

phar mail

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Roll out the power

High-performance
excipients for consistent,
low-dose formulation

Falsified Medicines Directive

Made in Germany: Glycine EMPROVE®

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CellPrime™ recombinant human lysozyme



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A universal seal of approval

The EXCiPACT™ certification scheme

When patient safety is your top priority, it clearly makes sense to verify *all* the ingredients in medications, not just some of them. Yet while active pharmaceutical ingredients are strictly regulated, there is still no formal legislation on the excipients that make up the bulk of most formulations. In fact, even the independent audit organizations who audit and certify those excipients use different standards. As a result, suppliers have to arrange (and pay for) multiple audits before marketing their products globally.

The new EXCiPACT™ certification scheme, introduced on January 25, 2012, will remedy this situation by granting an independent, one-stop 'seal of approval' by third-party auditors who follow the processes it defines. Thanks to EXCiPACT™, a single audit will be all it takes to prove an excipient complies with current GMP and GDP requirements. And since EXCiPACT™ certificates are recognized everywhere, including North America, they will make life simpler – and safer – all over the world.

Like the Rx-360 consortium, EXCiPACT™ is a voluntary, self-regulated industry initiative. Unlike Rx-360, however, it focuses entirely on excipients and involves a wide range of manufacturers, as well as distributors of excipients. To find out more about the EXCiPACT™ certification scheme, visit www.excipact.org



international excipients
certification

Caring for quality

New EMPROVE® api products: Urea cryst. and Potassium chloride

Since urea is so popular in skin creams and dermatological applications, we decided to help customers stay on the safe side – by becoming the first supplier to offer urea in EMPROVE® api quality with even higher purity. As a result, customers who order from us can now obtain the dossiers they need to use urea crystalline as an active – a Merck Millipore exclusive!

And because we've also added Potassium chloride, there are not one, but two good reasons to check out our growing EMPROVE® api portfolio.

Like all EMPROVE® api products, both new arrivals combine outstanding quality with tailor-made documentation that's designed to streamline approvals and reduce your time-to-market. For details visit: www.merck4pharma.com/urea

Only from us: Urea cryst. in EMPROVE® api with a Drug Master File.

Quality made in Germany

Our glycine in EMPROVE® exp quality

With so many customers seeking reliable supplies of top-quality glycine, we decided the best solution was to produce it ourselves – in Germany. As a result, you can now order Glycine EMPROVE® exp – straight from us, the manufacturer.

We deliver reliable supplies of top-quality glycine – made in Germany.

The new material is produced according to GMP guidelines. In terms of quality, Merck Millipore's glycine is better than ever thanks to its improved free-flowing characteristics. And since it's part of our EMPROVE® exp product family, it can save you time and money during registration too. The detailed, ready-to-use EMPROVE® exp dossier provides in-depth information on the manufacturing process, testing procedures, specification, stability data, and more besides. To find out more, visit www.merck4pharma.com/glycine



Stepping up safety

The new Falsified Medicines Directive

Falsified medicines are a major threat to global health and safety. Most of them are fake products that masquerade as the real thing, but can be much stronger or weaker – and are usually of dubious quality. The others are genuine products that were fine when packed, but have since become substandard due to incorrect transport, storage, or adulteration.

The new Falsified Medicines Directive, which was adopted by the EU Parliament in February 2011, will help protect patients and manufacturers alike by regulating the quality of APIs and excipients more strictly. Under the new rules, for example, drug manufacturers must make sure their excipients are

'fit for purpose' by verifying the appropriate GMP in advance, based on a formalized risk assessment. Authorities will also be able to inspect the premises of companies that make, import, or distribute excipients; in the case of manufacturers, this includes premises located outside the European Union.

EU member states have 18 months to transpose the directive into national law, and are likely to interpret it in different ways. So while we welcome the new directive as a step in the right direction, Merck Millipore will continue to press for a consistent, pan-European solution that would make patients safer still.

Putting safety first: the Falsified Medicines Directive.

The lowdown on low dose

Low dosage and Parateck® M

Did you know? One in five oral formulations now contains highly potent APIs in extremely low dosages. For tablet manufacturers, these 'highly potents' can be highly challenging too: the particles of low-dose APIs are far smaller than those of excipients, so it's much harder to achieve a stable, consistent mixture just by stirring the ingredients as segregation occurs. As a result, manufacturers often have to use wet or dry granulation processes, instead of the more economical direct compression method.

With their filamentary particle structure and greatly increased surface area, Parateck® M mannitol types help solving the issue by ensuring a consistent, stable mix even at dosages below 1%. And because it's so compressible, you can use the same product

for the preparation of high-dose forms as well. You are able to add up to 60% of non-directly compressible actives to your formula – and still produce uniform, homogeneous tablets that are hard and durable, yet disintegrate and dissolve fast.

Parateck® M excipients come in various grades suitable for direct compression, all with complete, ready-to-use EMPROVE® documentation. For details, contact your local sales representative today – or visit www.merck4pharma.com/parateckm

Parateck® M is ideal for direct compression of highly potents.

Extracting the benefits

CellPrime™ recombinant human lysozyme – for in-culture protein extraction

As any specialist will confirm, expressing protein in a bacterial system is easy; the hard part comes afterwards, when you need to extract it in a functional form. Now there's a new Merck Millipore product that meets this challenge and can improve your functional protein therapeutic yield dramatically: CellPrime™ recombinant human lysozyme (CellPrime™ rLysozyme).

CellPrime™ rLysozyme is a non-animal origin lysozyme designed specifically for use in biopharmaceutical production processes, diagnostic applications, and life science research. Compared to chicken lysozyme, it has four times greater activity per mg when lysing E.coli and Micrococcus, resulting in up to five times higher protein recovery.

As a non-animal origin product, CellPrime™ rLysozyme eliminates the risk of infectious disease transmission. And thanks to recombinant manufacturing, you can benefit from outstanding reliability and lot-to-lot consistency too. For details, visit www.merckmillipore.com/lysozyme

CellPrime™ rLysozyme means higher yields and lower risks for in-culture protein extraction.



Problem (dis)solved

How our API-grade meglumine enhances bioavailability

When you consider how closely organic counter-ions like meglumine interact with the drug substance itself, it obviously makes sense to use the best quality you can find. And when you order from Merck Millipore, you can be sure of getting the finest level available.

The reason is simple: Unlike many manufacturers who only produce technical grades, we can supply meglumine in API-grade according to the ICH Q7 guideline. This quality and purity makes our product ideal for use as a counter-ion that solubilizes APIs in the blood. And when used as a substitute for sodium in APIs, our meglumine can enhance the bioavailability of poorly soluble actives too.

The documentation for our API-grade meglumine is as unique as the product itself and includes both CEP and US-DMF. To find out more about this versatile material and its different applications, visit www.merck4pharma.com/meglumine

Only from us: API-grade meglumine according to the ICH Q7 guideline.



Uses for meglumine

- In X-ray imaging products
- To treat leishmaniasis (human and veterinary medicine)
- As an anti-inflammatory (veterinary medicine)
- As a counter-ion to solubilize APIs in the blood

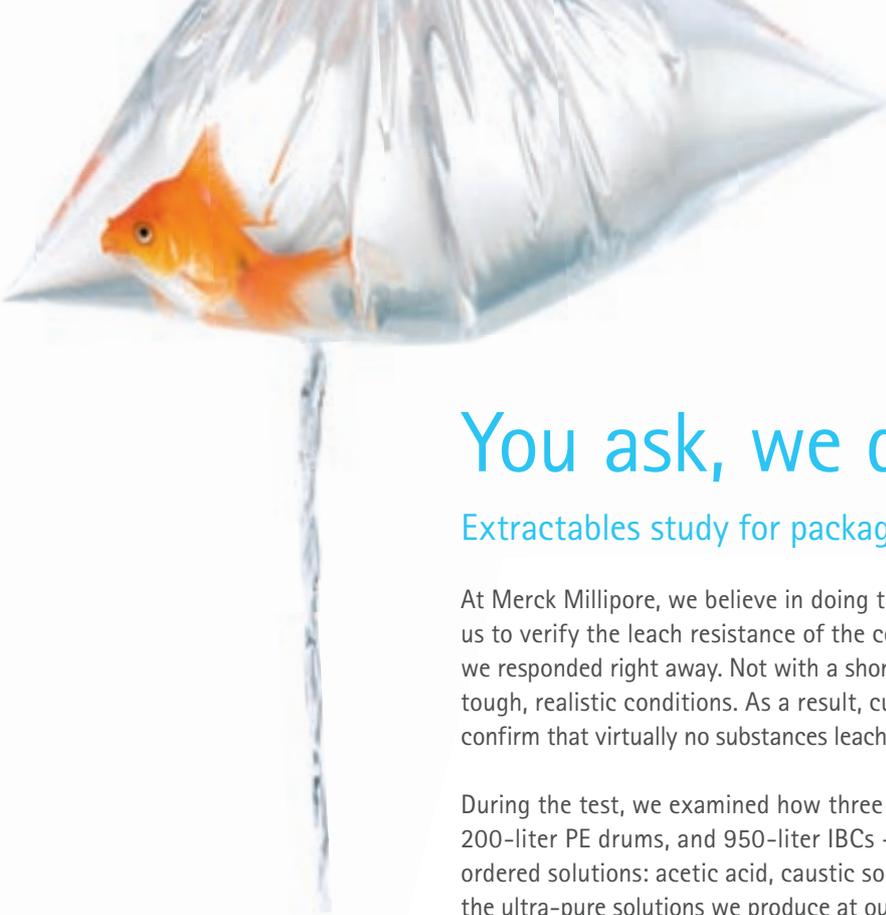
Breaking the bottleneck

Our tankless concept for downstream purification

For manufacturers, the biggest challenge in downstream purification is higher titers – or rather, the sheer volumes of buffers and holding tanks required to process them. Normally, the process involves changing the conditions of the drug pool in bulky storage tanks between process steps – a stop-and-go procedure that slows down your entire operation. Now, thankfully, there's a better way: our 'tankless application concept'.

This innovative Merck Millipore concept creates a smooth, tank-free workflow by eliminating the need for interim storage and processing completely. It works by connecting three unique technologies – one for each process step. In affinity, we use the chromatography resin ProSep® Ultra Plus. It has the greatest capacity of any commercial affinity resin on the market and is ideal for higher titers. In cation, we use Fractogel® and Eshmuno® – two smart resins that maintain good capacity across a wide range of process conditions. In the polishing step, our single-use flow-through ChromaSorb™ anion exchange membrane removes impurities at high salt concentration. The result? Seamless purification – with less waiting and no bottlenecks.

Faster, smoother purification – and a lot more space in your facility.



You ask, we deliver

Extractables study for packaging of GMP solutions

At Merck Millipore, we believe in doing things properly. So when biotech customers asked us to verify the leach resistance of the containers we use for CIP and process solutions, we responded right away. Not with a short letter, but with a rigorous, 12-month study under tough, realistic conditions. As a result, customers now receive detailed documentation to confirm that virtually no substances leach out of the packaging during transport and storage.

During the test, we examined how three popular packagings – our 25-liter PE containers, 200-liter PE drums, and 950-liter IBCs – responded to three of our most frequently-ordered solutions: acetic acid, caustic soda, and hydrochloric acid. These are just three of the ultra-pure solutions we produce at our new GMP process solutions plant in Darmstadt (Germany) in a clean room under GMP conditions, using highly purified water.

For details of how we tested and how well our candidates performed, visit www.merck4pharma.com/extractables

Quality products deserve documented quality packaging.

All wrapped up

Our new aluminum-coated PE media packaging

When it comes to keeping moisture out of sensitive cell culture media, we've got it all wrapped up. In fact, our PE packaging now does an even better job of protecting the quality of the goods inside.

The secret of our new solution lies in the new double wrapping. First, we seal the media inside a normal PE bag as usual. Then we seal everything inside a second PE bag with a special aluminum coating. This added protection eliminates the risk of the contents 'drawing' water from the surrounding air. The result is a Merck Millipore exclusive: a media packaging solution that's not just airtight and lightfast, but moisture-proof too.

Speaking of proof, recent data confirm that our new packs really do make a difference. For details, visit www.merck4pharma.com/mediapackaging

Airtight, lightfast, and moisture-proof: our new PE media packaging solutions.



Easy is right

The new Mobius® CellReady 200 L bioreactor

Looking for a single-use bioreactor that's reliable, robust, and easy to use? Our new Mobius® CellReady 200 L fits the bill perfectly. Designed to deliver reliable mammalian cell culture performance at pilot and clinical scale, this flexible new bioreactor is outstandingly simple to install and use and helps you work with confidence in a wide range of applications.

Thanks to innovative Mobius® SensorReady technology, you have more freedom than ever when monitoring and controlling your bioreactor process. Since the sensing and sampling takes place via an external recirculating loop, you can integrate a wide range of conventional and single-use sensor technologies easily – without having to customize bioreactor process containers.

Reliable, robust, and easy to use: the new Mobius® CellReady 200 L bioreactor.

The open architecture platform also provides more choice when it comes to automation. You can either opt for a turnkey system integrated with Finesse automation or for your own platform. For details of the new Mobius® CellReady 200 L bioreactor, visit www.millipore.com/cellready



Raising the standard

Our DMEM/F12 makes the difference

Just because it's a standard medium doesn't mean it comes with standard levels of quality and support. Take DMEM/F12 (for CHO media developments), for example: When you order this standard medium from us, you can be certain it contains only top-quality, non-animal raw materials. Most of them follow the EMPROVE® concept and are sourced from controlled sources that meet our own rigorous standards. And thanks to our unique documentation pack, you'll have all the data you need for approvals – right there on your desk.

As a standard medium, Merck Millipore DMEM/F12 contains a large number of strictly tested raw materials and can cover a wide range of applications straight off the shelf. But when you need more, we strive to exceed your expectations once again – by responding promptly to your request, then modifying our medium to your exact formulation. For details on DMEM/F12 and other Merck Millipore media, visit www.merck4pharma.com/DMEM/F12

Merck Millipore DMEM/F12: chemical purity, plus unique regulatory support.

Eating the elephant

Rebranding our portfolio with the new Merck Millipore logo

How do you eat an elephant? One bite at a time, according to the old saying. We don't know if that's true – but it certainly works for the 'mammoth' task we are currently involved in: rebranding our whole portfolio with the new Merck Millipore logo. While it's definitely work in progress, more and more products and materials now bear the new mark.

All of the products we label in Darmstadt have already switched, and most of the Material Safety Data Sheets (MSDS) and Certificates of Analysis (CoA) on our website www.merck-chemicals.com use the new logo too.

But while our logos and labels may be changing, you can rest assured that the products and services that carry them are exactly the same as before; the changes are purely visual. And to avoid any surprises, we promise to notify you as early as possible about any upcoming changes to familiar documentation or packaging.

If you'd like to learn more about the Merck Millipore brand, the choice is yours: Simply consult the latest product catalog, contact your local office, or visit www.merckmillipore.com

Coming along nicely: our Merck Millipore rebranding process.



Upcoming events 2012

March 19–22	PBP World Meeting	Istanbul, Turkey
March 19–22	BioPharma Asia	Singapore, Singapore
March 25–29	ACS Biochemical Technology Meeting	San Diego, USA
April 10–13	World Vaccine Congress	Washington, USA
April 18–19	BioProcess International	Prague, Czech Republic
April 24–25	ExcipientFest	San Juan, Puerto Rico
May 1–3	Interphex	New York, USA

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