

Meeting 28th May 2008

SPECIAL PREPARATIONS WORKSHOP

Assessment of Special Preparations

**An example of its practical applications in
the stainless steel industry**

Special Preparations

“During the mid-90s, Germany’s BK Tox proposed to classify metallic nickel as a workplace human carcinogen and to petition the EU to increase its hazard classification from a Category 3 to a Category 2 Carcinogen.

The nickel and stainless steel industries responded by challenging the scientific validity of the studies upon which these proposals were based. The issue was resolved by an agreement to undertake an inhalation of metallic nickel powder in rats. This study became the definitive inhalation assessment of metallic nickel and its outcome became an integral part of the EU Risk Assessment of nickel.

As part of the stainless steel industry’s “what if” analysis, it was agreed to conduct studies on nickel-containing stainless steels to determine their potential toxicity (including carcinogenicity)

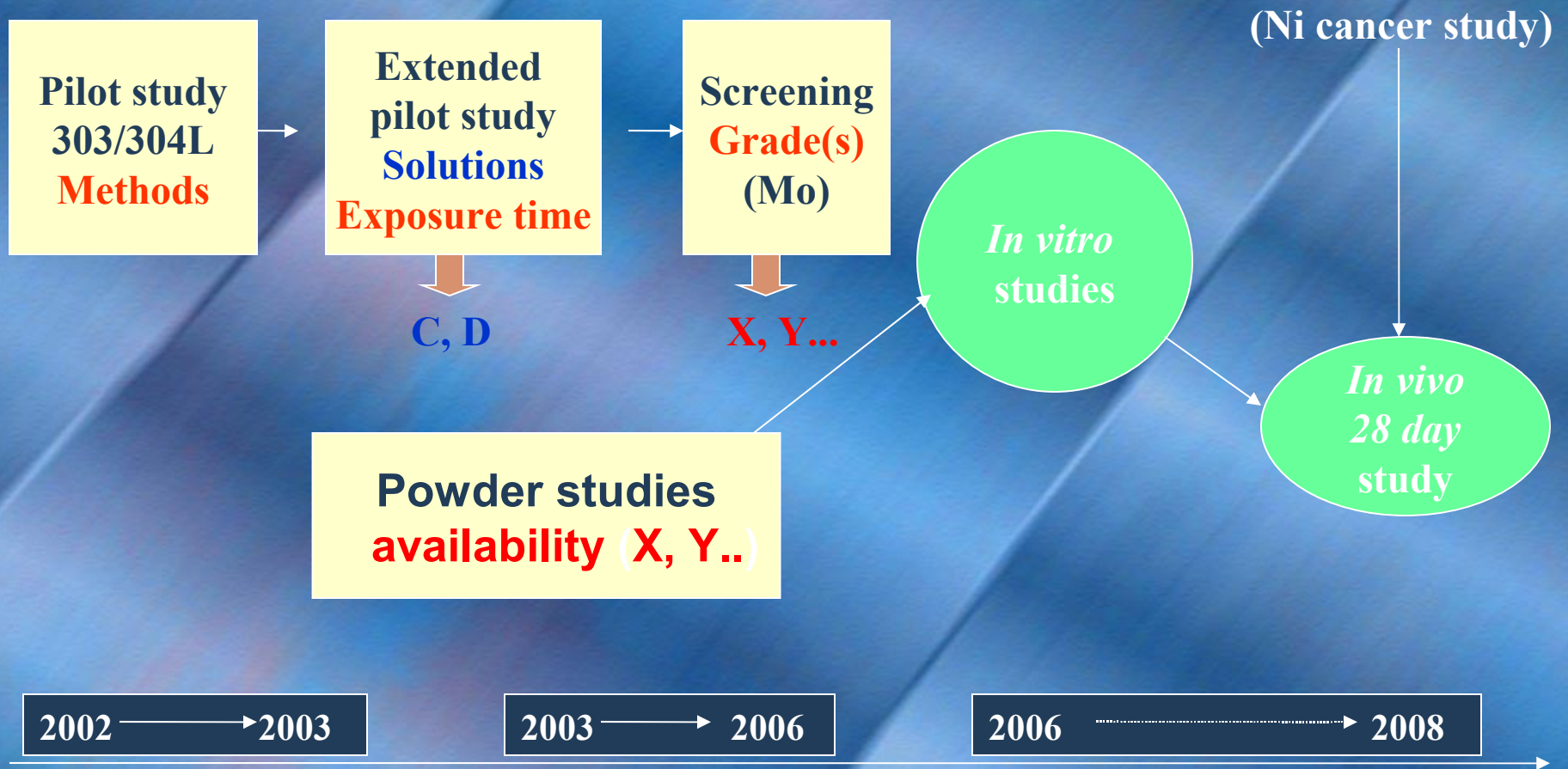
Special Preparations

Despite being offered US\$3,000,000 for a parallel inhalation study on stainless steel, the SSPG selected an iterative approach to the assessment of the toxicity potential of stainless steels in respect of inhalation exposure.

This approach consisted of the following steps:-

- (i) Pilot study to develop the methodology and establish its reliability*
- (ii) Extended pilot scheme with a wider range of biological fluids*
- (iii) Screening tests on representative massive forms of stainless steel grades in PBS, artificial sweat, and two lung fluids (Cytosol and ALF)*
- (iv) Selection of representative stainless steel for further testing*
- (v) Powder verses massive studies in several biological fluids*
- (vi) In vitro tests on one representative stainless steel*
- (vii) In vivo 28 day inhalation tests on stainless steel powder*

Stainless Steel studies – road map



Special Preparations

Grade	C	Si	Mn	P	S	Cr	Ni	Mo	N
2205	0.03	1.0 0	2.0	0.03 5	0.01 5	21-23	4.5-6.5	2.5-3. 5	0.10-0.2 2
201	0.015	1.0 0	5.5-7. 5	0.04 5	0.01 5	16-18	3.5-5.5	-	-
304	0.07	1.0 0	2.0	0.04 5	0.01 5	17-19.5	8.-10.5	-	0.11
310	0.025	1.5 0	2.0	0.04 5	0.03 0	24-26	19-22	-	-
316L	0.03	1.0 0	2.0	0.04 5	0.01 5	16.5-18.5	10.5-1 3	2.5-3	0.11
409	0.08	1.0 0	1.0	0.04 5	0.03 0	10.5-12	0.6	-	-
430	0.08	1.0 0	1.0	0.04 0	0.01 5	16-18	-	-	0.05-0.2 5

Special Preparations

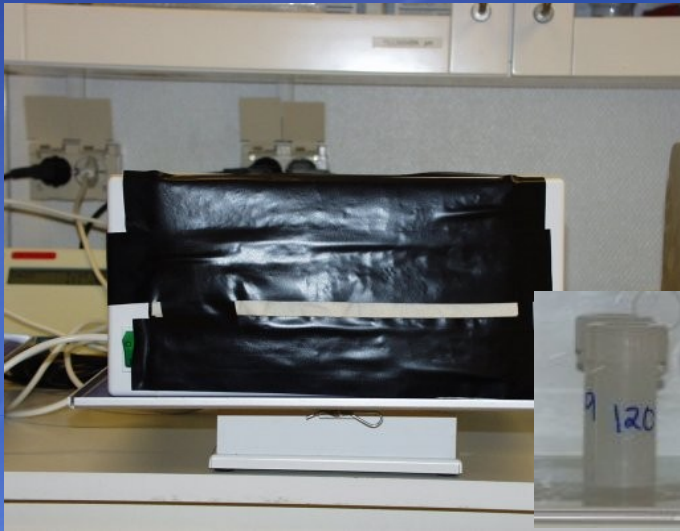
Artificial physiological solutions

Cytosol, artificial phagolysosomal fluid – pH 4.5-5.0
Gamble's solution, artificial interstitial fluid – pH 7.4

Immersion periods:



Special Preparations



Surface cleaning in RBS and
ultra pure water

Surface area:solution volume; 1:1
As-received and abraded (1200 P)
surface conditions

Dark conditions

~ 37°C

Shaking incubator, 30 rpm

Analysis: Metal release

⇒ ICP/MS-DRC

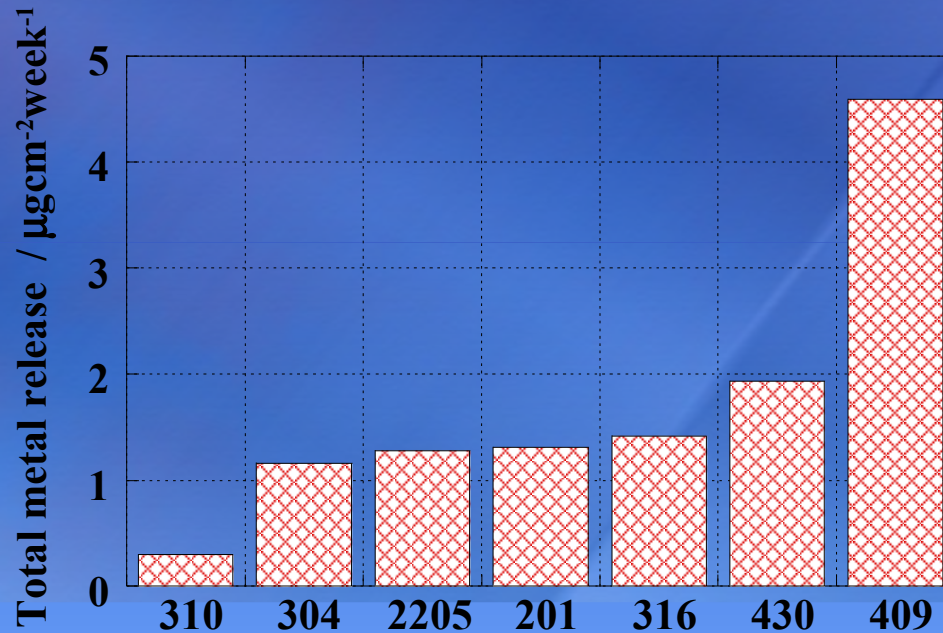
Surface composition

⇒ XPS

pH 4.5-5.0

Special Preparations

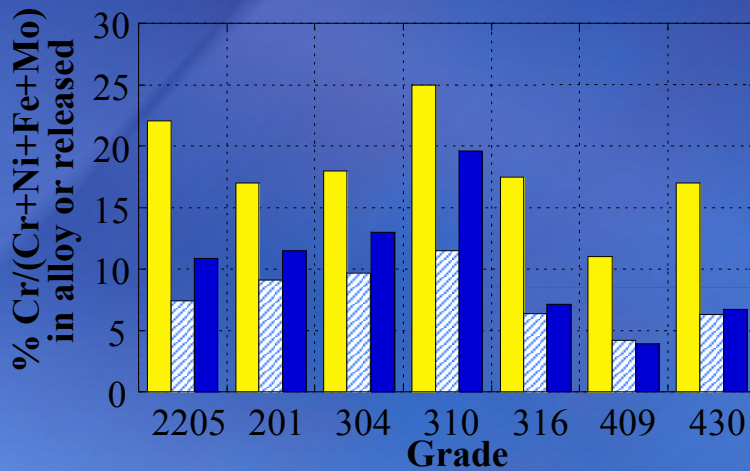
*Total metal release rates
(Ni+Cr+Fe+Mo) from all grades exposed during one
week in Cytosol.
(as-received surfaces)*



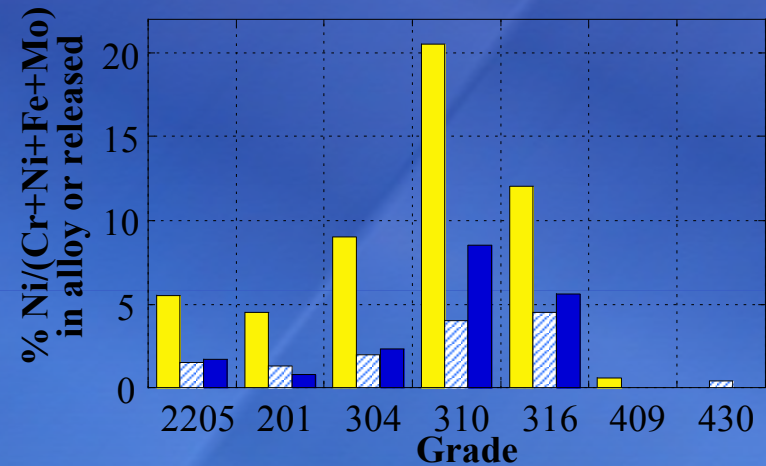
Special Preparations

Mass balance calculations based on release rates from as-received surfaces exposed in Cytosol and the bulk alloy composition.

chromium



nickel



The release of Cr and Ni is considerably lower than corresponding bulk alloy ratio for all grades investigated.

Stainless Steel studies – road map

