Photos given for information only.

h) IMGHC-LS-EH : Smooth surface Extra High profile High cohesivity gel pre-filled breast implants

CODE	SURFACE	PROFILE	VOLUME (cc)	DIAMETER (mm)	PROJECTION (mm)
IMGHC	SMOOTH	EXTRA-HIGH	115	79	36
IMGHC	SMOOTH	EXTRA-HIGH	135	83	38
IMGHC	SMOOTH	EXTRA-HIGH	165	88	41
IMGHC	SMOOTH	EXTRA-HIGH	195	91	43
IMGHC	SMOOTH	EXTRA-HIGH	215	96	44
IMGHC	SMOOTH	EXTRA-HIGH	245	99	45
IMGHC	SMOOTH	EXTRA-HIGH	265	104	46
IMGHC	SMOOTH	EXTRA-HIGH	285	106	47
IMGHC	SMOOTH	EXTRA-HIGH	305	109	48
IMGHC	SMOOTH	EXTRA-HIGH	335	112	49
IMGHC	SMOOTH	EXTRA-HIGH	365	115	52
IMGHC	SMOOTH	EXTRA-HIGH	395	119	53
IMGHC	SMOOTH	EXTRA-HIGH	445	123	54
IMGHC	SMOOTH	EXTRA-HIGH	475	126	56
IMGHC	SMOOTH	EXTRA-HIGH	515	130	58
IMGHC	SMOOTH	EXTRA-HIGH	555	134	59
IMGHC	SMOOTH	EXTRA-HIGH	615	138	60
IMGHC	SMOOTH	EXTRA-HIGH	705	142	66
IMGHC	SMOOTH	EXTRA-HIGH	755	146	67
IMGHC	SMOOTH	EXTRA-HIGH	805	149	70

I) IMGHC-TX-EH : TeXtured surface Extra High profile High cohesivity gel pre-filled breast implants

CODE	SURFACE	PROFILE	VOLUME (cc)	DIAMETER (mm)	PROJECTION (mm)
IMGHC	TEXTURED	EXTRA-HIGH	115	79	36
IMGHC	TEXTURED	EXTRA-HIGH	135	83	38
IMGHC	TEXTURED	EXTRA-HIGH	165	88	41
IMGHC	TEXTURED	EXTRA-HIGH	195	91	43
IMGHC	TEXTURED	EXTRA-HIGH	215	96	44
IMGHC	TEXTURED	EXTRA-HIGH	245	99	45
IMGHC	TEXTURED	EXTRA-HIGH	265	104	46
IMGHC	TEXTURED	EXTRA-HIGH	285	106	47
IMGHC	TEXTURED	EXTRA-HIGH	305	109	48
IMGHC	TEXTURED	EXTRA-HIGH	335	112	49
IMGHC	TEXTURED	EXTRA-HIGH	365	115	52
IMGHC	TEXTURED	EXTRA-HIGH	395	119	53
IMGHC	TEXTURED	EXTRA-HIGH	445	123	54
IMGHC	TEXTURED	EXTRA-HIGH	475	126	56
IMGHC	TEXTURED	EXTRA-HIGH	515	130	58
IMGHC	TEXTURED	EXTRA-HIGH	555	134	59
IMGHC	TEXTURED	EXTRA-HIGH	615	138	60
IMGHC	TEXTURED	EXTRA-HIGH	705	142	66
IMGHC	TEXTURED	EXTRA-HIGH	755	146	67
IMGHC	TEXTURED	EXTRA-HIGH	805	149	70

1.6 - REFERENCE TEXTS

1.6.1 Regulatory texts :

- ✓ European Directive N°93/42/CEE related to medical devices
- ✓ Statutory Order N°95-292 of March, 16th1995 related to medical devices
- ✓ Statutory Order N° 96-32 of January 15th1996 related to the vigilance reporting for medical devices
- ✓ European Pharmacopoeia

1.6.2 Quality Standards :

- ✓ ISO 9001 (1994) : Quality Systems / Models for quality assurance in design, development, production, installation and associated services
- ✓ EN 46001 (1996) : Quality Systems / Medical devices – Specific requirements related to the application of the EN 29001
- ✓ NF EN 724 (1995) : Guide in the application of the EN 29001 & EN 46001 Standards and the EN 29002 & EN 46002 Standards for non active medical devices
- ✓ 21 CFR part 820 (2002) : Code of Federal Regulations - Quality System Regulation
- ✓ NF EN 1441 (1998) : Medical Devices – Risk analysis

1.6.3 Technical Standards :

- ✓ ASTM D 412-97 (1997) : Standard Test Methods for Vulcanized Rubber and Thermoplastic rubbers and Thermoplastic Elastomers – Tension
- ✓ ASTM D 624-00 (2000) : Standard test method for the tear strength of conventional vulcanized rubber and thermoplastic rubbers
- ✓ ASTM F 604-94 (1994) : Standards specification for silicone elastomers used in medical applications.
- ✓ ASTM F 703-96 (1996) : Standard Specification for Implantable Breast Prostheses
- ✓ ISO 5893 (1993) : Rubber and plastic testing equipment – Types for traction, flexion and compression (constant translation speed) – Description
- ✓ **Standards presented under the general title « Evaluation of medical devices » gathering :**
  - NF EN ISO 10993-1 (1998) : Evaluation and testing
  - NF EN ISO 10993-2 (1998) : Animal welfare requirements
  - NF EN 30993-3 (1994) : Genotoxicity, Carcinogenicity and reproductive toxicity testing
  - NF EN 30993-4 (1994) : Test choice for interactions with blood
  - NF EN ISO 10993-5 (1994) : Test for in vitro cytotoxicity
  - NF EN 30993-6 (1995) : Test for local effects after implantation
  - NF EN ISO 10993-9 (1999) : Framework for identification and quantification of potential degradation products
  - NF EN ISO 10993-10 (1996) : Test for irritation and sensitization
  - NF EN ISO 10993-11 (1996) : Systemic toxicity testing
  - ISO/DIS 10993-12 (2001) : Sample preparation and reference materials
  - ISO 10993-13 (1998) : Identification and quantification of degradation products from polymeric medical devices
  - NF EN ISO 10993-16 (1997) : Design for toxico-kinetic studies of degradation products and leachable substances
  - ISO/DIS 10993-17 (1999) : Methods for the establishment of allowable limits for leachable substances using health based risk assessment
- ✓ ISO 11607 (1997) : Packaging for terminally sterilized devices
- ✓ NF EN 12180 (2000) : Non-active surgical implants –Morphological implants. Specific requirements related to breast implants
- ✓ NF EN 556-1 (2002) : Requirements for medical devices labeled « Sterile »
- ✓ NF EN 550 (1994) : Sterilization of medical devices. Validation and routine control for the ethylene oxide sterilization
- ✓ NF EN 861-1 (1997) : Materials and packaging systems for medical devices to be sterilized. Part 1 : General requirements and testing methods.
- ✓ NF EN 980 (1996) : Graphical symbols used for the medical device labeling
- ✓ NF EN 1041 (1998) : Information provided by the manufacturer with medical devices
- ✓ NF EN ISO 14630 (1998) : Non active surgical implants
- ✓ NF S 94-350 (1994) : Implantable breast implants

P.I.P.

POLY IMPLANTS PROTHESES
337 Avenue de Bruxelles - 83507 La SEYNE S/Mer - Tel : 04.94.10.98.10 - Fax : 04.94.10.98.11

Reference : SQ1/02 DOT 202	Index : H
Document title : TECHNICAL FILE – High cohesivity gel pre-filled breast implants	

DOCUMENT TITLE

TECHNICAL FILE

HIGH COHESIVITY GEL PRE-FILLED BREAST IMPLANTS

Source documents : SQ1/02 MAQ 001 - QUALITY ASSURANCE MANUAL
ISO 9001 - NF EN 46001
European Directive 93/42 CEE

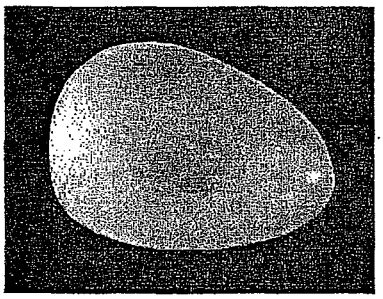
Index :	Date, pages concerned, purpose of the modification :
A	02/06/1998 : Initial edition
B	04/01/2000 : Updated further to C.A.R. n° AQ 99/04, AQ 99/22 and AQ 99/32
C	17/07/2000 : Updated further to C.A.R. n° AQ 00/11, AQ 00/35 and AQ 00/36
D	27/02/2001 : Updated further to C.A.R. AQ 00/58 - new parameters in production according to Project PR 00/09
E	06/06/2001 : Updated further to PR 00/010 : Locating system of asymmetrical & reconstruction profiles Asymmetrical IMGHC & GABGL range widening
F	24/08/2001 : Updated further to DIRQ 01/018 & PR 01/05 : Research of a bactericide exempt from glutaraldehyde to wash the implants
G	29/08/2002 : Updated further to : - RD 02-017-1 related to the modification of the acceptance criteria of the envelope mechanical features - The implementation of new biocompatibility tests
H	02/01/2003 : p.25, 43; Updated further to RD 02/013-7 and 8 : New texture of patches for textured breast implants implemented

Note : The paragraphs modified by the last order are printed with a stroke

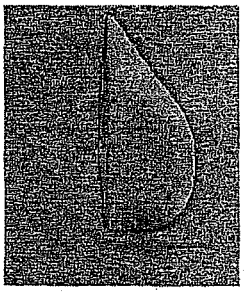
Written by :	Reviewed by :	Approved by :
Name M. BOUZIAN	Name A. GOSSE	Name J.C. MAS
Function Studies, R&D Engineer	Function Studies, R&D Leader	Function Technical Manager
Signature	Signature	Signature
	Name J. BUREL	
	Function Quality & Regulatory Affairs Manager	
	Signature	

TABLE OF CONTENTS

Photos given for information only.



PROFILE R

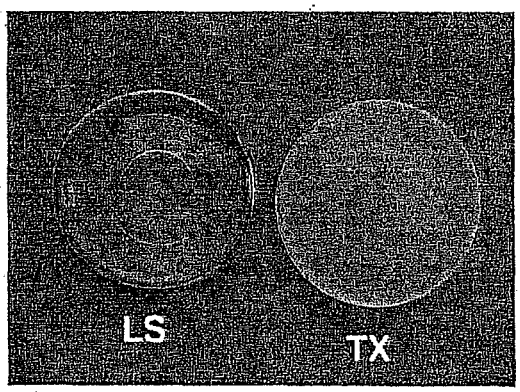


PROFILE R

1.5.2 – Surface :

The external structure of the high cohesivity gel pre-filled breast implant envelopes can be of two types :

- smooth surface (LS),
- textured surface (TX).



For asymmetrical and reconstruction profile breast implants :

Given the non symmetrical shapes of these profiles and taking into account the distortion applied to the prosthesis when introducing it into the body, a location system (tactile and visual) allows for guiding the surgeon when implanting the device so that it is positioned on the right side inside the patient body.

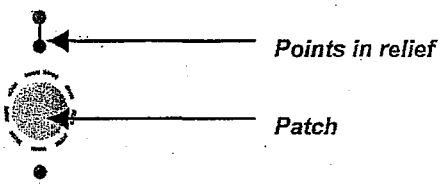
Smooth surface breast implants can slide, which is not disturbing for a hemispheral profile (symmetrical), but becomes so for asymmetrical and reconstruction profiles.

➢ Asymmetrical and reconstruction profile implants always have a textured surface.

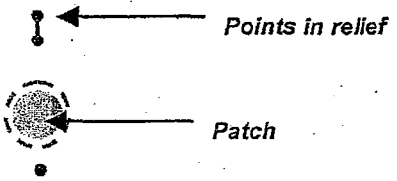
Tactile location system :

➢ For the submammary and axillary implantation incisions, the asymmetrical and reconstruction prosthesis has a tactile location system allowing to distinguish the top from the bottom.

These are points in relief in silicone elastomer at the back of the implant, on the patch side.
The top of the implant has two points in relief and the bottom one point.



Drawing of asymmetrical profile back



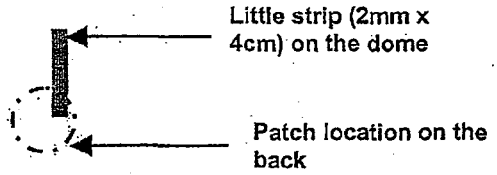
Drawing of reconstruction profile back

Visual location system :

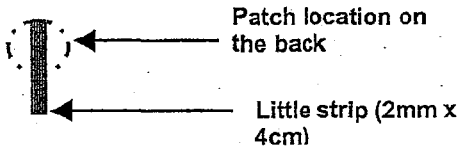
➢ For the peri-areolar implantation incision, the prosthesis has **a visual location system** on the implant dome (side opposed to the patch) allowing to position the implant in the right axis and also to locate the implant top or bottom.
This visual location system consists in the absence of texturing elements of rectangular shape, measuring out : 2 mm x 4cm.

This little strip is positioned :

- on the implant dome :
  - on asymmetrical profiles: on the implant superior half
  - on reconstruction profiles: on the implant inferior third
- it represents the prosthesis' vertical axis



Drawing of asymmetrical profile back



Drawing of reconstruction profile back

RECONSTRUCTION ASYMMETRICAL

1.5.3 – Volume :

The range of P.I.P.'s high cohesivity gel pre-filled breast implants gathers several volumes which, for a given profile are all achieved from an homothety of the previous volume.
The volume measurement unit is the cubic centimeter (cc).

Recapitulative tables for each type of implant are found in the next pages :

a) IMGHC-LS-S : Smooth surface standard profile high cohesivity gel pre-filled breast implant

CODE	SURFACE	PROFILE	VOLUME (cc)	DIAMETER (mm)	PROJECTION (mm)
IMGHC	SMOOTH	STANDARD	85	87	18
IMGHC	SMOOTH	STANDARD	105	92	20
IMGHC	SMOOTH	STANDARD	125	97	21
IMGHC	SMOOTH	STANDARD	145	102	23
IMGHC	SMOOTH	STANDARD	165	106	26
IMGHC	SMOOTH	STANDARD	185	108	27
IMGHC	SMOOTH	STANDARD	205	110	28
IMGHC	SMOOTH	STANDARD	225	114	29
IMGHC	SMOOTH	STANDARD	245	117	30
IMGHC	SMOOTH	STANDARD	265	124	31
IMGHC	SMOOTH	STANDARD	285	126	32
IMGHC	SMOOTH	STANDARD	305	128	33
IMGHC	SMOOTH	STANDARD	325	130	34
IMGHC	SMOOTH	STANDARD	345	132	35
IMGHC	SMOOTH	STANDARD	365	136	34
IMGHC	SMOOTH	STANDARD	415	141	35
IMGHC	SMOOTH	STANDARD	455	145	36
IMGHC	SMOOTH	STANDARD	505	150	37
IMGHC	SMOOTH	STANDARD	555	156	38
IMGHC	SMOOTH	STANDARD	605	160	39
IMGHC	SMOOTH	STANDARD	655	166	40
IMGHC	SMOOTH	STANDARD	705	172	41

b) IMGHC-LS-H : Smooth surface High profile High cohesivity gel pre-filled breast implants

CODE	SURFACE	PROFILE	VOLUME (cc)	DIAMETER (mm)	PROJECTION (mm)
IMGHC	SMOOTH	HIGH	90	80	29
IMGHC	SMOOTH	HIGH	130	84	32
IMGHC	SMOOTH	HIGH	150	90	34
IMGHC	SMOOTH	HIGH	170	94	35
IMGHC	SMOOTH	HIGH	190	98	36
IMGHC	SMOOTH	HIGH	210	102	37
IMGHC	SMOOTH	HIGH	230	105	38
IMGHC	SMOOTH	HIGH	250	109	39
IMGHC	SMOOTH	HIGH	270	112	40
IMGHC	SMOOTH	HIGH	290	115	41
IMGHC	SMOOTH	HIGH	310	118	42
IMGHC	SMOOTH	HIGH	330	121	43
IMGHC	SMOOTH	HIGH	350	126	44
IMGHC	SMOOTH	HIGH	390	128	45
IMGHC	SMOOTH	HIGH	430	135	46
IMGHC	SMOOTH	HIGH	470	142	47
IMGHC	SMOOTH	HIGH	510	146	48
IMGHC	SMOOTH	HIGH	570	151	49
IMGHC	SMOOTH	HIGH	620	157	50
IMGHC	SMOOTH	HIGH	680	160	51

c) IMGHC-TX-S : TeXtured surface Standard profile High cohesivity gel pre-filled breast implants

CODE	SURFACE	PROFILE	VOLUME (cc)	DIAMETER (mm)	PROJECTION (mm)
IMGHC	TEXTURED	STANDARD	85	87	18
IMGHC	TEXTURED	STANDARD	105	92	20
IMGHC	TEXTURED	STANDARD	125	97	21
IMGHC	TEXTURED	STANDARD	145	102	23
IMGHC	TEXTURED	STANDARD	165	106	26
IMGHC	TEXTURED	STANDARD	185	108	27
IMGHC	TEXTURED	STANDARD	205	110	28
IMGHC	TEXTURED	STANDARD	225	114	29
IMGHC	TEXTURED	STANDARD	245	117	30
IMGHC	TEXTURED	STANDARD	265	124	31
IMGHC	TEXTURED	STANDARD	285	126	32
IMGHC	TEXTURED	STANDARD	305	128	33
IMGHC	TEXTURED	STANDARD	325	130	34
IMGHC	TEXTURED	STANDARD	345	132	35
IMGHC	TEXTURED	STANDARD	365	136	34
IMGHC	TEXTURED	STANDARD	415	141	35
IMGHC	TEXTURED	STANDARD	455	145	36
IMGHC	TEXTURED	STANDARD	505	150	37
IMGHC	TEXTURED	STANDARD	555	156	38
IMGHC	TEXTURED	STANDARD	605	160	39
IMGHC	TEXTURED	STANDARD	655	166	40
IMGHC	TEXTURED	STANDARD	705	172	41

d) IMGHC-TX-H : TeXtured surface High profile High cohesivity gel pre-filled breast implants

CODE	SURFACE	PROFILE	VOLUME (cc)	DIAMETER (mm)	PROJECTION (mm)
IMGHC	TEXTURED	HIGH	90	80	29
IMGHC	TEXTURED	HIGH	130	84	32
IMGHC	TEXTURED	HIGH	150	90	34
IMGHC	TEXTURED	HIGH	170	94	35
IMGHC	TEXTURED	HIGH	190	98	36
IMGHC	TEXTURED	HIGH	210	102	37
IMGHC	TEXTURED	HIGH	230	105	38
IMGHC	TEXTURED	HIGH	250	109	39
IMGHC	TEXTURED	HIGH	270	112	40
IMGHC	TEXTURED	HIGH	290	115	41
IMGHC	TEXTURED	HIGH	310	118	42
IMGHC	TEXTURED	HIGH	330	121	43
IMGHC	TEXTURED	HIGH	350	126	44
IMGHC	TEXTURED	HIGH	390	128	45
IMGHC	TEXTURED	HIGH	430	135	46
IMGHC	TEXTURED	HIGH	470	142	47
IMGHC	TEXTURED	HIGH	510	146	48
IMGHC	TEXTURED	HIGH	570	151	49
IMGHC	TEXTURED	HIGH	620	157	50
IMGHC	TEXTURED	HIGH	680	160	51

e) IMGHC-TX-R : TeXtured surface Reconstruction profile High cohesivity gel pre-filled breast implants

CODE	SURFACE	PROFILE	VOLUME (cc)	LENGTH (mm)	WIDTH (mm)	PROJECTION MAXI (mm)
IMGHC	TEXTURED	RECONSTRUCTION	180	111	96	39
IMGHC	TEXTURED	RECONSTRUCTION	220	113	98	41
IMGHC	TEXTURED	RECONSTRUCTION	260	120	98	44
IMGHC	TEXTURED	RECONSTRUCTION	330	127	111	48
IMGHC	TEXTURED	RECONSTRUCTION	420	132	118	53
IMGHC	TEXTURED	RECONSTRUCTION	500	143	124	57
IMGHC	TEXTURED	RECONSTRUCTION	600	154	137	60

f) IMGHC-TX-AL : Textured surface Asymmetrical profile High cohesivity gel pre-filled breast implants- Left side

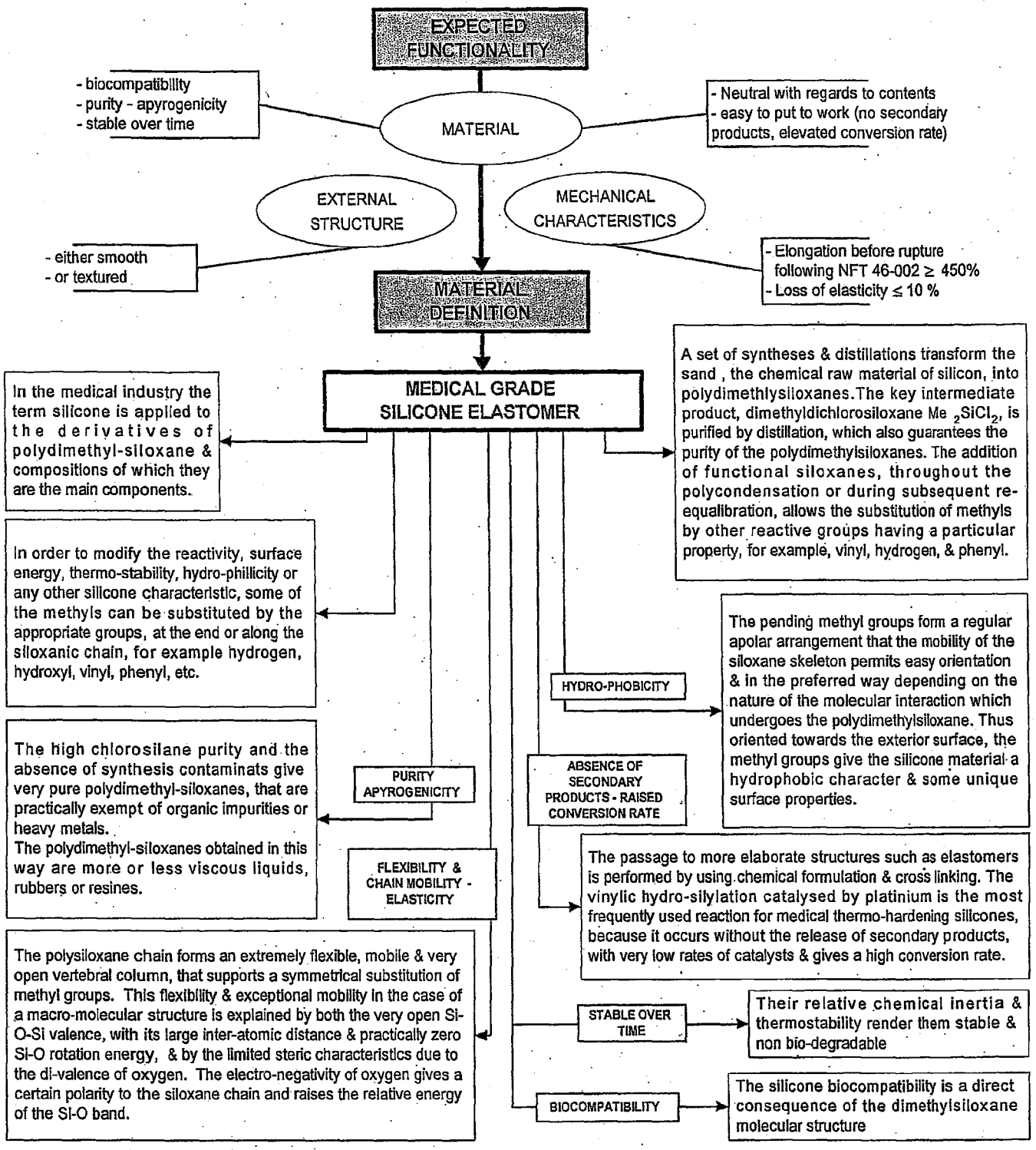
CODE	SURFACE	PROFILE	VOLUME (cc)	LENGTH (mm)	WIDTH (mm)	PROJECTION (mm)
IMGHC	TEXTURED	ASYMMETRICAL	200	109	86	36
IMGHC	TEXTURED	ASYMMETRICAL	230	114	89	39
IMGHC	TEXTURED	ASYMMETRICAL	245	119	93	42
IMGHC	TEXTURED	ASYMMETRICAL	260	125	98	44
IMGHC	TEXTURED	ASYMMETRICAL	280	130	102	46
IMGHC	TEXTURED	ASYMMETRICAL	300	135	107	48
IMGHC	TEXTURED	ASYMMETRICAL	330	138	110	50
IMGHC	TEXTURED	ASYMMETRICAL	370	143	115	52
IMGHC	TEXTURED	ASYMMETRICAL	400	148	119	54
IMGHC	TEXTURED	ASYMMETRICAL	450	153	124	56

g) IMGHC-TX-AR : TeXtured surface Asymmetrical profile High cohesivity gel pre-filled breast implants- Right side

CODE	SURFACE	PROFILE	VOLUME (cc)	LENGTH (mm)	WIDTH (mm)	PROJECTION (mm)
IMGHC	TEXTURED	ASYMMETRICAL	200	109	86	36
IMGHC	TEXTURED	ASYMMETRICAL	230	114	89	39
IMGHC	TEXTURED	ASYMMETRICAL	245	119	93	42
IMGHC	TEXTURED	ASYMMETRICAL	260	125	98	44
IMGHC	TEXTURED	ASYMMETRICAL	280	130	102	46
IMGHC	TEXTURED	ASYMMETRICAL	300	135	107	48
IMGHC	TEXTURED	ASYMMETRICAL	330	138	110	50
IMGHC	TEXTURED	ASYMMETRICAL	370	143	115	52
IMGHC	TEXTURED	ASYMMETRICAL	400	148	119	54
IMGHC	TEXTURED	ASYMMETRICAL	450	153	124	56

2.3.1 – Envelope :

a) General definition :



Pg 38 / 113
Vol 1

b) Choice of raw material

Silicone type : Polydimethyldiphenylsiloxane – medical grade silicone

Smooth envelope : NUSIL MED6 6400 (4 layers)
Textured envelope : NUSIL MED6 6400 (4 layers) + NUSIL MED6 6400 (last layer)

The technical specifications of the MED6 6400 are described in the forms [170].

c) Raw material biocompatibility – MED6 6400

The following tests were performed to evaluate biocompatibility on the raw materials and implemented by NAmSA for Nusil. *(NamSA : 9 Morgan Irvine – CA 92718)*

➢ ***Cytotoxicity***

(see [50])

The methodology used complies with the GLP (21 CFR 58).
Some material extracts are performed with some culture medium for cells and put in contact with mouse fibroblasts. The material is not cytotoxical.

➢ ***In vitro hemolysis***

(see [51])

The methodology used complies with the GLP (21 CFR 58).
Some material extracts are performed in some sodium chloride and put in contact with rabbit blood.
The material is not haemolytical.

➢ ***Toxicity by systemic injection***

(see [52])

The methodology used complies with the GLP (21 CFR 58) and the USP guidelines. Some material extracts are performed with some sodium chloride (SC) and cotton seed oil (CSO). They are then injected in mice by intraveinous route (SC) and by intraperitoneal route (CSO). Animals are regularly observed until 72 hours. No mortality occurred and there is no sign of systemic toxicity.

➢ ***Intradermic injection in the rabbit***

(see [53])

The methodology used complies with the GLP (21 CFR 58) and the USP guidelines. Some material extracts are performed with sodium chloride (SC) and cotton seed oil (CSO). They are injected to rabbits in intracutaneous. Animals are regularly observed until 72 hours to detect erythema and oedema. There is no irritation nor sign toxicity.

➢ ***Implantation in the rabbit***

(see [54])

The methodology used complies with the GLP (21 CFR 58) and the USP guidelines. The testing material is implanted in the muscle, in the rabbit. After 90 days, animals undergo euthanasia and the implantation sites are analyzed, histological examinations are performed. Implantation didn't provoke any significant macroscopic reaction and the implant was classified as non irritating from a microscopic point of view.

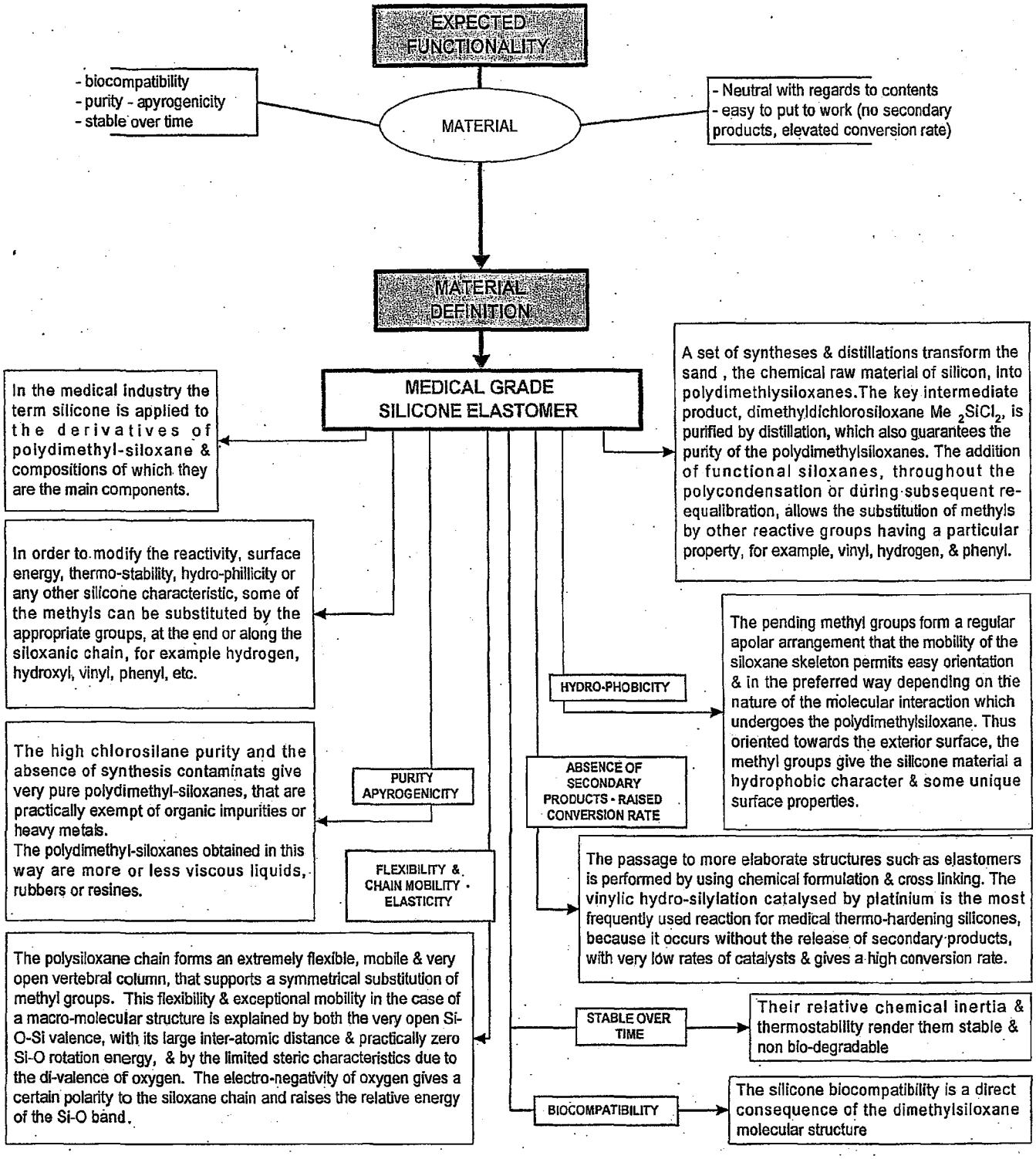
➢ ***Mutagenicity – Ames Test***

(see [55])

The methodology used is that of Ames and al. and complies with the GLP (21 CFR 58). Some material extracts are performed with some sodium chlorid (SC) and put in contact with the various strains of Salmonella thyphimurium. The extracts are not mutagenic.

2.3.2 - Closure patch

a) General definition



b) Choice of raw material

Type of silicone : Polydimethyldiphenylsiloxane – medical grade silicone

Closure patch : NUSIL MED6 6400

The technical specifications of the MED6 6400 are described in the form [170].

c) Raw material biocompatibility – MED6 6400

The following tests were performed to evaluate biocompatibility on the raw material and implemented by NamSA for Nusil. *(NamSA : 9 Morgan Irvine – CA 92718)*

➢ ***Cytotoxicity***

(see [50])

The methodology used complies with the GLP (21 CFR 58).
Some material extracts are performed with some culture medium for cells and put in contact with mouse fibroblasts. The material is not cytotoxical.

➢ ***In vitro hemolysis***

(see [51])

The methodology used complies with the GLP (21 CFR 58).
Some material extracts are performed in some sodium chloride and put in contact with rabbit blood.
The material is not haemolytical.

➢ ***Toxicity by systemic injection***

(see [52])

The methodology used complies with the GLP (21 CFR 58) and the USP guidelines. Some material extracts are performed with some sodium chloride (SC) and cotton seed oil (CSO). They are then injected in mice by intraveinous route (SC) and by intraperitoneal route (CSO). Animals are regularly observed until 72 hours. No mortality occurred and there is no sign of systemic toxicity.

➢ ***Intradermic injection in the rabbit***

(see [53])

The methodology used complies with the GLP (21 CFR 58) and the USP guidelines. Some material extracts are performed with sodium chloride (SC) and cotton seed oil (CSO). They are injected to rabbits in intracutaneous. Animals are regularly observed until 72 hours to detect erythema and oedema. There is no irritation nor sign of toxicity.

➢ ***Implantation in the rabbit***

(see [54])

The methodology used complies with the GLP (21 CFR 58) and the USP guidelines. The testing material is implanted in the muscle, in the rabbit. After 90 days, animals undego euthanasia and the implantation sites are analyzed, histo logical examinations are performed. The implantation didn't provoke any significant macroscopic reaction and the implant was classified as non irritating from a microscopic point of view.

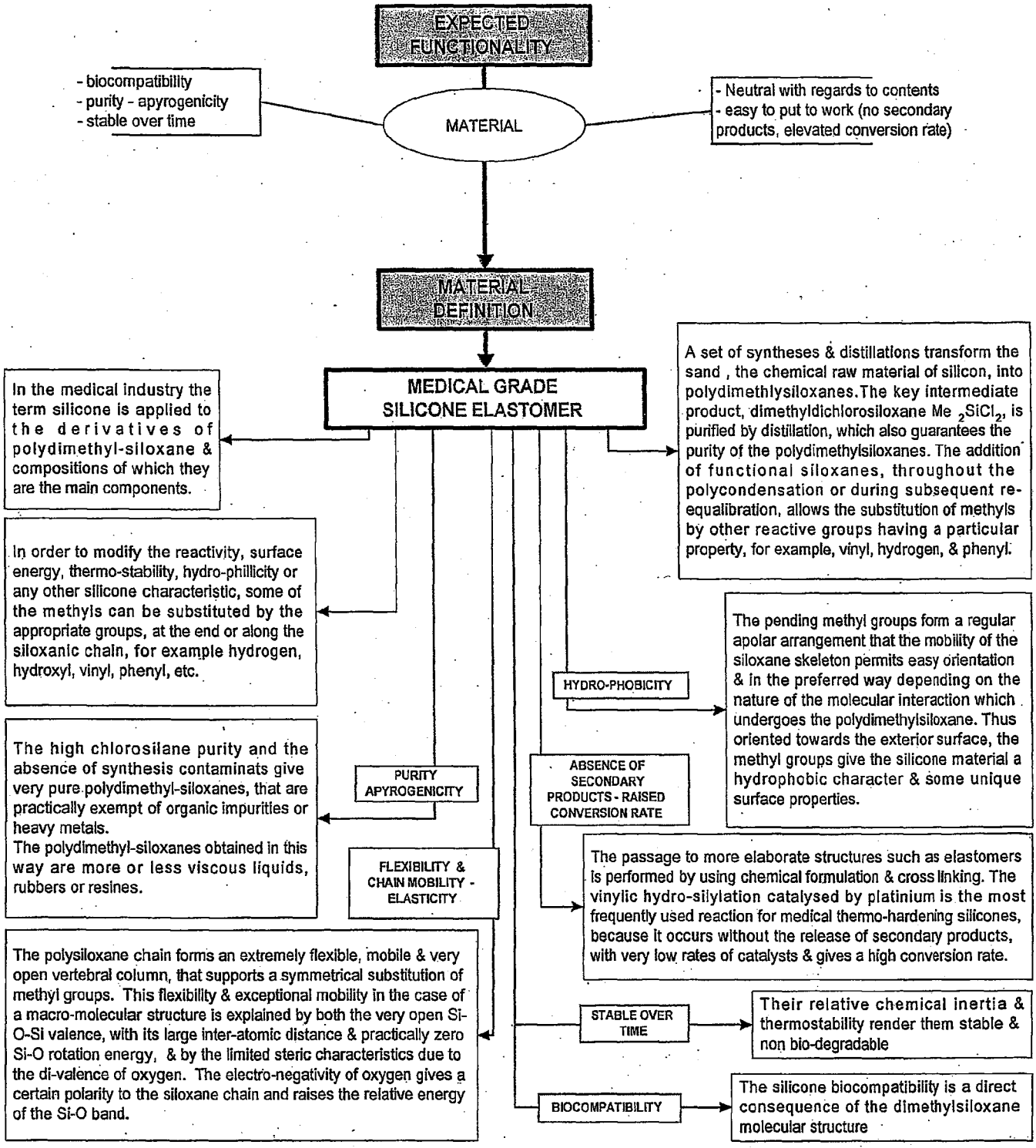
➢ ***Mutagenicity – Ames Test***

(see [55])

The methodology used is that of Ames and al. and complies with the GLP (21 CFR 58). Some material extracts are performed with some sodium chloride (SC) and put in contact with the various strains of Salmonella thyphimurium. The extracts are not mutagenic.

2.3.3 – Very first gluing layer on the envelope :

a) General definition



b) Choice of raw material

Tye pf silicone : Polydimethylmethylvinylsiloxane – medical grade silicone

Very first glue layer: NUSIL MED 6640

The technical specifications of the MED 6640 are described in the form [172].

c) Raw material biocompatibility – MED 6640

The following tests were performed to evaluate biocompatibility on the MED2 6640 and remain valid for the MED 6640. They were implemented by NamSA for Nusil.

(NamSA : 9 Morgan Irvine – CA 92718)

➢ ***Cytotoxicity***

(see [56])

Several in vitro biocompatibility tests were performed on the mouse. None of them could emphasize toxicity on the fibroblast cells of the mouse.

➢ ***In vitro hemolysis***

(see [57])

The In vitro hemolysis test by extraction in the sodium chloride show that the extracts considered are not hemolitic.

➢ ***Toxicity by systemic injection***

(see [58])

The test of systemic toxicity by extraction in the sodium chloride were performed in the mouse. The extracts considered didn't lead to any mortality and the systemic toxicity was not emphasized by these tests.

➢ ***Intradermic injection in the rabbit***

(see [59])

The toxicity test by intradermic injection in the rabbit were performed by extraction in the sodium chloride. The extracts didn't lead to any irritation and no toxicity was observed.

➢ ***Implantation in the rabbit***

(see [60])

The implantation didn't lead to any significant macroscopic reaction and the implant was classified as "no irritating" from a microscopical point of view.

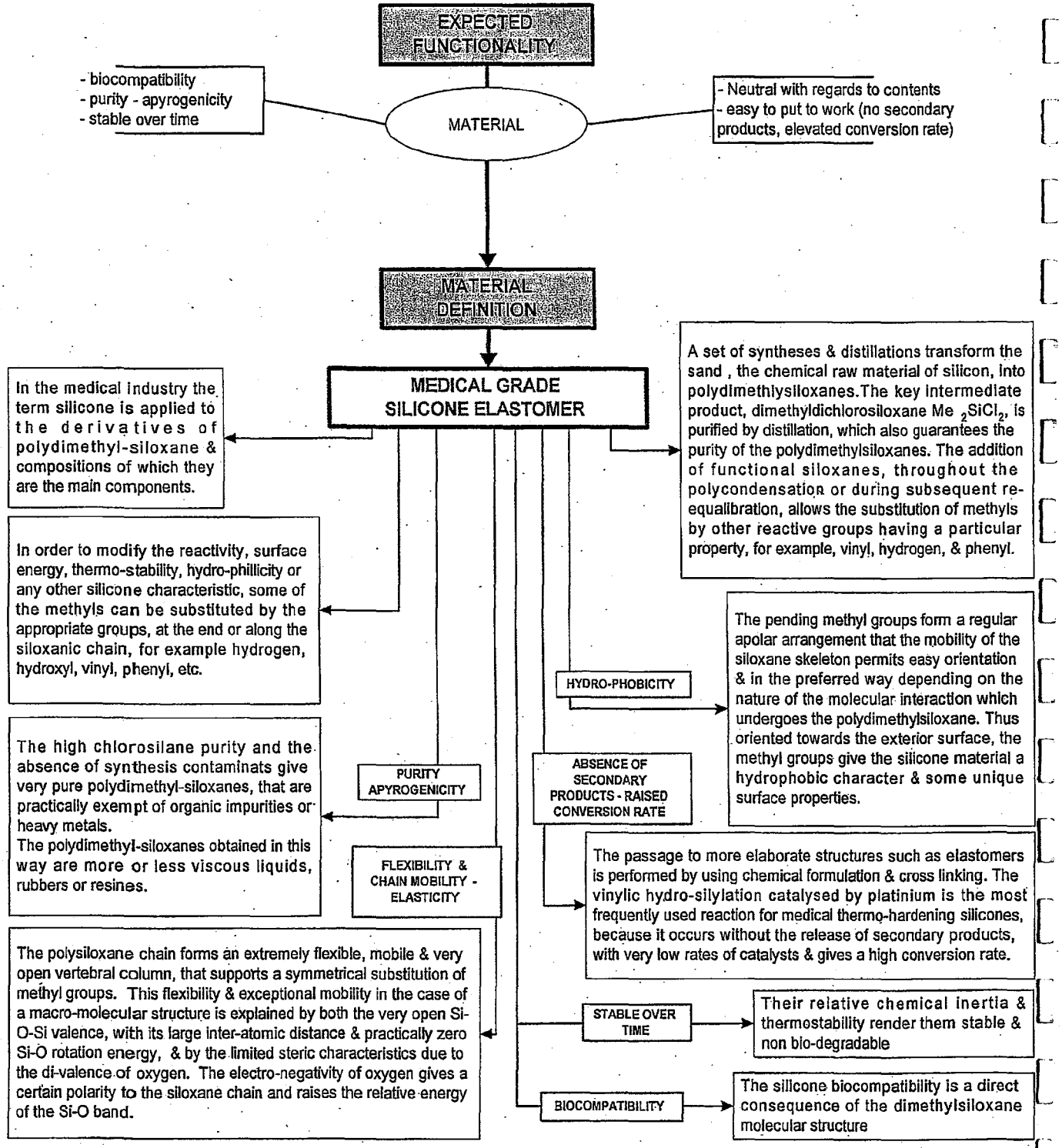
➢ ***Mutagenicity – Ames Test***

(see [61])

The mutagenicity tests by extraction in the sodium chloride showed that the extracts don't induce mutagenic changes in the salmonella typhimurium.

2.3.4 – Glue :

a) General definition



b) Choice of raw material

Type of silicone : Polydimethylmethylvinylsiloxane – medical grade silicone

Glue: NUSIL MED 2245

The technical specifications of the MED 2245 are described in the form [169].

c) Raw material biocompatibility – MED 2245

The following tests were performed to evaluate biocompatibility on the raw material and implemented by NamSA for Nusil. *(NamSA : 9 Morgan Irvine – CA 92718)*

➢ ***Cytotoxicity***

(see [90])

Several cytotoxicity tests were performed in vitro. None of them could emphasize toxicity on the fibroblast cells of the mouse.

➢ ***Toxicity by systemic injection***

(see [91])

The tests of systemic toxicity by extraction in the sodium chloride were performed in the mouse. The extracts considered didn't lead to any mortality and the systemic toxicity was not emphasized by these tests.

➢ ***Intradermic injection in the rabbit***

(see [92])

The toxicity tests by intradermic injection in the rabbit were performed by extraction in the sodium chloride. The extracts didn't lead to any irritation and no toxicity was observed.

➢ ***Implantation in the rabbit***

(see [93])

The implantation didn't lead to any significant macroscopic reaction and the implant was classified as "no irritating" from a microscopical point of view.

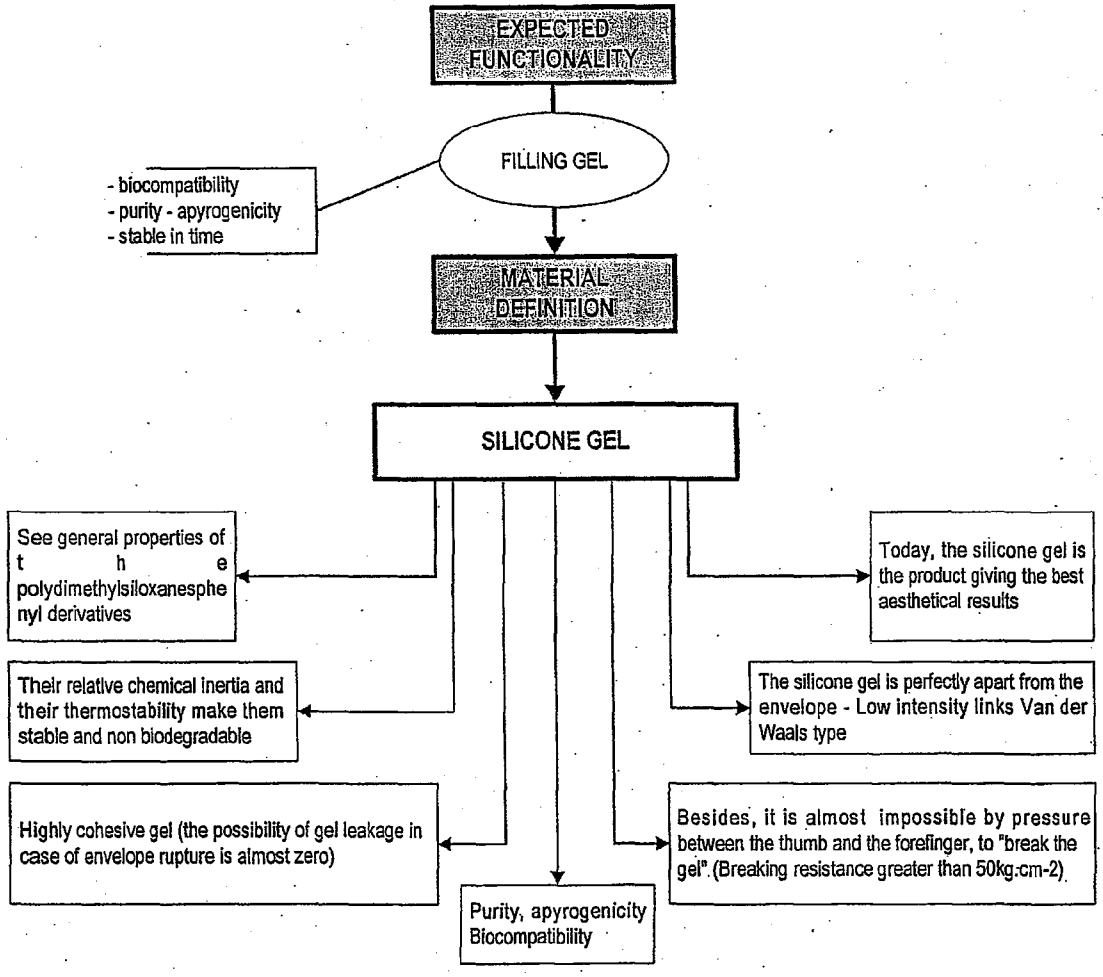
➢ ***Mutagenicity – Ames Test***

(see [94])

The mutagenicity tests by extraction in the sodium chloride showed that the extracts don't induce mutagenic changes in the salmonella typhimurium.

2.3.5 – Filler material :

a) General definition



b) Choice of raw material

Type of silicone : Polydimethylmethylvinylsiloxane – medical grade silicone

Filler material : NUSIL MED3 6300

The technical specifications of the MED3 6300 are described in the form [175].

c) Raw material biocompatibility – MED3 6300

The following tests were performed to evaluate biocompatibility on the raw material and implemented by NamSA for Nusil. *(NamSA : 9 Morgan Irvine – CA 92718)*

➢ ***Cytotoxicity***

(see [62])

The methodologies used comply with the GLP (21 CFR 58) and the ISO 10993-5 (1994) Standard.

Methodology in agarose :

The silicone gel is put in contact with the L-929 cells (mouse fibroblasts). After 24-hour incubation, the cells are observed with the microscope so as to detect any distortion, degeneration, detachment or cellular lysis. The material is not cytotoxic.

Methodology by extraction :

Some material extracts are performed with some culture medium for cells and put in contact with some mouse fibroblasts L-929. The cells are incubated for 48 hours. The material is not cytotoxic.

➢ ***In vitro hemolysis***

(see [63])

The methodology used complies with the GLP (21 CFR 58).

Some material extracts are performed in some sodium chloride (SC) and put in contact with some rabbit blood. The material is not haemolytical.

➢ ***Acute toxicity in the mouse***

(see [64])

The methodology used is in compliance with the GLP (21 CFR 58) and the ISO 10993-11 (1996).

Some material extracts are performed with some sodium chloride (SC), an alcoholized saline solution (AS), glycol polyethylene (PEG) and cotton seed oil (CSO). They are injected in mice by intraveinous route (SC) and (AS) and by intraperitoneal route (PEG) and (CSO). Animals are regularly observed until 72 hours. No mortality occurred and there are no signs of systemic toxicity.

➢ ***Intradermic injection in the rabbit***

(see [65])

The intra-cutaneous reactivity test was performed in accordance with the ISO 10993-10 Standard (1996).

Some material extracts are performed with some sodium chloride (SC), an alcoholized saline solution (AS), glycol polyethylene (PEG) and cotton seed oil (CSO). They are injected to rabbits by intra-cutaneous route. Animals are regularly observed until 72 hours to detect erythema and oedemas.There is no irritation nor sign of toxicity.

➢ ***Implantation in the muscle in the rabbit (7 and 90 days)***

(see [66])

The implantation test (1 week and 30 weeks) in the muscle was performed according to the ISO 10993-6 Standard (1995).

The testing material is implanted in the muscle in the rabbit.

Animals undergo euthanasia and the implantation sites are analyzed, histological examinations are performed. At 1 week, the implantation didn't provoke any significant macroscopic reaction and the implant was classified as slightly irritating from a microscopic point of view. At 30 weeks, the implantation didn't provoke any significant macroscopic reaction and the implant was classified as non irritating from a microscopical point of view

➢ ***Mutagenicity – Ames Test***

(see [67])

The methodology used is that of Ames and al. and complies with the GLP (21 CFR 58).

Some material extracts are performed with some sodium chloride (SC) and DMSO and are put in contact with various strains of Salmonella thyphimurium. Tests are performed with and without metabolic activation (S9 fraction). The silicone gel extracts are not mutagenic.

➢ ***Pyrogenicity test in the rabbit***

(see [47])

The pyrogenicity test was performed in accordance with the ISO 10993-11 Standard (1996).

A silicone gel extract was performed with some sodium chloride (SC) and injected to rabbits by intraveinous route. The rabbit temperature is regularly measured out for the 3 hours following the injection.

The silicone gel is declared non pyrogenic.

➢ ***Cutaneous irritation in the rabbit***

(see [48])

The cutaneous irritation test was performed in accordance with the ISO 10993-10 Standard (1996). The silicone gel is directly applied on the rabbit skin. The exposed sites are regularly observed (until 72 hours after gel withdrawal) to detect any sign of erythema or oedema.

The silicone gel is declared as non irritating.

➢ ***Sensitization test in the guinea pig***

(see [49])

The sensitization test was performed in accordance with the ISO 10993-10 Standard (1996).

The extracts of silicone gel are performed with some sodium chloride (SC) and cotton seed oil (CSO).

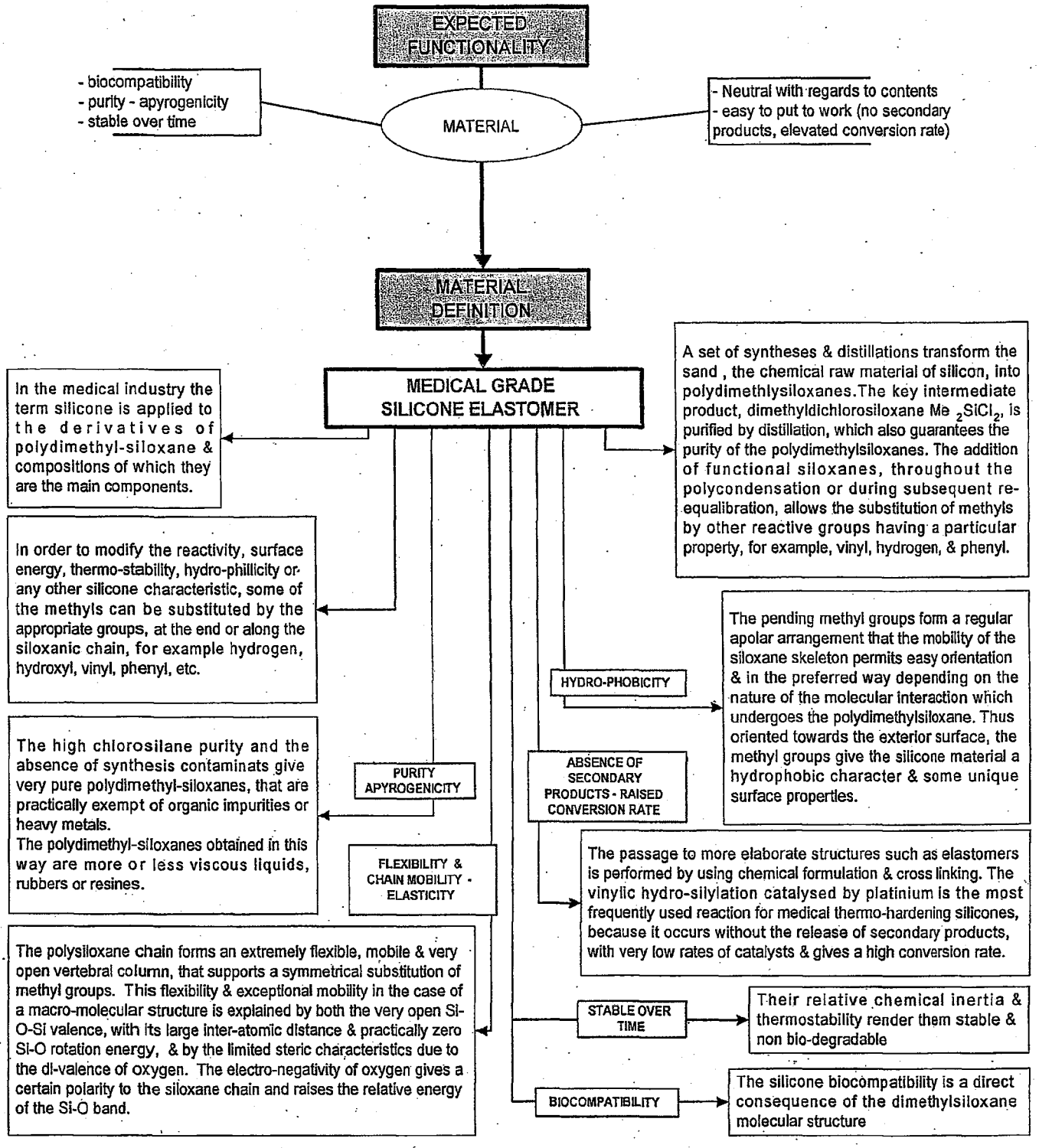
Induction I : Extracts are injected by intradermal route in the guinea pig

Induction II : At D6, injections are performed again on the same site as the first induction and 24 hours after the occlusive dressing containing the extract for a 48 hour time.

Test : 15 days after, occluded topical applications of the extract are performed on a never treated zone. The sensitization reaction is evaluated noting down the erythema and oedema. The silicone gel is not sensitizing.

2.3.6 – Closing solution :

a) General definition



b) Choice of raw material

Type of silicone : Organopolysiloxane RTV –silicone elastomer of medical grade

Closure solution : APPLIED SILICONE PN 40076
The technical specifications of the PN 40 076 are described in the form [174].

c) Raw material biocompatibility – PN 40076

The following biocompatibility tests were performed for « Applied Silicone Corporation »(320 W.Stanley Avenue Ventura - CA 93001) by NamSA et UBTL companies :

NamSA – 9 morgan Irvine, CA 92 718
UBTL, Inc – 520 Wakara Way – Salt Lake City, Utah 84108

➢ ***Cytotoxicity*** *(see [44])*

Cytotoxicity tests were performed in the fibroblast cells of the mouse from the material extracts (in some culture medium for cells). No cytotoxicity was observed.

➢ ***Intradermal irritation :*** *(see [40])*

Some material extracts were performed in sodium chloride at 0.9% (SC) and cotton seed oil (CSO). The extracts are injected in subcutaneous in rabbits. Under the testing conditions, no sign of toxicity nor irritation was observed.

➢ ***Systemic toxicity :*** *(see [41])*

The systemic toxicity test was performed in compliance with the USP guidelines. Some material extracts are performed in the sodium chloride (SC) and in the cotton seed oil (CSO). The extracts are injected by intraveinous (SC) and intraperitoneal (CSO) route in mice. No mortality nor signs of systemic toxicity were observed.

➢ ***Implantation :****(see [42])*

The implantation test in the muscle was performed in compliance with the USP guidelines. The elastomer was implanted in the rabbit for 90 days. After the animal sacrifice, macroscopic and microscopic (histopathology) observations of the implantation site were performed. The implantation didn't provoke any significant macroscopic reaction and the implant was classified as "non irritating" from a microscopic point of view.

➢ ***Chronic toxicity :*** *(see [46])*

A chronic toxicity study was performed implanting in subcutaneous in the rat the elastomer to test. No systemic toxicity (body weight, organ weight, haematology, biochemical analyses...) was noticed.

➢ ***Genotoxicity :*** *(see [43])*

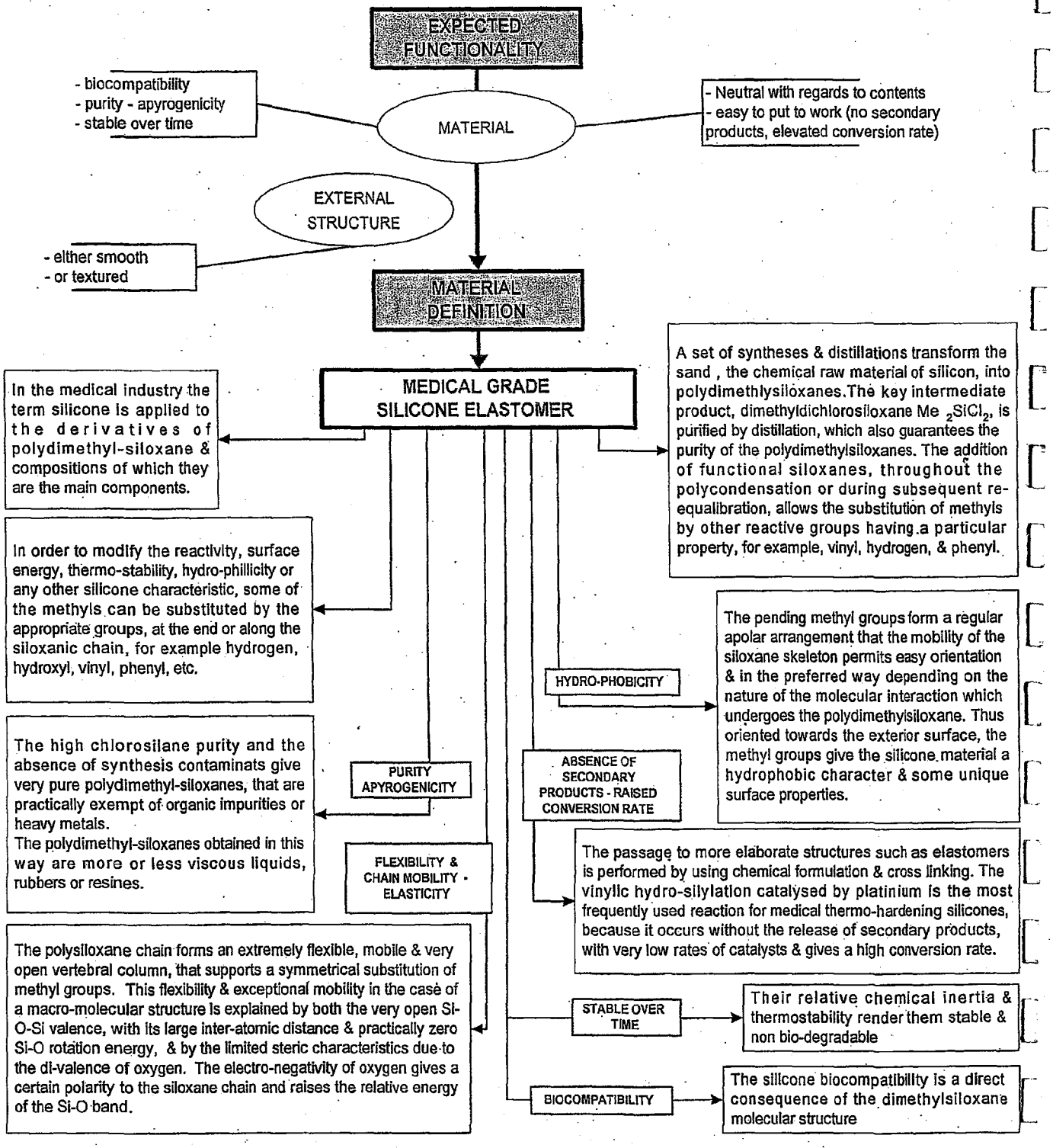
Some material extracts are performed in the sodium chloride and DMSO, and the evaluation of their mutagenic power is tested, in presence and absence of metabolic activation (S9). The extracts don't induce mutagen changes in the various strains of tested Salmonella typhimurium.

➢ ***Reproductive effects :*** *(see [45])*

A reproductive toxicity test was performed after implanting the elastomer in subcutaneous in female rats. After gestation, the foetus study didn't show any teratogenic effects.

2.3.7 – Finishing patch :

a) General definition



b) Choice of raw material

Type of silicone : Polydimethyldiphenylsiloxane – medical grade silicone elastomer

Finishing patch : NUSIL MED6 6400
The technical specifications of the MED6 6400 are described in the form [170].

c) Raw material biocompatibility – MED6 6400

The following biocompatibility tests were performed to evaluate biocompatibility on the raw material and performed by NamSA for Nusil (NamSa : 9 Morgan Irvine – CA 92718)

➢ ***Cytotoxicity***

(see [50])

The methodology used complies with the GLP (21 CFR 58).
Some material extracts are performed with some culture medium for cells and put in contact with mouse fibroblasts. The material is not cytotoxical.

➢ ***In vitro hemolysis***

(see [51])

The methodology used complies with the GLP (21 CFR 58).
Some material extracts are performed in some sodium chloride and put in contact with rabbit blood.
The material is not haemolytical.

➢ ***Toxicity by systemic injection***

(see [52])

The methodology used complies with the GLP (21 CFR 58) and the USP guidelines. Some material extracts are performed with some sodium chloride (SC) and cotton seed oil (CSO). They are then injected in mice by intraveinous route (SC) and by intraperitoneal route (CSO). Animals are regularly observed until 72 hours. No mortality occurred and there is no sign of systemic toxicity.

➢ ***Intradermic injection in the rabbit***

(see [53])

The methodology used complies with the GLP (21 CFR 58) and the USP guidelines. Some material extracts are performed with sodium chloride (SC) and cotton seed oil (CSO). They are injected to rabbits in intra cutaneous. Animals are regularly observed until 72 hours to detect erythema and oedema. There is no irritation nor sign of toxicity.

➢ ***Implantation in the rabbit***

(see [54])

The methodology used complies with the GLP (21 CFR 58) and the USP guidelines. The testing material is implanted in the muscle, in the rabbit. After 90 days, animals are submitted to euthanasia and the implantation sites are analyzed, histological examinations are performed. The implantation didn't provoke any significant macroscopic reaction and the implant was classified as non irritating from a microscopic point of view.

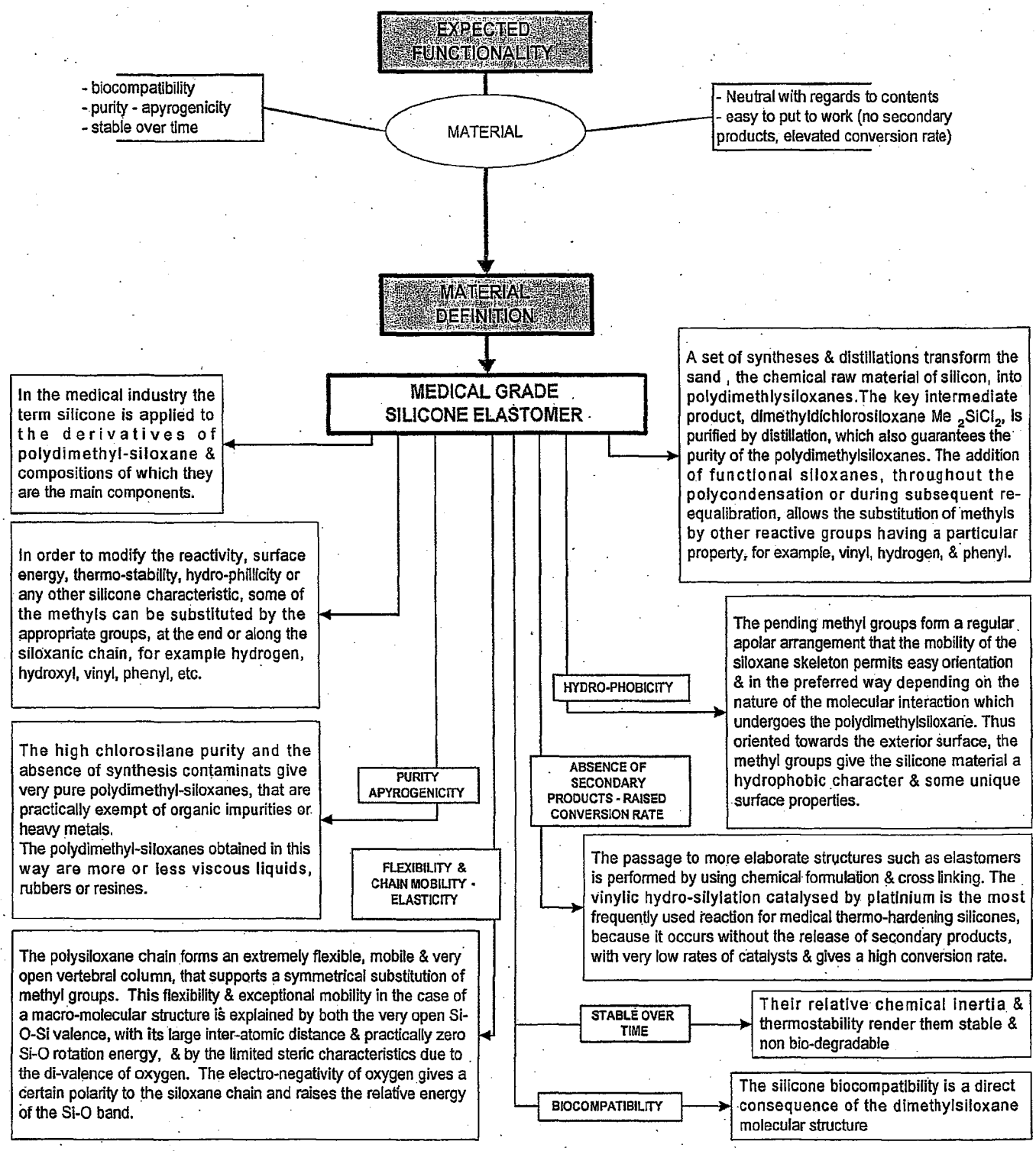
➢ ***Mutagenicity – Ames Test***

(see [55])

The methodology used is that of Ames and al. and complies with the GLP (21 CFR 58). Some material extracts are performed with some sodium chloride (SC) and put in contact with the various strains of Salmonella thyphimurium. The extracts are not mutagenic.

2.3.8 – Tactile location system : points in relief for Asymmetrical and Reconstruction profiles :

a) General definition



b) Choice of raw material

Type of silicone : Organopolysiloxane RTV – medical grade silicone elastomer

Points in relief : APPLIED SILICONE PN 40076
The technical specifications of the PN 40 076 are described in the form [174].

c) Raw material biocompatibility – PN 40076

The following biocompatibility tests were performed for « Applied Silicone Corporation »(320 W.Stanley Avenue Ventura - CA 93001) by NamSA and UBTL companies :

NamSA – 9 morgan Irvine, CA 92 718
UBTL, Inc – 520 Wakara Way – Salt Lake City, Utah 84108

➢ ***Cytotoxicity*** *(see [44])*
Cytotoxicity tests were performed in the fibroblast cells of the mouse from the material extracts (in some culture medium for cells). No cytotoxicity was observed.

➢ ***Intradermal irritation :*** *(see [40])*
Some material extracts were performed in sodium chloride at 0.9% (SC) and cotton seed oil (CSO). The extracts are injected in subcutaneous in rabbits. Under the testing conditions, no toxicity nor sign of irritation was observed.

➢ ***Systemic toxicity :*** *(see [41])*
The systemic toxicity test was performed in compliance with the USP guidelines. Some material extracts are injected in the sodium chloride (SC) and in the cotton seed oil (CSO). The extracts are injected by intraveinous (SC) and intraperitoneal (CSO) route in mice. No mortality nor signs of systemic toxicity were observed.

➢ ***Implantation :****(see [42])*
The implantation test in the muscle was performed in compliance with the USP guidelines. The elastomer was implanted in the rabbit for 90 days. After the animal sacrifice, macroscopic and microscopic (histopathology) observations of the implantation site were performed. The implantation didn't provoke any significant macroscopic reaction and the implant was classified as "non irritating" from a microscopic point of view.

➢ ***Chronic toxicity :*** *(see [46])*
A chronic toxicity study was performed implanting in subcutaneous in the rat the elastomer to test. No systemic toxicity (body weight, organ weight, haematology, biochemical analyses...) was noticed.

➢ ***Genotoxicity :*** *(see [43])*
Some material extracts are performed in the sodium chloride and DMSO, and the evaluation of their mutagenic power is tested, in presence and absence of metabolic activation (S9). The extracts don't induce mutagen changes in the various strains of tested Salmonella typhimurium.

➢ ***Reproductive effects :*** *(see [45])*

A reproductive toxicity test was performed after implanting the elastomer in subcutaneous in female rats. After gestation, the foetus study didn't show any teratogenic effects.

2.3.9 – Visual location system : absence of texturing elements for Asymmetrical and Reconstruction profiles:

The absence of texture is obtained by applying a teflon little strip (40 mm x 2 mm) prior to the texture phase. This strip, non adhering is then removed leaving a smooth trace having the features of the smooth envelope, as described in section 2.3.1.

The Teflon technical specifications are described in the form [167].

2.4 – ADDITIVES :

These are the solvents, the cleaning products or any other additives used in-process. An analysis (see section 3.4.6) allows for verifying they are no longer present in the finished product or the content is lower than the allowable limit of leachable substances in the human body established in the scope of the ISO/DIS 10993-17.2 (1999) Standard *: Biological evaluation of medical devices – Part 17 : Methods for establishing allowable limits of leachable substances using the health-related risk evaluation.*

2.4.1 – Xylene :

- Xylene is the dispersion agent of medical grade silicones supplied by Nusil company : the MED6 6400 used to manufacture the envelope, closure and finishing patches and the MED 6640 used as very first gluing layer.

- Some xylene bought by P.I.P. can also be added to adjust viscosity at the time of the dipping and texture phases. This product specifications are defined in the form [176].

2.4.2 – Heptane :

Heptane is used to adjust viscosity when manufacturing closure and finishing patches and to dissolve the glue. This product technical specifications are defined in the form [168].

2.4.3 – Ethanol :

Ethanol is used to clean the smooth envelopes after the mold removal. This product technical specifications are defined in the form [171].

2.4.4 – Isopropylic alcohol :

Isopropylic alcohol is used to clean the stamped finishing patches. This product technical specifications are defined in the form [173]

2.4.5 – Texturing agent :

The texturing agent is the calibrated saccharine used during the envelope texturing phase. This product technical specifications are defined in the form [177]

2.4.6 – Hydrogen peroxyde 10 volumes:

The hydrogen peroxyde 10 volumes (aqueous solution at 3% hydrogen peroxyde) is used at the finished product washing step prior to the final sterilization. This product technical specifications are defined in the form [182]

2.4.7 – Cyclohexane :

Cyclohexane is used after the gel reticulation to clean the patch. This product technical specifications are defined in the form [166].

3. – FINISHED PRODUCT CHARACTERISTICS

3.1 - PLANS

Type of product	*Product drawing*	*Nomenclature*	*Correspondence table*
IMGHC-LS-S	P1 0 IM 01 S 03 01 00	N1 0 IM 01 S 03 01 00	T1 0 IM 01 S 03 01 00
IMGHC-LS-H	P1 0 IM 01 H 03 01 00	N1 0 IM 01 H 03 01 00	T1 0 IM 01 H 03 01 00
IMGHC-LS-EH	P1 0 IM 01 EH 03 01 00	N1 0 IM 01 EH 03 01 00	T1 0 IM 01 EH 03 01 00
IMGHC-TX-S	P1 0 IM 02 S 03 01 00	N1 0 IM 02 S 03 01 00	T1 0 IM 02 S 03 01 00
IMGHC-TX-H	P1 0 IM 02 H 03 01 00	N1 0 IM 02 H 03 01 00	T1 0 IM 02 H 03 01 00
IMGHC-TX-R	P1 0 IM 02 R 03 01 00	N1 0 IM 02 R 03 01 00	T1 0 IM 02 R 03 01 00
IMGHC-TX-AR	P1 0 IM 02 A 03 01 00	N1 0 IM 02 A 03 01 00	T1 0 IM 02 A 03 01 00
IMGHC-TX-AL	P1 0 IM 02 A 03 01 00	N1 0 IM 02 A 03 01 00	T1 0 IM 02 A 03 01 00
IMGHC-TX-EH	P1 0 IM 02 EH 03 01 00	N1 0 IM 02 EH 03 01 00	T1 0 IM 02 EH 03 01 00

3.2 – BIOCOMPATIBILITY

The following tests were performed on the sterile finished product by the laboratories :

BIOMATECH
ZI de l'Islon – Rue Pasteur – 38670 Chasse sur Rhône – France

Or

LEMI
Technopôle Montesquieu – 33850 MARTILLAC - France

3.3.2 – Fatigue testing : (see [310])

The fatigue testing is a vertical and repetitive deformation test performed on an implant put between two plates which compress it in a cyclical way.

European Model – S 94-350 Standard (1994) :

- Production of alternated deformations of the implant according to a work surface parallel to the surface rest of the implant.
  These distortions are elicited by a moving surface.
- The moving plate is put on the implant and adjusted thanks to an adjusting screw until reaching a final height of the implant equal to 80% of its initial projection.
- The arm's run in its alternative movement is 40mm
- The testing time is 2 000 000 cyles at a frequency of 200 cycles per minute
- After the test described above, the envelope should not show tear or cracks or cut when observing it at a magnification 10.

In 1996, a standardized test was performed by the National Testing Laboratory LNE [310] in compliance with the S 94-350 (1994) experimental Standard : 3 implants of 210 cc (high profile) and 3 implants 205 cc (low profile) were submitted to the compression test (20% of the nominal height) at a 3.3 Hz frequency for 2 million cycles. The 6 implants tested didn't suffered any deterioration.

3.3.3 – Static impact resistance : (see [310])

European model –S 94-350 (1994) Standard :

The test of static impact resistance of a breast implant relies on the folowing rule :
- Vertical fall of a mass M on an implant,
- The prosthesis acceptance will be admitted in the basis of an energy at the impact time called "energy threshold"
- The implant should not break after the fall of the mass with a height corresponding to this energy threshold.

In 1995, a standardized test was performed by the National Testing Laboratory (LNE) [310] in accordance with the experimental standard S 94-350 (1994) on 6 implants of small volume (3 high profiles (90 cc) and 3 low profiles (85 cc) and 6 implants of medium volume (3 high profiles (210cc) and 3 low profiles (205cc)). A 4.4 kg mass was dropped from a falling height defined by the Standard according to the implant weight. None of the 12 implants broke.

3.3.4.- Gas permeability measurement: (see [320])

A permeability test with a constant volume was performed on a smooth envelope and on a textured envelope of breast implants according to the technical Stantdard NF T 46-037 (1979).
The lack of uniformity of the specimen thickness lead to an incertitude over the accuracy of the permeability coefficient of the tested elastomer. However, this rate is estimated at 10^{-15} m^2 $Pa^{-1}s^{-1}$.
The smooth implant membranes are more waterproof than the textured ones.

3.6 – IDENTIFICATION :

3.6.1 – Product identification :

The identification mark makes the product management during the packaging, storage and exit from the warehouse operations easier

The product is directly identified on the closure patch thanks to the following information :

- Company's name : PIP,
- Lot n°,
- Serial n°,
- Volume.

The mark and its position on the closure patch are defined in the definition drawing : P10IM00Z001110.

a) Lot n° composition

Chronological n°	*Last two digits of the current year*
123	00

This example (Lot n° : 12300) represents the 123rd lot of year 2000.

b) Serial number composition

All the items in the same lot have to be separately identifiable. During the manufacture, the implants are given a three digit sequential serial n°, allowing to distinguish each item.
The serial n° 001 represents the 1st lot item.

3.6.2 – Referencing and codification :

The referencing and article-codification system for PIP products helps assuring the coherence and homogeneity of these product designation.

The referencing system eases a simple and mnemonic identification of PIP products for PIP personnel, commercial attachés and customers.

The product reference should bear :

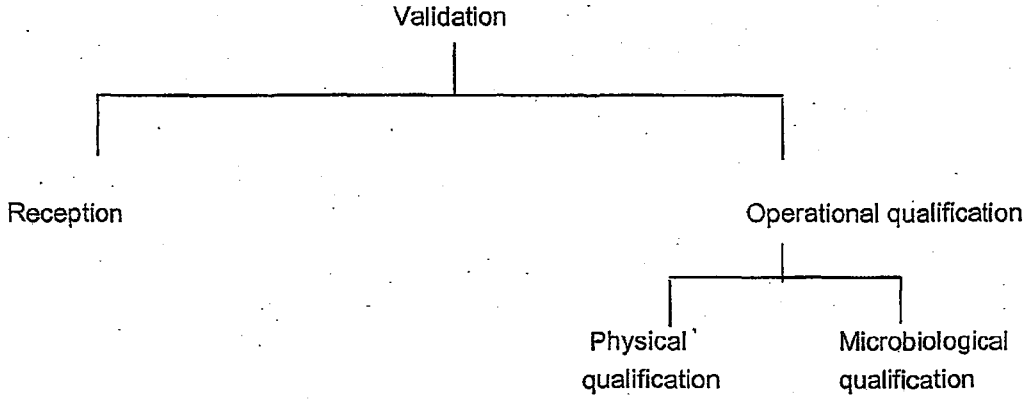
- An evocation of the product specific designation
- A qualification of the surface state (optional and that can be replaced by any information aimed at specifying the product nature)
- The profile nature (optional and that can be replaced by any information aimed at specifying the product nature)
- An indication on the product dimensions.

b) Definition of the UCC-EAN 128 bar code

This sytem is described in the procedure for referencing products [741].

										Data 3	Serial #
									ID 3	(21)	Data identifier 2 : Serial #
								Data 2	Lot #		
							ID 2	(10)			
						Data 1	Date of expiry				
					ID 1	(17)					
				Key	Calculated according to previous values						
			CIF	Article sequential #							
		CNUF	660312 (PIP) 716186 (RMI)								
	Country prefix	3 (France) 8 (RMI)									
Extension character	0										
Start	(01)										
Value											

Detail	Data identifier: EAN article code	France	CNUF attributed by Gencod to PIP	Article sequential #	Key for the control of 13 the 1st digits	Data identifier : Date of expiry	AAMMJJ	Data identifier: Lot #	Lot #	Data identifier 2 : Serial #	Serial #
Number of digits	2	1	6	5	1	2	6	2	5	2	3



• ***Reception***

The reception, which consists in showing that the equipment conforms to its specifications is performed when the cell is empty.

The following elements are determined :

- The physical operational factors of the sterilization process
- The air circulation profile in the cell
- The correct profile of the empty zone :
  - temperature profile of the internal surfaces and of the empty cell space (35 sensors)
  - relative humidity profile (12 sensors).

The number of sensors is used depending on the sterilization chamber volume in compliance with the NF EN 550 (1994) Standard.

These sensors are located where they can represent the maximum differences of relative humidity and temperature so as to identify the hot and cold points.

All the equipment used during the validation as well as the instruments for recording the parameters were previously calibrated.

• ***Operational qualification***

The microbiological operational qualification is performed thanks to the half-cycle method which helps determine the exposure time to Ethylene Oxide so that there is no survivor, the other parameters of the process remain constant, except the gas contact time.
Two additional experiments will be performed so as to confirm that the minimum time is adequate.

Considering a routine sterilization cycle in which a gas contact is 18 hours, the half cycle will have allowed to define a value of 9 hours as gas contact time, which is enough to find no survivor.

A short time cycle allowing to retrieve survivors will be performed so as to show that the retrieval technique is adequate. The gas contact time for the latter will be 10 minutes.

The contaminated products are spread out homogeneously in the sterilization load taking into account the points in which the sterilization conditions are harder to perform.
A buffer load is used for each cycle, so as to get a correctly loaded packaging zone.

Thirty five temperature sensors and twelve relative humidity sensors are used so as to obtain a whole profile of the sterilization load. The sensors are spread out homogeneously on the load.

The operational qualification occurred in two steps :

Microbiological part : The contaminated products were homogeneously spread out within the MXM buffer load, representative of the most loaded cycles; then sample analysis.

Physical part : Determination of the load whole profile by an homogeneous spread out of the captors within the MXM buffer load, representative of the most loaded cycles.

⇨ **HALF-CYLES**

Three half-cycles are performed under the following progress conditions :

Pre-packaging : One hour of heating with mixed ventilation to reach 45 °C -1°C +2°C (adjustment temperature) at the end of the pre-packaging operation. Humidification during the same period to reach a value of ≥40% at the end of the pre-packaging operation. This step is performed under atmospheric pressure.

Injection preparatory phase : Two vacuums at -450mbar +/- 50mbar with 5 security steps to avoid the packaging breaking out, followed for each one by an injection of azote until the atmospheric pressure.

Put under vacuum : Vacuum at -450mbar -/+ 50mbar with 5 security steps.

[825] SQ1/02 SYN 105 : Flow chart of subprocess "Controlling the quality of water"

[826] SQ1/02 SYN 104 : Flow chart of subprocess "Controlling the quality of air"

[827] SQ1/02 SYN 103 : Flow chart of subprocess "Controlling contamination linked to noxious substances"

[840] SQ1/13 PCD 001: Procedure for treating non-conformities

[860] SQ1/14 PCD 002 : Procedure for managing complaints

[861] SQ1/14 PCD 004 : Procedure for the recall of commercialized materials

[879] SQ1/15 FOR 607 : EEC Product information for the attention of surgeons - IMGHC

[880] SQ1/02 SYN 106 : Flow chart of the subprocess "Dispatch"

[881] SQ1/15 FOR 608 : CEE – Product information for the attention of patients - IMGHC

[882] SQ1/15 FOR 704 : CEE – Implantation slip / Operation slip

[883] SQ1/15 FOR 700 : CEE – Follow-up slip

[884] SQ1/15 FOR 705 : CEE – Implant bearer's identity card

[960] SQ1/19 PCD 001 : Procedure related to the receipt, storage and delivery by distributors and agents of products manufactured by P.I.P.