	Rossman *et al.* (1984)
BSD, *Bacillus subtilis rec* strains H17/M45, growth inhibition	–	0	325.0000	Nishioka (1975)
BSD, *Bacillus subtilis rec* strain H17, growth inhibition	+	0	325.0000	Kanematsu *et al.* (1980)
BSD, *Bacillus subtilis rec* strain H17, growth inhibition	(+)	0	325.0000	Kanematsu *et al.* (1980)
BSD, *Bacillus subtilis rec* strain H17, growth inhibition	(+)	0	325.0000	Kanematsu *et al.* (1980)
???, *Bacillus subtilis* strain NIG 1125, reverse mutation	–[a]	0	0.0000	Inoue *et al.* (1981)
SAO, *Salmonella typhimurium* TA100, reverse mutation	–	0	130.0000	Tso & Fung (1981)
SAO, *Salmonella typhimurium* TA100, reverse mutation	–	0	0.0000	Arlauskas *et al.* (1985)
SAO, *Salmonella typhimurium* TA100, reverse mutation	–	0	0.0000	Ogawa *et al.* (1986)
SA2, *Salmonella typhimurium* TA102, reverse mutation	–	–	40.0000	Wong (1988)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	0	0.0000	Arlauskas *et al.* (1985)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	40.0000	Wong (1988)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	0	0.0000	Arlauskas *et al.* (1985)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	0	65000.0000	Ogawa *et al.* (1986)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	+	–	0.0000	Wong (1988)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	0	20.0000	Mochizuki & Kada (1982)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	0	0.0000	Arlauskas *et al.* (1985)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–[a]	0	20.0000	Mochizuki & Kada (1982)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	0	0.0000	Arlauskas *et al.* (1985)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	0	0.0000	Ogawa *et al.* (1986)
SA9, *Salmonella typhimurium* TA98, reverse mutation	+	–	0.0000	Wong (1988)
SAS, *Salmonella typhimurium* TA2637, reverse mutation	–	0	65000.0000	Ogawa *et al.* (1986)
ECW, *Escherichia coli* WP2 *uvrA*, reverse mutation	–	0	0.0000	Arlauskas *et al.* (1985)
EC2, *Escherichia coli* WP2, reverse mutation	–[a]	0	20.0000	Kada & Kanematsu (1978)
SCG, *Saccharomyces cerevisiae* D7, gene conversion	+	0	1300.0000	Fukunaga *et al.* (1982)

Table 21 (contd)

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
Cobalt(II) salts (contd)				
SCG, *Saccharomyces cerevisiae* D7, gene conversion	(+)	0	0.0000	Singh (1983)
SCG, *Saccharomyces cerevisiae* D7, gene conversion	+	0	1500.0000	Kharab & Singh (1985)
SCF, *Saccharomyces cerevisiae*, petite mutation	+	0	130.0000	Lindegren *et al.* (1958)
SCF, *Saccharomyces cerevisiae* SBTD-2B, petite mutation	+	0	260.0000	Prazmo *et al.* (1975)
SCF, *Saccharomyces cerevisiae*, petite mutation	(+)	0	640.0000	Egilsson *et al.* (1979)
SCF, *Saccharomyces cerevisiae* D7, petite mutation	+	0	750.0000	Kharab & Singh (1987)
SCR, *Saccharomyces cerevisiae* S/M 13-D, erythromycin-resistant mut.	-	0	1300.0000	Putrament *et al.* (1977)
SCR, *Saccharomyces cerevisiae* D7, *ilv* gene mutation	-	0	1300.0000	Fukunaga *et al.* (1982)
SCR, *Saccharomyces cerevisiae* D7, *ilv* gene mutation	-	0	0.0000	Singh (1983)
SCR, *Saccharomyces cerevisiae* D7, *ilv* gene mutation	(+)	0	3000.0000	Kharab & Singh (1985)
PLM, *Pisum abyssinicum*, chlorophyll mutation	+	0	0.0000	von Rosen (1964)[b]
ACC, *Allium cepa*, chromosomal aberration	+	0	3.0000	Gori & Zucconi (1957)
???, *Allium cepa*, aneuploidy	+	0	0.0000	Gori & Zucconi (1957)
DIA, DNA strand breaks, Chinese hamster CHO cells	+	0	260.0000	Hamilton-Koch *et al.* (1986)
DIA, DNA cross-links, Novikoff hepatoma cells	(+)	0	130.0000	Wedrychowski *et al.* (1986)
G9H, Gene mutation, Chinese hamster V79 cells, *hprt* locus	(+)	0	26.0000	Miyaki *et al.* (1979)
G9H, Gene mutation, Chinese hamster V79 cells, *hprt* locus	+	0	0.0000	Hartwig *et al.* (1990)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus	-	0	57.0000	Amacher & Paillet (1980)
SIM, Sister chromatid exchange, mouse macrophage P388D1 cell line	+	0	13.0000	Andersen (1983)
T7S, Cell transformation, SA7/Syrian hamster embryo cells	+	0	35.0000	Casto *et al.* (1979)
T7S, Cell transformation, SA7/Syrian hamster embryo cells	+	0	55.0000	Casto *et al.* (1979)
DIH, DNA strand breaks, human white blood cells	+	0	6.5000	McLean *et al.* (1982)
DIH, DNA strand breaks, human diploid fibroblasts	+	0	650.0000	Hamilton-Koch *et al.* (1986)
DIH, DNA strand breaks, HeLa cells	+	0	0.0000	Hartwig *et al.* (1990)
SHL, sister chromatid exchanges, human lymphocytes	+	0	1.3000	Andersen (1983)

Table 21 (contd)

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
Cobalt(II) salts (contd)				
CHF, Chromosomal aberrations, human fibroblasts	-	0	0.0150	Paton & Allison (1972)
CHL, Chromosomal aberrations, human lymphocytes	-	0	0.6000	Voroshilin *et al.* (1978)
CIH, Chromosomal aberrations, human leukocytes	-	0	0.1500	Paton & Allison (1972)
AIH, Aneuploidy, human lymphocytes	+	0	3.7000	Resende de Souza-Nazareth (1976)
AVA, Aneuploidy, bone marrow and testes of male hamsters	+	0	400.0000	Farah (1983)[c]
Cobalt sulfides				
DIA, DNA strand breaks, Chinese hamster CHO cells	+	0	10.0000	Robison *et al.* (1982)
TCS, Cell transformation, Syrian hamster embryo cells	+	0	5.0000	Costa *et al.* (1982)
TCS, Cell transformation, Syrian hamster embryo cells	(+)	0	10.0000	Costa *et al.* (1982)
Cobalt(III) salts				
BSD, *Bacillus subtilis rec* strain H17, growth inhibition	(+)	0	1375.0000	Kanematsu *et al.* (1980)

[a]Antimutagenic effect
[b]Or as EDTA chelate
[c]Injected intraperitoneally over nine days

proportion of the cobalt (from either the metal or the oxide) retained after inhalation has a biological half-time in the order of years, were obtained by other investigators (Newton & Rundo, 1970; Hedge *et al.*, 1979).

Measurements of cobalt, chromium and nickel in blood and urine from persons with metallic hip replacements containing a high proportion of these metals have repeatedly shown elevated levels of one or several of them compared to controls or prior to surgery (Coleman *et al.*, 1973; Jones *et al.*, 1975; Hildebrand *et al.*, 1985; Braun *et al.*, 1986; Hildebrand *et al.*, 1988). [The Working Group noted that the analytical accuracy of several of the earlier studies was not confirmed.]

Sunderman *et al.* (1989) measured the concentrations of chromium, cobalt and nickel in serum and urine samples collected from patients who had undergone bone surgery and had received metallic hip or knee prostheses. Patients were followed for up to two years. The concentration of chromium in serum and urine remained essentially unchanged, whereas the concentration of nickel was markedly increased in both urine and serum collected shortly after the operation (1-14 days). The cobalt concentration, however, displayed a relatively small, slow increase in serum and blood. The highest concentrations were seen after two and 22 months in two patients who had loosening of their prosthesis.

(ii) *Toxic effects*

Pulmonary effects have been regarded as the major occupational problem in relation to cobalt, particularly in the hard-metal industry where cobalt-containing dust is generated. Two types of lung lesions may develop—interstitial fibrosis (so-called 'hard-metal pneumoconiosis') and occupational asthma (Demedts & Ceuppens, 1989). Hard-metal pneumoconiosis is a severe and progressive type of pneumoconiosis which may develop after several years of exposure to cobalt-containing dust at concentrations of 0.1-2 mg/m^3 (for reviews, see Elinder & Friberg, 1986; Sprince *et al.*, 1988). As the dust in the hard-metal industry always contains agents in combination with cobalt (tungsten carbide and sometimes other metals such as titanium and tantalum), it has been questioned whether cobalt is solely responsible for the observed health effects (Brooks, 1981). Diamond polishers exposed to fine dust containing cobalt and diamond had severe lung fibrosis (Demedts *et al.*, 1984).

Symptoms and signs of obstructive lung disease can develop as a result of occupational exposure to cobalt-containing dust during the production of hard metal (Coates & Watson, 1971, 1973; Bech, 1974; Scherrer & Maillard, 1982), but these were also observed in workers in a porcelain factory using cobalt dye (Raffn *et al.*, 1988) and among diamond polishers (Gheysens *et al.*, 1985). This condition, which usually improves after cessation of exposure, is considered to be of allergic origin (Sjögren *et al.*, 1980). Provocation tests with cobalt usually induce a typical

asthmatic reaction (Hartmann *et al.*, 1982). Shirakawa *et al.* (1989) examined eight workers who developed asthma after having worked in a Japanese hard-metal plant. The total number of workers was about 400. The eight asthmatic workers all reacted with a drop in peak expiratory flow rate after an inhalation challenge with cobalt chloride. In four of them, it was possible to identify specific IgE antibodies towards cobalt-conjugated human albumin. This finding supports the hypothesis that cobalt hypersensitivity has a role in hard-metal asthma.

Histopathological findings in lung biopsies from workers with fibrosis (hard-metal pneumoconiosis) and/or obstructive problems (hard-metal asthma) have been published (Coates & Watson, 1971, 1973; Davison *et al.*, 1983; Demedts *et al.*, 1984; Anttila *et al.*, 1986; Cugell *et al.*, 1990). Typical microscopic findings include advanced fibrosis and desquamative interstitial pneumonia of the giant-cell type (Coates & Watson, 1971; Anttila *et al.*, 1986).

Cobalt has an erythropoietic effect and has been used for the treatment of anaemia (Berk *et al.*, 1949; Duckham & Lee, 1976). Berk *et al.* (1949) gave patients about 100 mg cobalt in the form of cobalt chloride three times a day for several weeks and recorded vomiting and anorexia in some patients, but only mild symptoms in the alimentary tract were seen as side-effects of the treatment in others. Duckham and Lee (1976) used a lower dose of cobalt chloride (25-50 mg cobalt per day) and observed fewer side effects. Polycythaemia has also been reported in heavy drinkers of cobalt-fortified beer (Morin *et al.*, 1971; Alexander, 1972).

Endemic outbreaks of cardiomyopathy with mortality rates of up to 50% were described among heavy consumers (up to 10 l per day) of cobalt-fortified beer (Morin & Daniel, 1967; Kesteloot *et al.*, 1968; Morin *et al.*, 1971; Alexander, 1972). As the daily dose of cobalt ingested by heavy beer drinkers (a few milligrams) was certainly excessive compared to the normal daily intake of cobalt (around 5-50 μg/day), but considerably lower than the doses prescribed to patients with anaemia, it was suggested that the cardiomyopathy had a multicausal origin (Morin & Daniel, 1967; Balazs & Herman, 1976). Three cases of cardiomyopathy, two of which were fatal, were described in workers exposed industrially to cobalt (Barbořík & Dusek, 1972; Kennedy *et al.*, 1981; Alušík *et al.*, 1982).

There are some indications that workers in hard-metal plants have increased morbidity and mortality from cardiovascular disease. Alexandersson and Atterhög (1980) examined workers exposed to cobalt-containing dusts at concentrations of 0.01-0.06 mg/m^3. Symptoms of dyspnoea, 'heavy breathing' and 'tightness in chest' were more prevalent in exposed workers than in controls, but no pulmonary dysfunction was found. In a recent study of 3163 workers exposed to cobalt-containing dusts at concentrations ranging from 0.001 to up to 11 mg/m3 for at least one year, Hogstedt and Alexandersson (1990) found an excess of deaths

from ischaemic heart disease (standardized mortality ratio (SMR), 169; 95% confidence interval (CI), 96-275) among workers who had been exposed to 0.02-11 mg/m3 cobalt for at least 10 years (see also p. 445).

Cobalt may provoke allergic dermatitis (Camarasa, 1967). Of 853 patch-tested workers, about 7% showed allergic reactions to 1% cobalt chloride (Fischer & Rystedt, 1983). Cobalt allergy, which is usually found in people who suffer from other skin allergies and/or eczema (Rystedt & Fischer, 1983), is also seen in other occupational groups, such as offset printers and construction workers handling cobalt-containing cement (Goh *et al.*, 1986).

Cobalt and nickel released from orthopaedic or dental prostheses may precipitate allergic reactions, with local effects and inflammation (Jones *et al.*, 1975; Fernandez *et al.*, 1986; Thomas *et al.*, 1987).

(iii) *Effects on reproduction and prenatal toxicity*

The spontaneous abortion rate appeared to be increased in women who either worked in metal smelting or had spouses working in the metallurgical industry. Exposure to cobalt, arsenic, copper, zinc and sulfur was considered possible in the work setting (Hemminki *et al.*, 1983). [The Working Group noted that the contribution of cobalt, if any, to the increase in abortion rate was not separately identified.]

(iv) *Genetic and related effects*

No data were available to the Working Group.

3.3. Case reports and epidemiological studies of carcinogenicity in humans

(*a*) *Implanted medical devices*

The first report of development of a sarcoma at the site of a stainless-steel plate prosthesis for a fracture of the humerus was made in 1956 (McDougall, 1956). There have been 17 further reports of single cases of malignant neoplasia at the site of implants of metal-containing fracture plates or joint prostheses. The metal material used was unknown in four cases, stainless-steel in three cases and cobalt-containing alloys in 10 cases. The period between implantation and tumour development ranged from one to 30 years. The tumours described were various types of sarcoma in 14 cases (Delgado, 1958; Castleman & McNeely, 1965; Dube & Fisher, 1972; Arden & Bywaters, 1978; Tayton, 1980; Bagó-Granell *et al.*, 1984; Lee *et al.*, 1984; Penman & Ring, 1984; Swann, 1984; Weber, 1986; Hughes *et al.*, 1987; Ryu *et al.*, 1987; Martin *et al.*, 1988; Ward *et al.*, 1990), one carcinoma (Mazabraud *et al.*, 1989) and lymphoma in two cases (McDonald, 1981; Dodion *et al.*, 1983).

Incident cancers were recorded for a cohort of 1358 persons who received a total hip replacement in New Zealand in the period 1966-73 and were followed up

for six months to 17 years (mean, 10.5 years) to the end of 1983 (Gillespie *et al.*, 1988). Total cancer incidence was similar to that expected (164 observed *versus* 179.4 expected on the basis of general population rates; SMR, 91 [95% CI, 78-107]). While the overall cancer risk within 10 years of hip replacement was significantly low (SMR, 74; 95% CI, 61-90, based on 107 observed cases), the risk after 10 or more years was significantly high (SMR, 160; 95% CI, 122-209, based on 57 cases). There was a significant overall increase in the incidence of tumours of the lymphatic and haematopoietic system (21 observed *versus* 12.5 expected; SMR, 168; 95% CI, 106-260). When the five lymphatic and haematopoietic malignancies diagnosed within two years of hip replacement were excluded, this SMR fell to 151 (16 *versus* 10.6 expected [95% CI, 86-245]). There were significant deficits of breast cancer (six observed *versus* 16.6 expected; SMR, 36; 95% CI, 14-82) and of colorectal cancer (21 observed *versus* 33.8 expected; SMR, 62; 95% CI, 39-96). [No specific information on the composition of the hip prostheses was provided.]

(*b*) *Occupational exposure*

Schulz (1978) reported a cobalt-containing giant-cell tumour of the buccal membrane in a mineral-oil refinery employee five months after a single accidental exposure to dust containing cobalt[II] phthalocyanine.

Saknyn and Shabynina (1970, 1973) examined mortality rates among workers at four nickel plants in the USSR in 1955-67. The workers were exposed to cobalt, but also to various nickel and arsenic compounds. A two- to four-fold increase in the risk for lung cancer was reported. The risks relative to those of inhabitants in the towns in which the plants were located were increased in various parts of the plants, including the cobalt shops (relative risks, 5-13), where there was exposure to cobalt dust but also to nickel sulfates, nickel chlorides and arsenic compounds. A 1.5-3.3-fold increase in stomach cancer risk was also noted. [The observed numbers of deaths were not given, and no allowance was made for potential confounding factors.]

Cuckle *et al.* (1980) studied mortality in 297 men employed in two departments opened in 1937 and 1938 at a nickel refinery in the UK. In one department, a wet treatment plant, nickel sulfate, copper sulfate, 'cobaltic hydrate' and precious metal concentrates were manufactured; in the other, a chemical production department, a range of compounds of nickel, cobalt and selenium were produced. The men had all been first employed in the refinery in or after 1933 and had worked in one or other of the departments for at least 12 months before 1960. They were followed up to 30 June 1980. Overall, there were 105 deaths (SMR, 109 [95% CI, 89-132]). There were 13 deaths from lung cancer (SMR, 131 [95% CI, 70-224]); six of the men who died from lung cancer [SMR, 154; 95% CI, 57-336] had been employed in the precious metal concentration section of the wet treatment plant. When the expected number

of lung cancer deaths was estimated from death rates in rural districts of Glamorganshire (where the refinery was located), rather than in the population of England and Wales as a whole, the SMR was [172; 95% CI, 92-295]. Excess mortality from lung cancer occurred mainly less than 20 years from first employment in the refinery (SMR, 178 [95% CI, 65-387]) and among men who had been employed for six or more years (SMR, 138 [95% CI, 55-283]). Among the 1173 workers employed in the whole refinery in or after 1930 (International Committee on Nickel Carcinogenesis in Man, 1990), those first employed in 1930-39 had a SMR for lung cancer of 154 (95% CI, 97-233), those first employed in 1940-49 a SMR of 130 (95% CI, 71-218) and those first employed after 1950 a SMR of 77 (95% CI, 33-152). Cuckle *et al.* (1980) did not attribute any increase in risk in this cohort to exposure to cobalt.

Mur *et al.* (1987) followed up 1143 workers with at least one year of employment betwen 1950 and 1980 in an electrochemical plant producing cobalt and sodium in France. Altogether, 24.9% of the cohort were migrants (mainly North Africans and Italians). Vital status was established for 99.5% of the French-born workers and for 81.3% of the migrants. A total of 213 deaths occurring before 1981 was identified; cause of death was determined for 80% by interview with attending physicians and from hospital records. After adjustment for unknown causes of death (assuming that the distribution by cause of death was similar to that of cases with known cause of death), a SMR of 90 (95% CI, 44-159, based on nine cases) was observed for the total cohort for cancer of the lung, using mortality rates for France as a reference. For workers employed only in cobalt production, the SMR for lung cancer was 466 (95% CI, 146-1064, based on four observed cases). [The migrants may have had different rates of lung cancer from French-born workers, but the proportion of migrant workers in the different departments of the plants was not reported.] A case-control analysis was performed of lung cancer cases and controls, matched for year of birth, year of death and smoking habits. [The quality and manner of collection of information on smoking is unclear.] An odds ratio of 4.0 [95% CI, 1.6-9.9; calculated by the Working Group using an unmatched analysis] was associated with ever having worked in cobalt production. Workers in cobalt production were also exposed to unknown levels of forms of nickel and arsenic. [It is not known whether workers in other areas also had such exposure. No analysis based on latency or duration of exposure was presented.]

Hogstedt and Alexandersson (1990) reported on 3163 male Swedish workers with at least one year of exposure to cobalt-containing hard-metal dust at one of three hard-metal manufacturing plants in 1940-82 who were followed up during the period 1951-82. There were four categories of exposure (with estimated ambient air concentrations prior to 1970): occasionally present in rooms where hard metal was handled (less than 2 $\mu g/m^3$ Co); continuously present in rooms where hard metal

was handled, but own work not involving hard metal (1-5 μg/m^3 Co); manufacturing hard-metal objects (10-30 μg/m^3 Co); and exposed to cobalt in powder form when manufacturing hard-metal objects (60-11 000 μg/m^3 Co). No specific information was given on exposure to other substances in this cohort, but the workers were exposed to a number of substances that are used in the production of hard metal, such as tungsten carbide. There were 292 deaths among persons under 80 years of age during the study period; the SMRs relative to that of the male Swedish population were 96 (95% CI, 85-108) for mortality from all causes and 105 (95% CI, 82-132) for all incident tumours (73 cases). There were 17 cases of lung cancer *versus* 12.7 expected (SMR, 134; 95% CI, 77-213). With more than 10 years of exposure time and more than 20 years since first exposure, there were seven cases of lung cancer *versus* 2.5 expected (SMR, 278; 95% CI, 111-572); there were three cases of cancer of the lung *versus* 1.3 expected in the two lower exposure groups, and four cases of lung cancer *versus* 1.2 expected in the two higher exposure groups. A survey carried out at the end of the 1970s among hard-metal workers in Sweden showed that their smoking habits were not different from those of the male Swedish population (Alexandersson, 1979).

4. Summary of Data Reported and Evaluation

4.1 Exposure data

Cobalt is widely distributed in the environment; it is the thirty-third most abundant element in the earth's crust. Cobalt is obtained primarily as a by-product of the mining and processing of copper and nickel ores and is a constituent of about 70 naturally occurring oxide, sulfide, arsenide and sulfoarsenide minerals. Cobalt is extracted from ore and concentrated by pyrometallurgical, hydrometallurgical and electrolytic processes alone or in combination. Refined metallic cobalt is available to the industrial market as cathodes and to a lesser extent as powders; oxides and other compounds are also available.

Cobalt compounds have been used as pigments in glass and ceramics in many countries for thousands of years. Since the beginning of the twentieth century, the major uses of cobalt have been in the production of metal alloys, such as superalloys and magnetic alloys, as well as high-strength steels and hard-metal cemented carbides. At the end of the 1980s, about one-third of the cobalt used was in the production of cobalt chemicals, which are used primarily as catalysts and pigments.

The main route of occupational exposure is *via* the respiratory tract by inhalation of dusts, fumes and mists containing cobalt. Exposures have been measured in hard-metal production, processing and use and in porcelain painting. Occupational exposure to cobalt is regulated in many countries.

Cobalt occurs in vegetables *via* uptake from soil, and vegetables account for the major part of human dietary intake of cobalt. Animal-derived foods, particularly liver, contain cobalt in the form of vitamin B_{12}. Cobalt is also found in air, water and tobacco smoke. Human tissues and fluids normally contain low levels of cobalt, which may be increased as a result of occupational exposures. Cobalt concentrations in tissue, serum and urine can be increased in patients with implants made of cobalt-containing alloys. Cobalt-containing particles have been detected in tissues immediately adjacent to such prostheses.

4.2 Experimental carcinogenicity data

Cobalt metal powder was tested in two experiments in rats by intramuscular injection and in one experiment by intrathoracic injection, producing sarcomas at the injection site.

A finely powdered *cobalt-chromium-molybdenum alloy* was tested in rats by intramuscular injection, producing sarcomas at the injection site. In two other experiments in rats, coarsely or finely ground cobalt-chromium-molybdenum alloy implanted in muscle or pellets of cobalt-chromium-molybdenum alloy implanted subcutaneously did not induce sarcomas. Implantation in the rat femur of three different *cobalt-containing alloys*, in the form of powder, rod or compacted wire, resulted in a few local sarcomas. In another experiment, intramuscular implantation of polished rods consisting of three different cobalt-containing alloys did not produce local sarcomas. In an experiment in guinea-pigs, intramuscular implantation of a *cobalt-chromium-molybdenum alloy* powder did not produce local tumours.

Intraperitoneal injection of a *cobalt-chromium-aluminium spinel* in rats produced a few local malignant tumours, and intratracheal instillation of this spinel in rats was associated with the occurrence of a few pulmonary squamous-cell carcinomas.

In two experiments in rats, intramuscular injection of *cobalt[II] oxide* powder produced sarcomas at the injection site. In an experiment in mice, intramuscular injection of cobalt oxide powder did not produce local tumours. Intratracheal instillation of cobalt oxide powder in rats was associated with a few benign and malignant pulmonary tumours. In a study limited by poor survival, hamsters administered a cobalt oxide dust by inhalation showed no increase in the incidence of pulmonary tumours. In two experiments in rats by subcutaneous and intraperitoneal injection, cobalt oxide powder produced local malignant tumours.

Cobalt[II] sulfide powder was tested in one study in rats by intramuscular injection, producing a high incidence of local sarcomas.

Cobalt[II] chloride was tested in one study in rats by repeated subcutaneous injection, producing many local and a few distant subcutaneous sarcomas.

Cobalt[II,III] oxide was tested in one experiment in hamsters to determine the effects of various particulates on carcinogenesis induced by *N*-nitrosodiethylamine. Intratracheal instillation of cobalt[II,III] oxide did not increase the incidence of pulmonary tumours over that in appropriate control groups.

Studies in mice and rabbits with *cobalt naphthenate* could not be evaluated.

In a screening test for lung adenomas by intraperitoneal injection, *cobalt[III] acetate* did not increase the incidence of lung tumours in strain A mice.

Interpretation of the available evidence for the carcinogenicity of cobalt in experimental animals was difficult because many of the reports failed to include sufficient details on results of statistical analyses, on survival and on control groups. Further, statistical analyses could not be performed by the Working Group in the absence of specific information on survival and on whether the neoplasms were fatal. Nevertheless, weight was given in the evaluation to the consistent occurrence of tumours at the site of administration and to the histological types of tumours observed.

4.3 Human carcinogenicity data

A number of single cases of malignant tumours, mostly sarcomas, have been reported at the site of orthopaedic implants containing cobalt. In one cohort study of people with a hip prosthesis, there was a significant increase in the incidence of lymphatic and haematopoietic malignancies, and significant deficits of breast and colorectal cancers. Overall cancer incidence was significantly lower than expected in the first 10 years after surgery, but significantly higher than expected after 10 or more years. No data were provided on the composition of the prostheses in this study.

Four cohort studies on the association between industrial exposure to cobalt and death from cancer were reviewed, two of which provided information for the evaluation. In a French electrochemical plant, there was a significant increase in the risk for lung cancer among workers in cobalt production, who were also exposed to nickel and arsenic, but not among workers in other departments of the factory. In a study in Sweden of hard-metal workers with documented exposure to cobalt-containing dusts, a significant increase in lung cancer risk was seen in people exposed for more than 10 years whose exposure had begun more than 20 years previously.

Interpretation of the available evidence on the possible association between occupational exposure to cobalt and cancer in humans is made difficult by the fact that in three of the four studies there was concurrent exposure to other potentially

carcinogenic substances, including forms of nickel and arsenic. In the Swedish study, there was concurrent exposure to other components of hard-metal dust.

4.4 Other relevant data

Occupational exposure to cobalt-containing dusts can cause fibrotic changes in the lung and can precipitate asthma. Cardiotoxic effects have been reported in exposed humans; in particular, cardiomyopathy can occur after prolonged oral intake.

Cobalt[II] chloride reduced fertility in male mice.

Cobalt[II] compounds had weak or no genetic effect in bacteria; some cobalt[III] complexes with heterocyclic ligands were active.

In single studies with an extensive range of eukaryotes, including animal and human cells *in vitro*, cobalt[II] compounds induced DNA damage, mutation, sister chromatid exchange and aneuploidy. Gene conversion and mutation in eukaryotes and DNA damage in human cells were observed in several studies. There was some evidence that these compounds can also induce aneuploidy in hamsters *in vivo*. In single studies, cobalt[II] sulfide induced DNA damage and transformation in cultured mammalian cells.

4.5 Evaluation[1]

There is *inadequate evidence* for the carcinogenicity of cobalt and cobalt compounds in humans.

There is *sufficient evidence* for the carcinogenicity of cobalt metal powder in experimental animals.

There is *limited evidence* for the carcinogenicity of metal alloys containing cobalt, chromium and molybdenum in experimental animals.

There is *sufficient evidence* for the carcinogenicity of cobalt[II] oxide in experimental animals.

There is *limited evidence* for the carcinogenicity of cobalt[II] sulfide in experimental animals.

There is *limited evidence* for the carcinogenicity of cobalt[II] chloride in experimental animals.

There is *inadequate evidence* for the carcinogenicity of cobalt-aluminium-chromium spinel, cobalt[II,III] oxide, cobalt naphthenate and cobalt[III] acetate in experimental animals.

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[1]For definition of the italicized terms, see Preamble, pp. 30-33.

Overall evaluation

Cobalt and cobalt compounds *are possibly carcinogenic to humans (Group 2B).*

5. References

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