DAC® an anti-bacterial bio-absorbible hydrogel

DAC® is a hydrogel barrier to infection containing hyaluronic and polylactic acid. DAC® confers protection against bacterial colonisation and biofilm formation. DAC® has applications in:

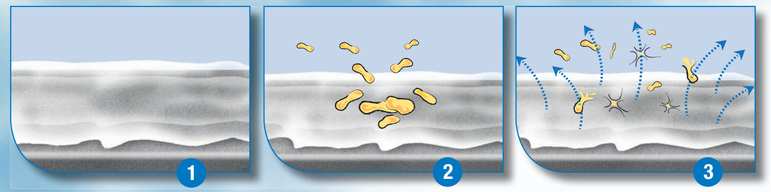
- **Prevention of prosthetic implant infection**
- **Prevention of osteo-syntetic devices infection**

DAC® hydrogel can be combined with an antimicrobial agent which may further enhance prevention of bacterial colonisation and inhibition of biofilm formation.

DAC® is supplied as a powder requiring reconstitution prior to use. In addition to the barrier effect described above, combination with an antibiotic such as 2% vancomycin introduces a complementary antimicrobial activity. The hydrogel disaggregates within approximately 72 hours releasing the antibiotic. Early disaggregation of the hydrogel avoids inhibition of implant osseointegration (17; 18).

DAC® effect

The combination of DAC® hydrogel with an antibiotic agent alters the dynamics of the 'race to the surface'. The hydrogel barrier acts as a physical deterrent to bacterial adherence. The hydrogel then disaggregates releasing the antibiotic at the target site of action. These two effects combine to inhibit the early stages of implant colonisation by bacteria.



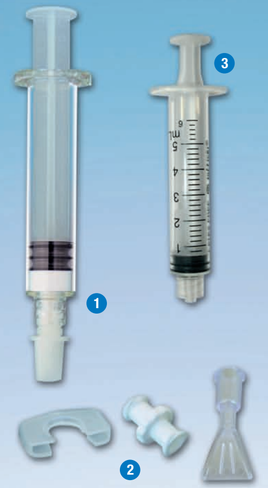
N.B. In these images the grey area represents the implant surface.

The protection achieved with DAC® hydrogel may be described in three stages:

1- Immediately before implantation. The implant surface is spread with DAC® hydrogel combined with an antibiotic.

2- Immediately after implantation. Bacteria attempt to colonise the surface of the implant but adherence is inhibited by the presence of the DAC® hydrogel.

3- Minutes after implantation. DAC® hydrogel begins to disaggregate releasing the antibiotic at the target site.



Kit DAC®

(Codice DAC003000)

is composed of:

COMPONENT	DESCRIPTION
1. 1x syringe prefilled with DAC® powder in a double sterile envelope (CodeDAC3000).	5ml sterile syringe with luer-lock connector containing 300mg DAC® hydrogel as a sterile powder for reconstitution. Contains hyaluronic acid and polylactic acid.
2. 1x accessories set in a double sterile envelope (Code CDM3000).	Sterile accessories set comprising 1x connector, 1x backstop, 1x spreader.
3. 1x 5ml syringe in a sterile blister pack.	Graduated 5ml syringe with luer-lock connector.

The syringe and accessories are packed in double sterile packaging to facilitate use within a sterile operative field.

Bibliography:

1. Australian National Joint Register 2012 Report.
2. Swedish National Joint Register 2012 Report.
3. K. Bozic and Others. The Epidemiology of Revision Total Hip Arthroplasty in the United States. JBJS (Am), 2009; 91(1): 128-133.
4. K. Bosic and Others. The Epidemiology of Revision Total Knee Arthroplasty in the United States. CORR. 2010 Jan; 468 (1): 45-51.
5. P. Bohm, T. Holy. Is there a future for hinged prostheses in primary total knee arthroplasty? A 20-years survivorship analysis of the Blauth Prosthesis. JBJS (Br) VOL. 80-B, NO. 2, March 1998
6. S.M Madely and Others. Charnley total hip arthroplasty with use of improved techniques of cementing. The results after a minimum of fifteen years of follow-up. JBJS (Am) 1997 Jan; 79 (1): 53-64
7. E Salvati and Others. Infection rates after 3175 total hip and total knee replacements performed with and without a horizontal unidirectional filtered air-flow system. JBJS (Am). 1982 Apr; 64 (4): 525-35.
8. Tim Bongartz and Others. Incidence and Risk Factors of Prosthetic Joint Infection After Total Hip or Knee Replacement in Patients With Rheumatoid Arthritis. Arthritis & Rheumatism (Arthritis Care & Research) Vol. 59, No. 12, December 15, 2008, pp 1713-1720.
9. Richard Iorio and Others. Diabetes Mellitus, Hemoglobin A1C, and the Incidence of Total Joint Arthroplasty Infection. The Journal of Arthroplasty 2012 May; 27(5):726-9.
10. Gino M.M.J. Kerkhoffs and Others. The Influence of Obesity on the Complication Rate and Outcome of Total Knee Arthroplasty: A Meta-Analysis and Systematic Literature Review. The Journal of Bone & Joint Surgery, Oct 2012, Volume 94, Issue 20.
11. M.V. Ragni and Others. Postoperative infection following orthopaedic surgery in human immunodeficiency virus-infected hemophiliacs with CD4 counts < or = 200/mm3. The Journal of Arthoplasty 1995 Dec; 10 (6): 716-21.
12. N. Davis and others. Intraoperative bacterial contamination in operations for joint replacement. JBJS (Br) 1999 Sep;81(5):886-9.
13. G.W. Costeron. How Bacteria Stick. Sci Am. 238:86-95, 1978.
14. A.G. Gristina; G.W. Costeron. Bacterial adherence to biomaterials and tissue. The significance of its role in clinical sepsis. JBJS (Am) 1985 Feb;67(2):264-73.
15. A.G. Gristina and Others. Biomaterial-Centered Infection: Microbial Adhesion vs. Tissue Integration. Science 1987:237; 1588
16. A.G. Gristina and Others. Infections from biomaterials and implants: a race for the surface. Med Prog Technol. 1988-1989; 14 (3-4): 205-24.
17. C. L. Romanò, G. Giammona, R. Giardino and E. Meani. Atibiotic-Loaded Resorbable Hydrogel Coating For Infection Prophylaxis of Orthopaedic Implants. Preliminary Studies. J Bone Joint Surg Br 2011 vol. 93-B no. SUPP III 337-338.
18. Rapporto di Prova n° 14/12 del 23/10/2012_ prova di valutazione degli effetti locali all'iniezione nel canale endomidollare femorale dell' idrogelo "DAC" - UNI EN ISO 10993-6_IOR, Bologna. Unpublished Internal Document.
19. C.L.Romanò. A or B Host – Does it matter? Podium presentation 10th Efort meeting, 3-6 June 2009, Vienna, Austria.
20. C.L. Romanò, L. Drago, M. Haensch, J. Stuick, L. Van Mellaert, K. Mallzos, M. Fini, E. Meani. Prevention of implant-related infections using a resorbable antibacterial hydrogel coating: in vitro and in vivo study. 32nd Annual Meeting European Bone and Joint Infection Society. 12-14 September 2013, Prague.
21. C.L. Romanò, L. Drago, M. Haensch, J. Stuick, L. Van Mellaert, K Mallzos, M. FINI, E. Meani. Disposable anti-bacterial coating for prevention of implant-related infections in orthopaedics 34th Sicot Orthopaedic World Congress, 17-19 October 2013, Hyderabad, India.
22. Romanò, L. Drago, M. Haensch, J. Stuick, L. Van Mellaert, K Mallzos, M. FINI, E. Meani. Antibacterial resorbable coating of orthopaedic implants: an in vitro and in vivo study. CORS meeting, 13-16 October, Venice, Italy.

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DAC®

THE HYDROGEL BARRIER TO INFECTION

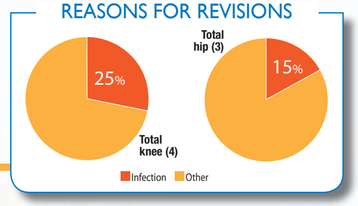
NOVAGENIT®

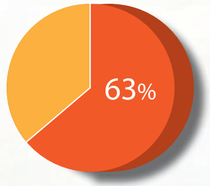
The burden of infections

Infection is the most common cause for failure of primary total knee implants, and the third most common cause of failure for primary total hip implants (1;2;3;4). Infection is reported as occurring in 0.5% to 4% of such cases (5;6;7).

Risk factors include (19):

- Autoimmune disease e.g. Rheumatoid arthritis (8)
- Diabetes (9)
- Obesity (10)
- Immunosuppression (11)





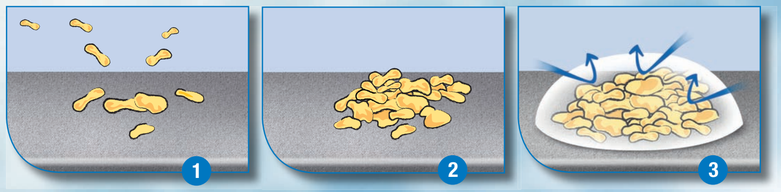
Percentage of surgical fields showing evidence of bacterial contamination.

Intraoperative bacterial contamination

In spite of modern aseptic procedure, the risk of peri-operative bacterial contamination cannot be completely eliminated. One study showed that 63% of surgical fields show evidence of bacterial contamination. (12)

The mechanism of infection

The race to the surface. Contamination at the time of surgery can lead to colonisation of the implant surface with bacteria. If unchecked, these bacteria will begin to cooperate and form biofilm. This may lead to the formation of a bacterial colony which is resistant to attack by antimicrobial agents and to the patient's immune system. (13;14;15;16)



N.B. In the above images the grey area represents the surface of the implant

The sequelae of bacterial contamination following implantation of a surgical implant can be described in three stages:

1- Immediately. Bacteria begin to adhere to the surface of the implant.

2- Within minutes. These bacteria begin to multiply and further attach themselves to the surface of the implant.

3- Within 24 hours. Adherent bacteria begin to interact and cooperate, beginning the processes which lead to biofilm production.

DAC® kit preparation

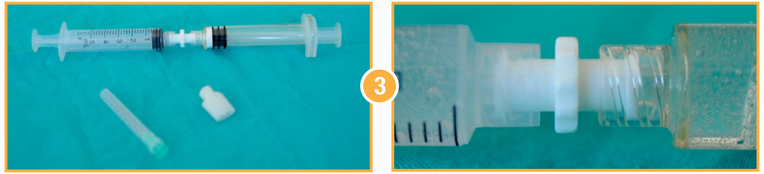
Preparation should be carried out within a sterile field

The below described procedure must be performed within a sterile field

BEFORE STARTING THIS PROCEDURE THE ANTIBIOTIC SOLUTION (NOT INCLUDED IN THE KIT) SHOULD BE PREPARED ACCORDING TO AN APPROPRIATE PROTOCOL TO A TOTAL VOLUME OF 5 MLS.

Open the blister pack containing the empty graduated syringe and draw up the 5ml of prepared antibiotic solution. Remove the needle and replace it with the luer-lock connector.

Open the syringe containing the DAC® powder. Slightly retract the syringe piston (0.5cm) and gently tap the syringe to loosen the powder, making reconstitution easier.
The backstop (extension flange) may be attached to the syringe for easier handling if required.



Remove the cap from the syringe containing the DAC® powder and connect it to the syringe containing the antibiotic solution.

Hold the two syringes vertically with the syringe containing the antibiotic positioned above the syringe containing the DAC® (this orientation enables a more homogeneous hydrogel formation). Slowly transfer the antibiotic solution into the syringe containing the DAC® powder, by gently pressing on the piston of the syringe containing the antibiotic solution whilst withdrawing the piston on the syringe containing the DAC® powder. Once the antibiotic solution has been added to the powder the two syringes may be held horizontally. Transfer gently from one syringe to the other (around 15 times) until a clear, homogeneous hydrogel has formed. Leave to rest in the syringe for 5-10 minutes before detaching the connector and the empty graduated syringe. The hydrogel is now ready for use.

DAC HYDROGEL APPLICATION

ATTACH THE SPREADER NOZZLE TO THE SYRINGE CONTAINING THE DAC® HYDROGEL AND APPLY EVENLY TO THE SURFACE OF THE IMPLANT.

DAC® animal validation studies

The efficacy of the DAC® has been validated through a series of in vitro and in vivo anumal studies (20; 21; 22) (*).

A study performed by the Department of Experimental Surgery of the Rizzoli Orthopaedic Institute, Bologna validated the efficacy of the DAC® hydrogel using an animal model.

A group of adult rabbits received a femoral intra-medullary (IM) nail covered with DAC® reconstructed with a 2% solution of Vancomycin. That group, together with a control group, also operated with an IM nail, received an IM injection of 0,2 x 10^6 CFU (colony forming units) of methicillin resistant staphylococcus aureus (MRSA).

Both groups received a pre and post-operative systemic antibiotic therapy with 2% Vancomycin.

Tab.1

	Reduction in Bacterial load (%)		
	Medullary canal	Bone	Nail
DAC® with Vancomycin	99,95	99,95	99,96

Bacterial load percentage reduction vs. controls obtained with DAC® reconstructed with 2% Vancomycin solution.

Tab.2

	CFU	
	Emo+	Emo-
Control group	>1,00x10^7	>1,00x10^7
Hydrogel DAC® with Vancomycin	0	0

Systemic bacterial load 7 days post-op.
Emo+: Blood culture under aerobic conditions
Emo-: Blood culture under anaerobic conditions

7 days post-surgery , bone, medullary canal (Tampon) and nail bacterial load was measured, and a blood culture was made for both groups.

Results

- The use of DAC® reconstructed with a 2% solution of Vancomycin led to a decrease in bacterial load of 99.95% in the bone, nail and medullary canal treated animals vs. the controls. (Tab.1)
- None of the animals treated with hydrogen DAC® with 2% Vancomycin developed any systemic infection, while all the controls showed signs of it in spite of the systemic antibiotic coverage. (Tab. 2)

Conclusions

The use of the hydrogel DAC® reconstructed with a solution of 2% Vancomycin showed to be effective reducing the bacterial load of 99.95% and preventing the development of a systemic infection even in presence of high bacterial contaminations.

(*) Data available on file at Novagenit srl