



# APV Focus Group Drug Delivery

Combining Science & Technology to Create Advanced Drug Delivery Systems

INTERNATIONAL ASSOCIATION FOR PHARMACEUTICAL TECHNOLOGY

NEWSLETTER | ISSUE 2/2008

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## DRUG DELIVERY EVENTS

Provided by Christoph Blümer

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### APV course: Poorly Water Soluble Drugs: Successful Formulation Approaches

Basle (CH), November, 04<sup>th</sup> - 05<sup>th</sup> 2008

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### Drug Formulation Technologies

London (UK), November, 04<sup>th</sup> - 05<sup>th</sup> 2008

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### Current Trends in Dosage Form Development and Biologics Formulation

San Diego, California (US), January 15<sup>th</sup> - 16<sup>th</sup> 2009

[Details](#)

### 14th International Symposium on Recent Advances in Drug Delivery Systems

Salt Lake City, Utah (US), February, 15<sup>th</sup> - 18<sup>th</sup> 2009

[Details](#)

***[Suggest a meeting to be announced!](#)***

## DRUG DELIVERY PRODUCTS

Provided by Dr. Louise Rosenmayr-Templeton

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### CIMZIA™ INJECTION (UCB Pharma)

The Spring of 2008 brought both good and bad news for UCB Pharma, with respect to its PEGylated anti-Tumor Necrosis Factor (anti-TNF- $\alpha$ ) product, Cimzia™. In April the injection, containing 200 mg certolizumab pegol, received approval from the FDA for the treatment of moderate to severe active Crohn's disease in patients who have not responded to conventional therapies. However, one month earlier the EMEA's Committee for Medicinal Products for Human Use had issued a final negative opinion on the product. The reasons for this decision were general safety concerns regarding the risk-benefit ratio of treatment with Cimzia™ in Crohn's (EMEA Press Release 20.03.2008). The product is already marketed for this indication in Switzerland and the company has filed a submission for its use in the treatment of rheumatoid arthritis with the FDA, with an European filing expected soon.

Certolizumab is a humanised Fab' fragment whose circulatory half-life has been extended by attachment to 40 kDa (approx.) polyethylene glycol. The Fab' fragment can be expressed in *E coli*, and therefore the product is likely to have lower production costs than if it contained a whole antibody. Cimzia™ is administered once every 4 weeks after an initial series of 3 injections in the first month. In addition to active, the preservative-free formulation contains sucrose, lactic acid and polysorbate, and is supplied as a lyophilized powder for reconstitution with water for injection.

Further Information: <http://www.ucb-group.com/>

### LUVOX® CR CAPSULES (Solvay Pharmaceuticals/Jazz Pharmaceuticals)

Solvay Pharmaceuticals received approval from the FDA in February 2008 for a controlled release formulation of their Luvox® product containing Fluvoxamine Maleate (100 mg and 150 mg) for the treatment of obsessive compulsive disorder and social anxiety disorder. The formulation is based on Elan's proprietary SODAS® (Spheroidal Oral Drug Absorption System) technology. It contains drug loaded sugar spheres which have been coated with a controlled release polymer (ammonio methacrylate copolymer type B). By combining beads with different release rates, the dissolution profile of the formulation can be altered to allow once daily dosing.

Solvay Pharmaceuticals licensed the rights to market Luvox® CR and Luvox® in the US to Jazz Pharmaceuticals in 2007 while retaining them in other territories. The license agreement requires Jazz Pharmaceuticals to pay Solvay Pharmaceuticals \$20 million as a result of the approval of Luvox® CR. The ex-factory sales for Luvox® CR in the US are estimated to be worth \$40 to \$60 million in 2008.

Further Information: <http://www.solvay.com/> and <http://www.jazzpharmaceuticals.com/>

### PRISTIQ™ EXTENDED RELEASE TABLETS (Wyeth Pharmaceuticals)

The FDA approved Wyeth's selective serotonin and noradrenaline uptake inhibitor, Pristiq™, for major depressive disorder in Feb 2008. The tablets contain 50mg or 100mg Desvenlafaxine (base) as the succinate salt in an extended release formulation containing hypromellose. Desvenlafaxine is the major metabolite of Venlafaxine, the active compound in Wyeth's highly successful Effexor® products. Since Desvenlafaxine, unlike Venlafaxine, does not require processing through the CYP2D6 metabolic pathway, it has the advantage that it will not interfere with the metabolism of other drugs processed by this enzyme.

Effexor®, which had worldwide sales of almost \$3800 million in 2007, is coming off patent in 2010 and Wyeth hopes to reduce the impact of generic competition on its anti-depressant portfolio by introduction of the Desvenlafaxine formulation. Analysts are currently projecting that Pristiq™ will achieve annual sales of \$900 million by 2012.

Further Information: <http://www.wyeth.com/>

## DRUG DELIVERY COMPANIES

Provided by Gerben Moolhuizen

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### NOVOSOM AG (Halle/Saale, Germany)

#### Fact sheet:

Founded:	1999
Location:	Halle/Saale, Germany
Ownership:	Private (main investor: IBG Beteiligungsgesellschaft mbH, Mittelständische Beteiligungsgesellschaft, undisclosed private Investors)
Employees:	20
Key technology:	<p><b>SMARTICLES® - charge reversible liposomes for RNAi Therapeutics.</b></p> <p>Smarticles are a new class of liposomes: fully charge-reversible particles. They are negatively charged under physiological conditions. However, as the pH drops down to 5 or 4 during endocytosis (the process whereby cell absorbs the liposome from the outside by engulfing it with its cell membrane), the vector surface becomes neutral and eventually positively charged. This unique property offers the advantage of stable and aggregate-free travel within the bloodstream. The acidification from endocytosis switches the charge of Smarticles, leading to membrane fusion and the escape of the cargo from the endosome. This provides a known and controllable mechanism for endosomal escape, a required feature for siRNA delivery. The company has siRNA delivery data in liver, inflammation and oncology.</p>
Products:	<p>Novosom's CD40 antagonist is an antisense oligonucleotide targeting CD40 mRNA combined with the Smarticles technology. CD40 is a validated target for both inflammatory diseases and B-cell cancers; development planned for indications such as Crohn's disease, transplant, rheumatoid arthritis, cancer and multiple sclerosis. Current status: Commencement of IND enabling studies</p> <p>Second lead candidate: Micromethason, a micro-dose formulation of dexamethasone phosphate for the treatment of inflammation. Status: pre-clinical proof-of-concept demonstrated.</p>
Development status:	<p><b>TECHNOLOGY</b></p> <p>Smarticles - have completed IND enabling studies including toxicology in 2 species, including primates. Additionally, Smarticles have been upscaled and produced under GMP conditions. The technology achieved a successful IND in Oncology in March 2008 "IND Filing of Partner ProNAi Therapeutics".</p> <p><b>PRODUCT</b></p> <p>CD40 Antagonist - Novosom has completed several indicative studies that establish the in vivo safety of the formulation and demonstrated superior efficacy to TNF-a antibodies in a variety of models of inflammatory diseases (Crohn's disease, transplant and rheumatoid arthritis). Initial</p>

	GLP toxicity studies have shown very high tolerability of the carrier. In rodents, Smarticles have shown targeted transfection in liver, spleen and lungs as well as small molecule delivery to sites of inflammation, all via the systemic route. Local applications have shown antisense delivery in inflammatory bowel diseases and in a transplant model. Rheumatoid arthritis data created with antisense provided by Isis Pharmaceuticals has been presented in numerous conferences.
Partnerships:	<b>Boehringer-Ingelheim:</b> RNAi delivery with for targets in the liver and lung. <b>ProNAI Therapeutics, Inc.:</b> Delivery of a new class of nucleic-acid drugs based on DNA interference (DNAi™) in oncology. IND granted by FDA; Smarticles-encapsulated DNAi product candidate about to enter the clinic. <b>Isis Pharmaceuticals, Inc.:</b> In-licensing of CD40 antisense antagonist <b>Various ongoing collaborations</b> with US, EU and Asian pharmaceutical and biotech companies involving RNAi, Antisense and DNA therapeutics
Website:	<a href="http://www.novosom.com">http://www.novosom.com</a>
Contact:	Elias Papatheodorou – CEO Weinbergweg 22 D-06120 Halle/Saale (Germany) Phone: +49 (0) 345 55 59 836 Fax: +49 (0) 345 55 59 846 e-mail: <a href="mailto:info@novosom.com">info@novosom.com</a>

## DRUG DELIVERY TERMINOLOGY

Provided by Dr. Karsten Cremer

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### ABSORPTION WINDOW

***A site or region in the gastrointestinal tract where a particular drug substance is preferentially absorbed.***

[Write a comment on this definition](#)

Most drug substances used for oral administration are absorbed by passive diffusion. Due to its high specific surface area, the proximal regions of the small intestine, i.e. duodenum and jejunum, are usually those from which such drug substances are relatively best absorbed; in practice, the duodenum may be less relevant because of its short length (resulting in a short duodenal transit time). In any case, absorption from the ileum is often slower, and many compounds are rather poorly absorbed from the colon. Drug substances whose absorption from the upper small intestine, but not from the more distal segments is acceptable are said to exhibit an "absorption window".

It is important to note that some compounds are sufficiently permeable to be absorbed from all segments of the small bowel and even the ascending colon, but are subject to an intestinal first-pass effect (see below) which is often most pronounced in the proximal small intestine. These compounds may have a greater bioavailability when delivered to the distal small bowel or ascending colon. In this case, the term "absorption window" would not be appropriate as the "window" effect is not related to absorption itself, but to subsequent processes. Instead, the broader term "bioavailability window" should be used.

German: [Absorptionsfenster](#)

French: [Provide a translation](#)

Spanish: [Provide a translation](#)

### FIRST-PASS EFFECT

***The elimination of a non-negligible fraction of an absorbed amount of a drug substance before it reaches the systemic blood circulation.*** [Write a comment on this definition](#)

According to the IUPAC Gold Book, a first-pass effect is "Biotransformation and, in some cases, elimination of a substance in the liver after absorption from the intestine and before it reaches the systemic circulation." This definition is somewhat too narrow since metabolic or non-metabolic elimination of the compound can, and often does, occur in the intestinal mucosa rather than in the liver only. An example of a drug substance exhibiting an intestinal first-pass effect is midazolam, which undergoes substantial metabolic degradation as a substrate of intestinal cytochrome P450-3A4 (CYP3A4); grapefruit juice, which reduces the intestinal CYP3A4 activity, remarkably increases the bioavailability of this drug.

German: n/a

French: [Provide a translation](#)

Spanish: [Provide a translation](#)

[Suggest a term to be defined](#)  
[Suggest a definition](#)

**ELIAS FATTAL** is professor of Pharmaceutical Technology at the University of Paris-X in Châtenay-Malabry, France, and has been President of the Association de Pharmacie Galénique Industrielle (APGI) since 2003. He received his Pharmacy Degree (1983), and Ph.D. (1990) from the University of Paris-XI. After visiting the Department of Biopharmaceutical Sciences, University of California, San Francisco as a post-doctoral student for Frank Szoka (1990-1991), he became associate Professor (1992) and full Professor at the school of pharmacy of the University of Paris-XI (2000). Elias Fattal leads the research group "Drug targeting and delivery of poorly stable active drugs" in the CNRS research unit, UMR CNRS 8612. He is also vice-chair of this department.



His research activity deals with the design of nano- and microtechnologies for the delivery of peptides/proteins and nucleic acids. His special expertise deals with oral administration of proteins and vaccines and the design of delivery systems for antisense oligonucleotides. In recent years his research has included the ocular delivery of nucleic acids and the use of cyclodextrins as absorption enhancing agents.

He is the author and co-author of around 150 publications and book chapters and 11 patents. In 1999, he received the Colloidal Drug Carrier Award (at the 5th Expert meeting on Colloidal Drug Carriers, Berlin, Germany) and the Pharmaceutical Sciences World Congress (PSWC) Research Achievement Award in 2007. He was also elected honorary member of the APV (*Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik*) in 2005. He is also corresponding member of the National Academy of Pharmacy. Elias Fattal is the co-editor of the journal of Drug Delivery Science and Technology, the European Editor of the Journal of Biomedical Nanotechnology. He serves on the editorial board of several pharmaceutical journals (Journal of Pharmaceutical Sciences, European Journal of Pharmaceutical Sciences, American Journal of Drug Delivery, and Expert Opinion on Drug Delivery, The Open Biomedical Engineering Journal) and nanotechnology dedicated journals (NanoBiotechnology, International Journal of Nanomedicine).

## FEATURED ARTICLE

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### INTRA-ARTICULAR APPLICATION OF DRUGS – STATUS QUO AND PERSPECTIVES

By Sebastian Rudolf and Wolfgang Friess

Department of Pharmacy, Pharmaceutical Technology and Biopharmaceutics, Ludwig Maximilian University, Munich

#### Anatomy and physiology of the knee joint [1]

Joints are essential for enabling motility and stability. They are classified into synarthroses, amphiarthroses and diarthroses (synovial joints), whereas the latter ones are most frequently affected by osteoarthritis (OA) or rheumatoid arthritis (RA). The typical construction of a synovial joint is exemplified by the knee joint in figure 1. The two bones are held together by a capsule and several ligaments. The inner surface of the capsule is lined out by the synovium, while the space between the hyaline cartilage, which completely covers the surface of the bone, is filled out with a clear and viscous liquid, called synovial fluid (SF), containing electrolytes, glucose, hyaluronic acid (HA) and proteins. The SF's functions are the nutrition of the blood vessel-free cartilage and the prevention of friction between the surfaces of the articular cartilage during movement, using the long glycosaminoglycan HA as lubricant. HA is produced by the synovium and continuously excreted into the joint cavity. But the synovium, forming a complex system of capillaries and lymphatics, furthermore has other important functions, as for example the clearance of unwanted particles/substances and the supply with ultrafiltrate from the plasma.

#### Synovial fluid (SF)

The composition of SF in the knee joint is very similar to that of plasma with one exception: the presence of considerable amounts of HA. Table 1 compares some SF parameters of healthy humans with those of OA and RA patients.

In OA and RA patients not only a significant increase in total SF volume and SF temperature but also a simultaneous decrease in HA concentration and HA molecular weight can be detected, which leads to an increase in SF pressure and to a decrease in viscosity, both resulting in pain aggravation. Additionally, in RA patients pH is shifted to a lower value which is not really surprising, since RA is recognized as an inflammatory disease. This decrease in pH is responsible for the accumulation of orally taken NSAIDs in SF of RA patients [4].

SF undergoes continuous turnover by trans-synovial flow into synovial lymph vessels, wherefrom it is mainly transported into circulation by the vena cava superior [1,5]. This mechanism seems to be the most important elimination pathway for high-molecular substances located in SF. Complete replacement of water and protein is observed within a

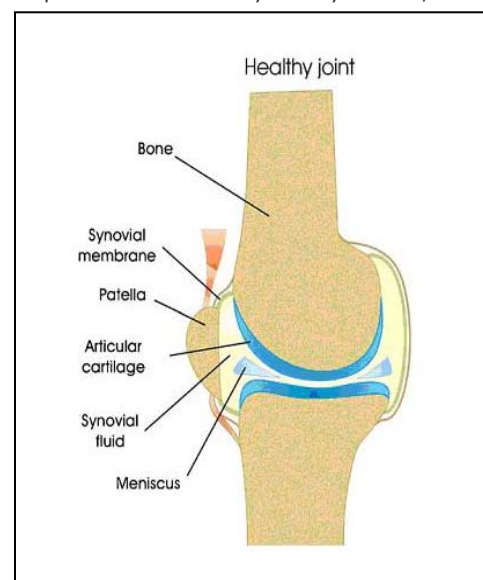


Figure 1:  
Construction of a healthy knee joint [1]

period of approximately 2 hours (e.g. clearance of albumin: 0.04 ml/min [1,5]). It is not only very interesting, but also rather curious that elimination via lymph drainage seems to be size-independent [2,5]. Brown, Cooper and Bluestone found that plasma albumin (66 kDa) and IgM (~900 kDa) leave SF at the same rate [6]. In contrast, clearance of the polyanion HA is considered to be slower, with an estimated turnover in joints of 0.5-2.0 days [7,8]. Unfortunately, RA patients show a much greater protein (albumin: 0.07 ml/min [5]) and drug clearance, while in OA patients such accelerated elimination has not been reported yet [1,5].

**Table 1: Characteristics of human SF under normal, OA and RA conditions [1,2,3]**

	Normal	OA	RA
<b>SF volume (knee)</b>	0.5-2.0 ml	> 3.5 ml	> 3.5 ml (100ml)
<b>Osmolarity</b>	296 mOsm/l	296 mOsm/l	296 mOsm/l
<b>Viscosity</b>	> 300 mPas (thixotrop)	< 300 mPas	1-10 mPas
<b>pH</b>	7.4	7.4	6.7-7.4
<b>Total protein conc.</b>	10-30 g/l	15-35 g/l	> 40 g/l
<b>HA conc.</b>	3.5 g/l	< 2.2 g/l	< 2.2 g/l
<b>MW of HA</b>	4-10 MDa	1-2 MDa	1-2 MDa
<b>SF temperature</b>	~34°C	>36°C	>36°C

### Intra-articular (IA) application [1]

Intra-articular (IA) application is defined as an administration of a small amount of substance (approximately 2-3 ml) into a joint cavity generally by using a needle. Hence it is a special form of parenteral application.

The affected site has to be well disinfected prior to injection, in order to prevent infections. The placement of the needle should be only performed by experienced physicians, as there exist some studies reporting that almost a third of all conducted knee injections are inaccurate (para-articular injection). Aspiration of SF at the time of injection is recommended for several reasons: First, it prevents the tissue cylinder, formed when the syringe penetrates the tissue, from entering the joint space, second, it reduces the pressure within the joint space leading often to an improvement of pain, and third, it allows the removal of SF for laboratory diagnostics. The injection should be administered slowly and a 24-h post-injection rest is recommended to increase the residence time of the injected substance [9].

#### Advantages of IA injection:

- *Drug targeting: possibility of reaching high drug concentrations at the side of action by applying only low amounts of drug, resulting in a reduction of systemic side effects and treatment expenses.*
- *Feasibility of applying drugs with low oral bioavailability (e.g. drugs of low solubility, proteins).*

#### Disadvantages of IA injection:

- *Discomfort and pain for patient.*
- *Increased risk of serious joint infections, sepsis or cartilage damage.*
- *Therefore only a limited number of 3-4 IA injections per year is recommended.*  
→ *Enormously rapid clearance of IA injected drugs (small molecules and proteins).*

The limited number of recommended IA injections and the short retention time of IA injected drugs require the development of sustained release formulations for IA use.

Further requirements for IA applied drugs are sterility, freedom of pyrogens, freedom of particles, isotony (290-420 mOsm/l) and pH of 5-9.

### Current products for IA use [1,2,10,11]

Currently, there are two major substance classes on the German market that are approved for IA application: glucocorticoids (dexamethasone, betamethasone, triamcinolone) and sodium hyaluronate/hyaluronic acid (HA). Table 2 lists some products from the German "Rote Liste".

**Table 2: Glucocorticoids and HA containing drugs for IA use (selection)**

Substance class	Product example
Glucocorticoids	Dexabene <sup>®</sup> , Fortecortin <sup>®</sup> Inject (solutions) Celestan <sup>®</sup> Depot, Diprosone <sup>®</sup> , Volon <sup>®</sup> A (crystal suspensions) Lipotalon <sup>®</sup> (liposome emulsion)
Sodium hyaluronate/Hyaluronic acid	Viscoseal <sup>®</sup> (0.5% HA) Hyalart <sup>®</sup> (MW ~ 1 MDa; 1.0% HA) Synvisc <sup>®</sup> (= Hylan G-F20 <sup>1</sup> , cross-linked, MW = 6-7 MDa; 1.0% HA) Hyalubrix <sup>®</sup> (1.5% HA) Durolane <sup>®</sup> (biosynthetically produced, twice stabilized)

<sup>1</sup> Hyalans (hyaluronan derivatives) are produced by chemically cross-linking hyaluronan chains, whereas cross-linking does not affect the carboxylic and N-acetyl groups [15].

To achieve longer glucocorticoid retention times in SF, two different classes of sustained release formulations were developed, namely crystal suspensions and a liposome emulsion. As the SF clearance of solid particles is negligible, the majority of glucocorticoid drugs for IA use are formulated as crystal suspensions of very poor aqueous solubility. Their SF retention durations lie between 2-4 weeks. The only liposomal formulation available for IA injection is Lipotalon® with dexamethason-21-palmitate as active ingredient. Since the 1970s it is known that palmitic acid-derivative of cortisol in liposomes shows a prolonged residence in SF [1]. A study with liposomes containing radioactive-labelled MTX demonstrated that they accumulate in the synovial membrane and slowly release their active compound [12]. For Lipotalon® a mean joint residence time of 4-8 days is reported [13]. Recently, Chopra et al. reviewed the use of liposomal drugs in the treatment of RA [14].

HA (fig. 2) belongs to a group of substances known as glycosaminoglycans (GAGs) and is built up of a repeating disaccharide unit of glucuronic acid and N-acetylglucosamine in an unbranched chain [1]. Native HA has a MW of 4-10 MDa and provides optimal viscoelastic properties to SF, where it is found in high concentration (3.5g/l): At low shear rates it behaves as a viscous liquid (lubricant function), whereas at high shear rates it acts as an elastic solid (shock absorber function) [1,15]. In joints affected by OA, the molecular weight and concentration of HA are diminished (Table 1), leading to an increase in friction between the cartilage during movement. As a result, an IA application of high-molecular

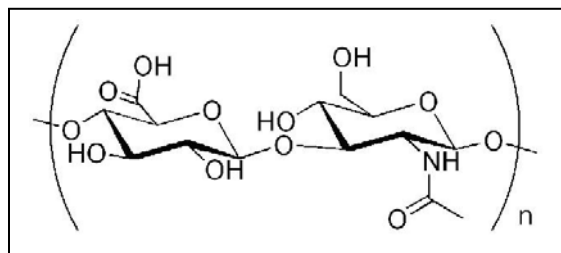


Figure 2: Chemical structure of HA

HA gels (MW > 4 MDa) has been postulated to be a rational option for symptomatic OA treatment (concept of viscosupplementation). But HA also seems to have direct anti-inflammatory effects in joints affected by OA. It is reported that high-molecular HA shall inhibit PGE2 synthesis, modulate cytokine expression, decrease activation of joint pain fibres, stimulate endogenous HA synthesis and act as a scavenger of free radicals [1,2,11].

One disadvantage of the low-molecular HA products (MW ~ 1 MDa) is that they mostly have to be injected up to 5 times over 5 weeks. In contrast, Synvisc® requires only 3 injections over 3 weeks due to its higher molecular weight achieved by cross-linking. For Durolane®, which is based on the NASHA® technology (non animal stabilized hyaluronic acid), it is claimed to reduce pain and increase mobility for up to 6 months requiring just one single injection [11]. Another critical point is the allergic potential of HA products that are isolated from rooster combs. Biosynthesized products like Durolane® do not bear this allergic risk and should be used in susceptible patients. Furthermore biotechnologically obtained HA is free of potential animal pathogens (bird flu virus, prions).

### HA in IA drug delivery

Because of its extraordinary biological compatibility (immunologically inert, completely biodegradable) and its viscoelasticity, HA is well suited for the use as a biopolymer for drug delivery systems [7,11,15]. Although a successful application of HA for topical sustained drug release systems is reported (gentamicin, betaxolol) [15], the IA application of HA still remains a critical issue, since – as already mentioned above – after IA application HA is cleared extremely rapidly (t<sub>0.5</sub>=10-12 h; turnover: 0.5-2.0 days) [16,17]. One solution for this problem could be the chemical modification of HA, for example by cross-linking [18,19]. But to date, there are no clinical studies available documenting efficiency and safety (e.g. immunological reactions) of these new HA derivatives.

### Future IA formulations

To achieve long-term drug exposure within the SF, beside different established formulations such as hydrogels (e.g. made of cross-linked macromolecules), also novel approaches such as lipid based formulations (liposomes) and nano- or microparticles are currently in development [1]. For drugs of very poor water solubility, the development of a suspension is the most obvious formulation option.

Many efforts are also being made to develop effective IA formulations for both well-known (NSAIDs, morphine, local anesthetics) and new drug substances (immunosuppressants, biologicals) [1].

### Summary

IA drug application provides lots of advantages like an initially high local drug concentration, the possibility of drug dose reduction, the avoidance of (serious) systemic side effects, the reduction of drug interactions and the targeted treatment of selective joints, leading not only to a reduction of treatment costs (e.g. by prevention of expensive operations) but also to more gentle and effective treatment options for OA and RA patients that often suffer from nagging pains.

To ensure the highest security level for the patients, only experienced orthopaedists should conduct IA injections in a limited number per year.

So far, glucocorticoids and sodium hyaluronate are available on the German market for IA administration. Nevertheless, the development of new IA formulations with novel drug substances is strongly promoted in order to disclose new treatment strategies for OA and RA patients.

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## DRUG DELIVERY LITERATURE

Provided by Dr. Karsten Cremer

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### RECENTLY PUBLISHED LITERATURE REVIEWS IN THE FIELD OF DRUG DELIVERY

**Tumour-targeted nanomedicines: principles and practice.** Lammers T, Hennink WE, Storm G. *Br J Cancer*. 2008 Aug 5;99(3):392-7.

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**Prodrugs in cardiovascular therapy.** Sandros MG, Sarraf CB, Tabrizian M. *Molecules*. 2008 May 14;13(5):1156-78.

**Progress in drug delivery to the central nervous system by the prodrug approach.** Pavan B, Dalpiaz A, Ciliberti N, Biondi C, Manfredini S, Vertuani S. *Molecules*. 2008 May 1;13(5):1035-65.

**Reprogrammed viruses as cancer therapeutics: targeted, armed and shielded.** Cattaneo R, Miest T, Shashkova EV, Barry MA. *Nat Rev Microbiol*. 2008 Jul;6(7):529-40.

**Drug delivery to brain tumors.** Blakeley J. *Curr Neurol Neurosci Rep*. 2008 May;8(3):235-41.

**Antibacterial nanomedicine.** Yacoby I, Benhar I. *Nanomed*. 2008 Jun;3(3):329-41.

**Quantum dots for tumor-targeted drug delivery and cell imaging.** Misra RD. *Nanomed*. 2008 Jun;3(3):271-4.

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The APV Drug Delivery Focus Group (APV DD) is a section of the APV (Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik e.V. / International Association for Pharmaceutical Technology), a major European society for those sharing a professional interest in pharmaceutical sciences. The Focus Group was established in 2003 in response to the increasing importance of drug delivery within modern pharmaceuticals.

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**COMBINING SCIENCE AND TECHNOLOGY TO CREATE ADVANCED DRUG DELIVERY SYSTEMS**

**OUR MISSION STATEMENT:**

Modern drug delivery research and development is a truly multidisciplinary approach and must combine all relevant scientific, technical, medical and regulatory aspects required for the design, preparation, testing, manufacturing and registration of drug delivery systems and their components. It is the mission of the APV Drug Delivery Working Group to foster and promote all aspects of research and development required to transform drug molecules into safe, applicable and acceptable drug delivery systems, which provide therapeutic benefit, convenience to the patient and improve patient compliance.

**Our mission includes in particular the following tasks:**

- Thoroughly understanding the physical-chemical and biopharmaceutical properties of the drug substance to be delivered and the components of the drug delivery system
- Understanding the biological barriers and the interactions of the drug molecule and its delivery system with the biological environment and the biological target including PK/PD and PK/safety relationships
- Research on excipients, materials and technologies required for the design, preparation and manufacturing of drug delivery systems for a selected route of administration
- Development and understanding of methods for in vitro and in vivo evaluation of drug delivery systems and their components
- Knowledge of regulatory requirements for clinical testing, manufacturing and registration of drug delivery systems

**All disciplines relevant to the above mentioned areas of drug delivery R&D are invited to contribute to the APV Drug Delivery Group:**

Pharmaceutics, Biopharmaceutics, Analytics, Biology, Physical Chemistry, Biochemistry, Physics, Engineering Sciences, Nano Technology, Material Sciences, Polymer Science, Toxicology, Drug Safety, Clinical Research, Drug Regulatory Affairs, etc.

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