El Lunes de Patentes (Patent Mondays)

Barcelona, Spain

September 29, 2008

AstraZeneca v. Mylan and Esteve
The Omeprazole II US Patent Case
An Eight Year Patent Conflict About a Best-Selling Prilosec® (Losec® in Europe) Drug

James H. Wallace, Jr.
Mark A. Pacella
Partners
1776 K Street, N.W.
Washington, D.C.
Tel: (202) 719-7000
Fax: (202) 719-7049
www.wileyrein.com

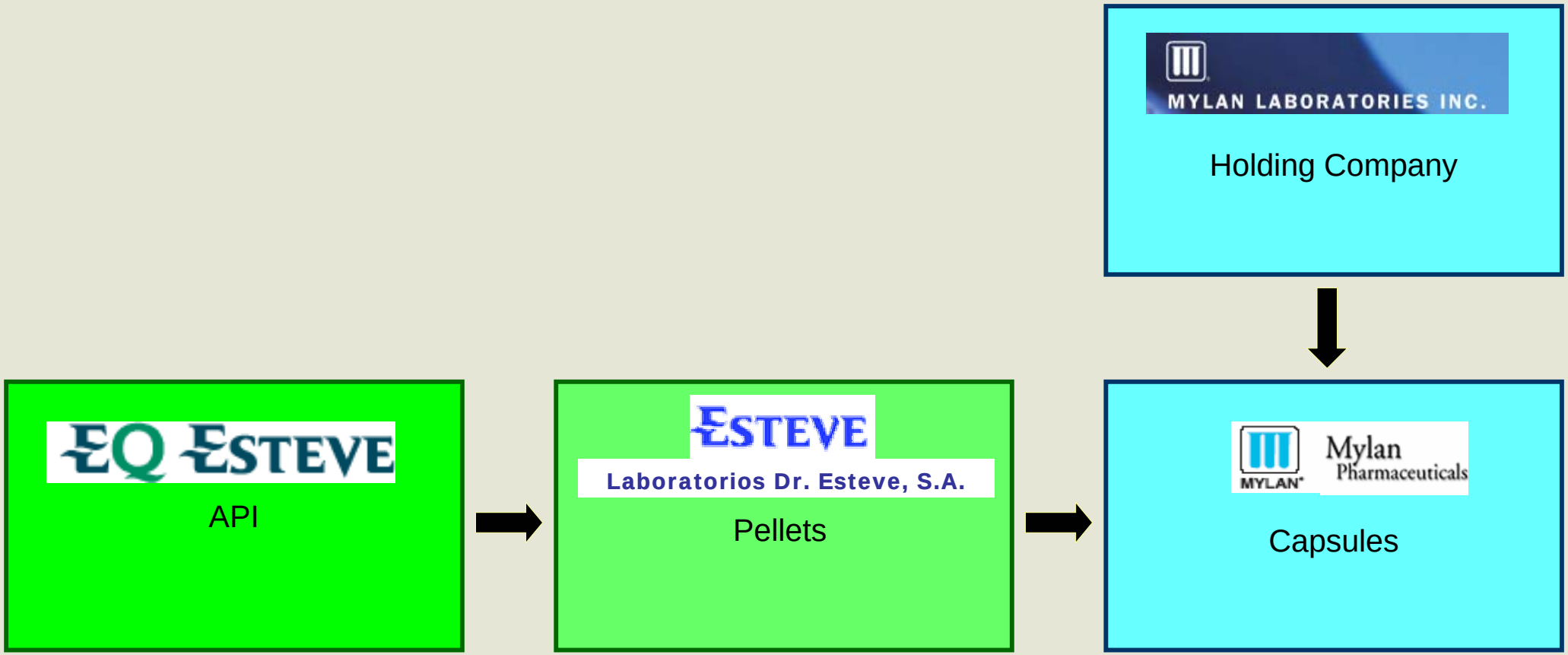
Overview

- Chronology of the case
- Design around avoids infringement
- Foreign supplier liability – before launch and after launch
- Foreign supplier discovery issues – as non-defendant third party and as defendants
- Testing finished products and intermediates
- “At Risk” sales prior to adjudication

Chronology of the Case

September 7, 2000:	Complaint Filed
April 3 – June 14, 2006:	Trial
May 31, 2007:	Trial Court Decision
May 6, 2008:	Oral Argument CAFC
June 10, 2008:	CAFC Decision

The Mylan/Esteve Defendants



Classic Design Around

Esteve carefully reviewed the Astra patents 15 years ago to develop a non-infringing formulation that is independently protected by two U.S. patents (5,626,875 and 6,780,436)

The Problem Solved by Astra's Patents

- Omeprazole is acid labile
- There must be protection from stomach acids
- Enteric coat prevents exposure in stomach
- Because enteric coat is itself acidic, to protect omeprazole
    - add alkaline reacting compound ("ARC") to omeprazole
    - put a protective layer containing, e.g., HPMC between omeprazole and enteric coat
- Protective layer protects omeprazole from acids in enteric coat and protects enteric coat from ARC drug layer.

United States Patent [19]
Lovgren et al.

[11] **Patent Number: 4,786,505**
[45] **Date of Patent: Nov. 22, 1988**

[54] **NEW PHARMACEUTICAL PREPARATION FOR ORAL USE**

[75] Inventors: **Kurt L. Lovgren**, Mölnlycke; **Ake G. Pilbrant**, Kungsbacka, both of Sweden; **Mitsuru Yasumura**; **Satoshi Morigaki**, both of Hyogo, Japan; **Minoru Oda**, Ohita, Japan; **Naohiro Ohishi**, Fukuoka, Japan

[73] Assignee: **Aktiebolaget Hassle**, Sweden

[21] Appl. No.: **40,491**

[22] Filed: **Apr. 20, 1987**

[30] **Foreign Application Priority Data**

Apr. 30, 1986 [GB] United Kingdom 8610572

[51] **Int. Cl.**[4] **A61K 9/22**; A61K 9/32
[52] **U.S. Cl.** **424/468**; 424/475; 424/479; 424/480; 424/482
[58] **Field of Search** 424/480, 482, 468, 475, 424/479; 427/2, 3

[56] **References Cited**

U.S. PATENT DOCUMENTS

2,540,979 2/1951 Clymer et al. 167/82
4,685,919 8/1987 Amidon et al. ..... 427/2 X

FOREIGN PATENT DOCUMENTS

0005129 10/1979 European Pat. Off. .
1204363 8/1964 Fed. Rep. of Germany .
1617615 5/1966 Fed. Rep. of Germany .
2336218 5/1979 Fed. Rep. of Germany .
3046559 12/1980 Fed. Rep. of Germany .
WO85/03436 8/1985 PCT Int'l Appl. .
1485676 9/1977 United Kingdom .

Primary Examiner—Michael Lusignan
Attorney, Agent, or Firm—Brumbaugh, Graves, Donohue & Raymond

[57] **ABSTRACT**

Pharmaceutical preparation containing omeprazole together with an alkaline reacting compound or an alkaline salt of omeprazole optionally together with an alkaline compound as the core material, one or more subcoating layers comprising inert reacting compounds which are soluble or rapidly disintegrating in water, or polymeric, water soluble filmforming compounds, optionally containing pH-buffering alkaline compounds and an enteric coating as well as a process for the preparation thereof and the use in the treatment of gastrointestinal diseases.

14 Claims, No Drawings

DEFENDANT'S EXHIBIT M/EX1

stability of the formulations according to Examples I, II and V is not acceptable, since a discolouration, showing a degradation of omeprazole, occours during short storage at an elevated storage temperature (Examples I and II) or already during the enteric coating process (Example V).

If the amount of alkaline substances in the cores is increased to a level where omeprazole has an acceptable storage stability (Example III) or if an alkaline reacting salt of omeprazole is used in the preparation of the cores (Example IV), then, without the separating layer of the invention, the resistance to dissolution in acid media becomes unacceptably low and much or all of the active substance will degrade already in the stomach and thus, it has no effect on the gastric acid secretion.

When the preparation is carried out according to the invention as for instance in Example 4, a good resistance towards gastric juice as well as a good stability during long-term storage is obtained. This is in contrast with the formulations in Examples I, II and III where either an acceptable acid resistance or an acceptable storage stability can be achieved—but not both. The same comparison can be made between the formulations according to Examples 7 and 8 according to the invention and

administration of the omeprazole suspension and at further four times with a 10-minutes interval after the drug intake. The concentration of omeprazole in blood plasma was assayed by high pressure liquid chromatography (Persson, Lagerström and Grandevik. Scand J Gastroenterol 1985, 20, (suppl 108), 71–77. The mean plasma concentrations are given in Table 6.

TABLE 6

The plasma concentrations (μmol/l) after 20 mg single oral doses of omeprazole given as hard gelatin capsules according to Example 3 and as a suspension of micronized omeprazole in sodium bicarbonate solution.

Time (min)	Capsules	Suspension
10		0.84
20		0.90
30	0.03	0.84
45		0.64
60	0.22	0.44
90	0.36	0.24
120	0.39	0.13
150	0.29	
180	0.20	0.04
210	0.10	
240	0.05	0.01
300	0.02	0
360	0.01	
420	0	

We claim:

1. An oral pharmaceutical preparation comprising

(a) a core region comprising an effective amount of a material selected from the group consisting of omeprazole plus an alkaline reacting compound, an alkaline omeprazole salt plus an alkaline reacting compound and an alkaline omeprazole salt alone;

(b) an inert subcoating which is soluble or rapidly disintegrating in water disposed on said core region, said subcoating comprising one or more layers of materials selected from among tablet excipients and polymeric film-forming compounds; and

(c) an outer layer disposed on said subcoating comprising an enteric coating.

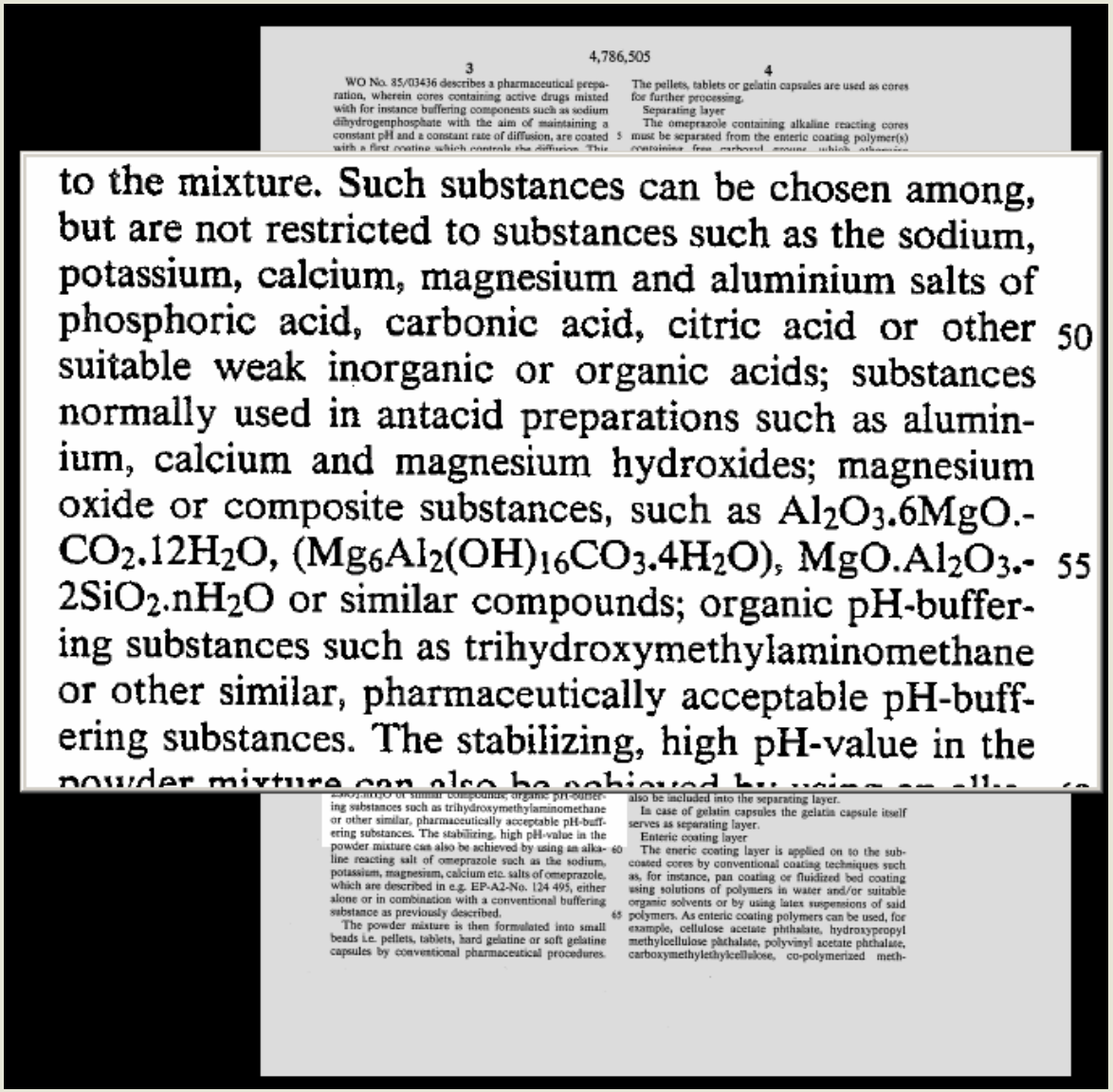
day.

In another experiment the same volunteers were administered 20 mg of omeprazole in the form of a suspension of micronized omeprazole in a sodium bicarbonate water solution. In order to reduce the degradation of omeprazole in the stomach to a minimum, sodium bicarbonate solution was given to the subjects just before the

4. A preparation according to claim 3 wherein the subcoating comprises hydroxypropyl methylcellulose, hydroxypropyl cellulose or polyvinylpyrrolidone.

5. A preparation according to claim 1 wherein the alkaline core comprises omeprazole and pH-buffering alkaline compound rendering to the micro-environment of omeprazole a pH of 7–12.

Examples Of ARCs – Do Not Include Talc, HPMC or TEA



4,786,505

3

WO No. 85/03436 describes a pharmaceutical preparation, wherein cores containing active drugs misted with for instance buffering components such as sodium dihydrogenphosphate with the aim of maintaining a constant pH and a constant rate of diffusion, are coated with a first coating which controls the diffusion. This

4

The pellets, tablets or gelatin capsules are used as cores for further processing.

Separating layer

The omeprazole containing alkaline reacting cores must be separated from the enteric coating polymer(s) containing free carboxyl groups which otherwise

to the mixture. Such substances can be chosen among, but are not restricted to substances such as the sodium, potassium, calcium, magnesium and aluminium salts of phosphoric acid, carbonic acid, citric acid or other suitable weak inorganic or organic acids; substances normally used in antacid preparations such as aluminium, calcium and magnesium hydroxides; magnesium oxide or composite substances, such as $Al_2O_3.6MgO.CO_2.12H_2O$, $(Mg_6Al_2(OH)_{16}CO_3.4H_2O)$, $MgO.Al_2O_3.2SiO_2.nH_2O$ or similar compounds; organic pH-buffering substances such as trihydroxymethylaminomethane or other similar, pharmaceutically acceptable pH-buffering substances. The stabilizing, high pH-value in the powder mixture can also be achieved by using an alka-

$Al_2O_3.6MgO.CO_2.12H_2O$, $(Mg_6Al_2(OH)_{16}CO_3.4H_2O)$, $MgO.Al_2O_3.2SiO_2.nH_2O$ or similar compounds; organic pH-buffering substances such as trihydroxymethylaminomethane or other similar, pharmaceutically acceptable pH-buffering substances. The stabilizing, high pH-value in the powder mixture can also be achieved by using an alkaline reacting salt of omeprazole such as the sodium, potassium, magnesium, calcium etc. salts of omeprazole, which are described in e.g. EP-A2-No. 124 495, either alone or in combination with a conventional buffering substance as previously described.

The powder mixture is then formulated into small beads i.e. pellets, tablets, hard gelatine or soft gelatine capsules by conventional pharmaceutical procedures.

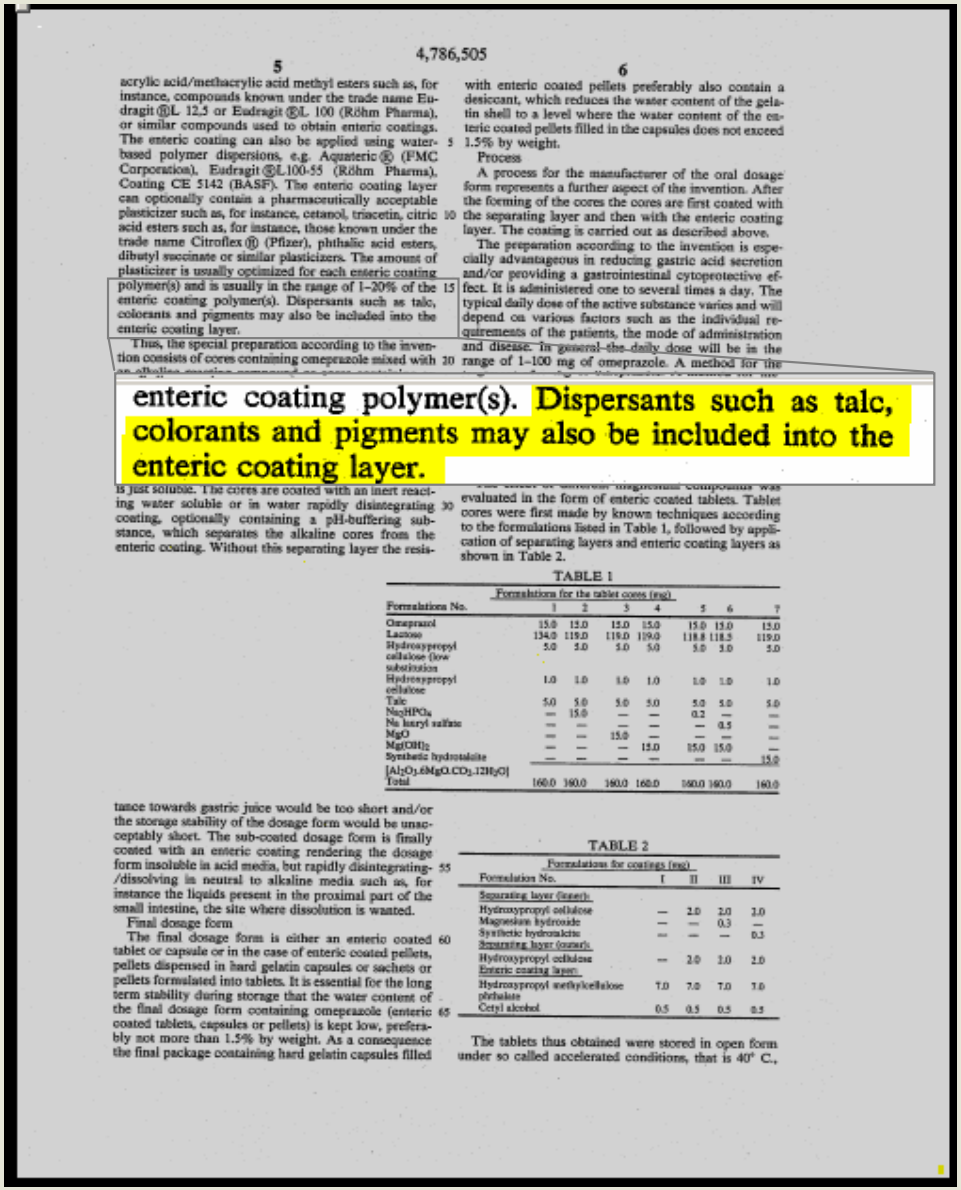
also be included into the separating layer.

In case of gelatin capsules the gelatin capsule itself serves as separating layer.

Enteric coating layer

The enteric coating layer is applied on to the sub-coated cores by conventional coating techniques such as, for instance, pan coating or fluidized bed coating using solutions of polymers in water and/or suitable organic solvents or by using latex suspensions of said polymers. As enteric coating polymers can be used, for example, cellulose acetate phthalate, hydroxypropyl methylcellulose phthalate, polyvinyl acetate phthalate, carboxymethylethylcellulose, co-polymerized meth-

The Patents Distinguish Talc From "ARCs"



4,786,505

5 6

acrylic acid/methacrylic acid methyl esters such as, for instance, compounds known under the trade name Eudragit ®L 12,5 or Eudragit ®L 100 (Röhm Pharma), or similar compounds used to obtain enteric coatings. The enteric coating can also be applied using water-based polymer dispersions, e.g. Aquateric ® (FMC Corporation), Eudragit ®L100-55 (Röhm Pharma), Coating CE 5142 (BASF). The enteric coating layer can optionally contain a pharmaceutically acceptable plasticizer such as, for instance, cetanol, triacetin, citric acid esters such as, for instance, those known under the trade name Citroflex (ß) (Pfizer), phthalic acid esters, dibutyl succinate or similar plasticizers. The amount of plasticizer is usually optimized for each enteric coating polymer(s) and is usually in the range of 1–20% of the enteric coating polymer(s). Dispersants such as talc, colorants and pigments may also be included into the enteric coating layer.

Thus, the special preparation according to the invention consists of cores containing omeprazole mixed with an alkaline reacting compound or compounds, which is just soluble. The cores are coated with an inert reacting water soluble or in water rapidly disintegrating coating, optionally containing a pH-buffering substance, which separates the alkaline cores from the enteric coating. Without this separating layer the resistance towards gastric juice would be too short and/or the storage stability of the dosage form would be unacceptably short. The sub-coated dosage form is finally coated with an enteric coating rendering the dosage form insoluble in acid media, but rapidly disintegrating-/dissolving in neutral to alkaline media such as, for instance the liquids present in the proximal part of the small intestine, the site where dissolution is wanted.

Final dosage form

The final dosage form is either an enteric coated tablet or capsule or in the case of enteric coated pellets, pellets dispensed in hard gelatin capsules or sachets or pellets formulated into tablets. It is essential for the long term stability during storage that the water content of the final dosage form containing omeprazole (enteric coated tablets, capsules or pellets) is kept low, preferably not more than 1.5% by weight. As a consequence the final package containing hard gelatin capsules filled with enteric coated pellets preferably also contain a desiccant, which reduces the water content of the gelatin shell to a level where the water content of the enteric coated pellets filled in the capsules does not exceed 1.5% by weight.

Process

A process for the manufacturer of the oral dosage form represents a further aspect of the invention. After the forming of the cores the cores are first coated with the separating layer and then with the enteric coating layer. The coating is carried out as described above.

The preparation according to the invention is especially advantageous in reducing gastric acid secretion and/or providing a gastrointestinal cytoprotective effect. It is administered one to several times a day. The typical daily dose of the active substance varies and will depend on various factors such as the individual requirements of the patients, the mode of administration and disease. In general the daily dose will be in the range of 1–100 mg of omeprazole. A method for the

enteric coating polymer(s). Dispersants such as talc, colorants and pigments may also be included into the enteric coating layer.

evaluated in the form of enteric coated tablets. Tablet cores were first made by known techniques according to the formulations listed in Table 1, followed by application of separating layers and enteric coating layers as shown in Table 2.

TABLE 1

Formulations No.	Formulations for the tablet cores (mg) 1	2	3	4	5	6	7
Omeprazol	15.0	15.0	15.0	15.0	15.0	15.0	15.0
Lactose	134.0	119.0	119.0	119.0	118.8	118.5	119.0
Hydroxypropyl cellulose (low substitution	5.0	5.0	5.0	5.0	5.0	5.0	5.0
Hydroxypropyl cellulose	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Talc	5.0	5.0	5.0	5.0	5.0	5.0	5.0
Na_2HPO_4	—	15.0	—	—	0.2	—	—
Na lauryl sulfate	—	—	—	—	—	0.5	—
MgO	—	—	15.0	—	—	—	—
$Mg(OH)_2$	—	—	—	15.0	15.0	15.0	—
Synthetic hydrotalcite $[Al_2O_3.6MgO.CO_2.12H_2O]$	—	—	—	—	—	—	15.0
Total	160.0	160.0	160.0	160.0	160.0	160.0	160.0

TABLE 2

Formulation No.	Formulations for coatings (mg) I	II	III	IV
Separating layer (inner):				
Hydroxypropyl cellulose	—	2.0	2.0	3.0
Magnesium hydroxide	—	—	0.3	—
Synthetic hydrotalcite	—	—	—	0.3
Separating layer (outer):				
Hydroxypropyl cellulose	—	2.0	2.0	2.0
Enteric coating layer:				
Hydroxypropyl methylcellulose phthalate	7.0	7.0	7.0	7.0
Cetyl alcohol	0.5	0.5	0.5	0.5

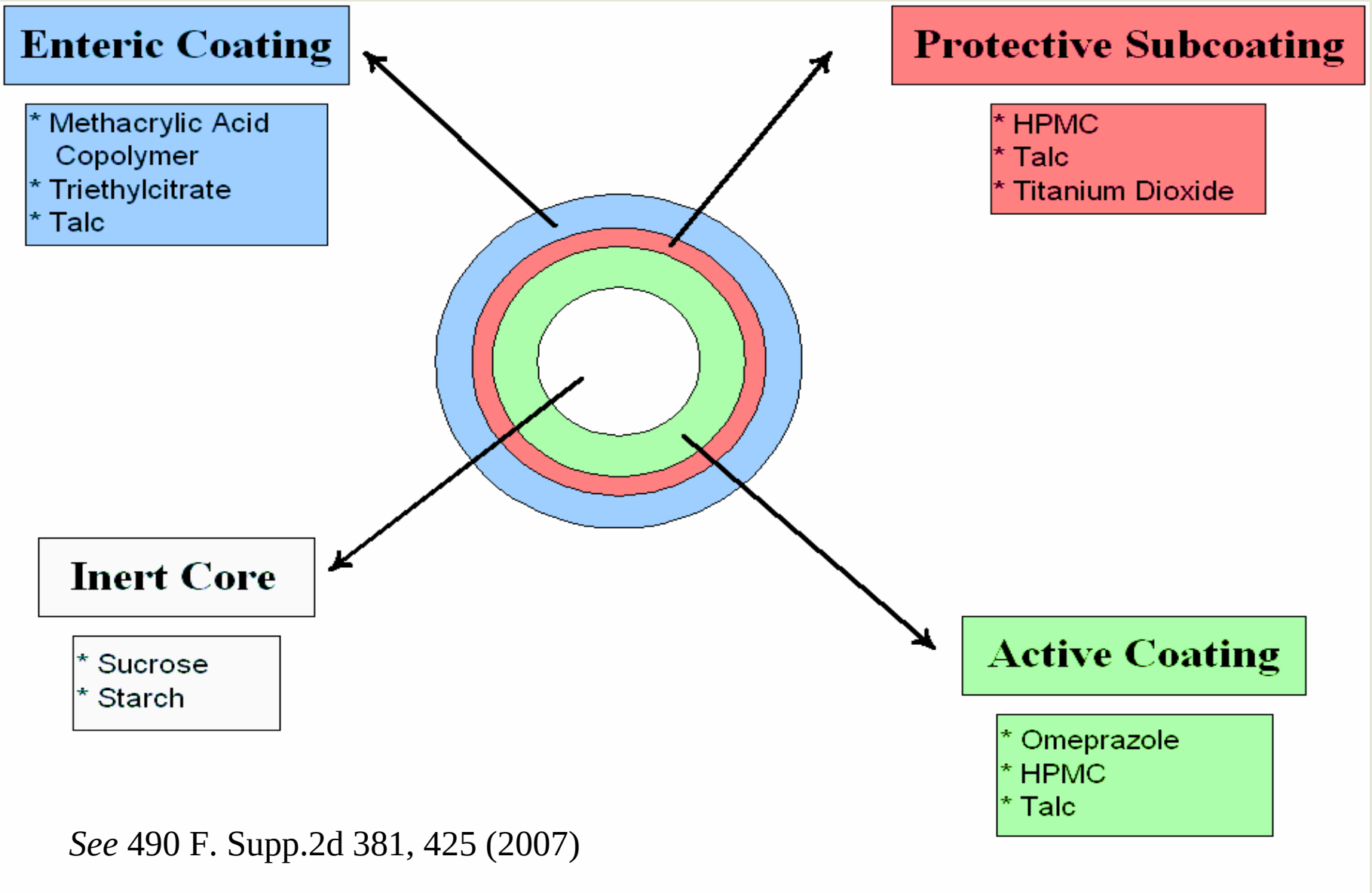
The tablets thus obtained were stored in open form under so called accelerated conditions, that is 40° C.,

Esteve Design Around

- Esteve project leaders used patent disclosures to carefully avoid ARCs and instead included HPMC and talc in the Omeprazole layer
- Esteve formulation relies on limiting exposure to moisture, including effective physical barriers, for stability – not chemical stabilization
- Esteve received ‘875 Patent for its novel ARC-free formulation

Impact of Design Around

- The selection and location of the ingredients forced Astra to make inconsistent and indefensible arguments
- It asserted that the HPMC and Talc in the active ingredient core provided impurities that are ARCs to that layer but it also argued that the very same HPMC and Talc that are in the protective subcoating met the patent's limitation for that layer that they be inert!
- The court did not accept this argument



See 490 F. Supp.2d 381, 425 (2007)

Liability Of The Foreign Supplier Before Launch
Hatch-Waxman Act

- Statutory safe Harbor for acitivies relating to submission for FDA approval
  35 U.S.C. 271(e)(1)
- Filing ANDA creates artificial act of infringement
  35 U.S.C. 271(e)(2)(A)
- Limited Pre-launch Remedies
  - court order prohibiting FDA approval before patent expiration
  - injunction against commercial activities

  35 U.S.C. 271(e)(4)(A), (B)

Liability Of The Foreign Supplier Before Launch
Inducing Infringement

- "Whoever actively induces infringement of a patent shall be liable as an infringer." -- 35 U.S.C. 271(b)
- Supplier of a product or component may be liable for inducing infringement if the patentee shows:
  - there has been direct infringement; and
  - the supplier knowingly induced the infringing acts with the specific intent to encourage the direct infringement

Liability Of The Foreign Supplier Before Launch
Mylan/Esteve's Omeprazole Case

- Sep 2000: Astra sued Mylan based on filing ANDA
- Jan 2003 (pre-launch): Astra sought consent to add EQ and LDE as parties – Mylan refused
- Astra moved to amend its complaint to add EQ/LDE as parties – motion denied

Liability Of The Foreign Supplier Before Launch
Astra's Theory of Inducement

- Submission of omeprazole DMF and authorization for Mylan to reference the DMF in the ANDA
- Collaboration with Mylan in developing the ANDA product
- Providing assistance to Mylan in preparing its ANDA
- Supplying raw materials and pellets to be used in the ANDA product
- Providing raw materials and documentation used to support the ANDA batches relied on for FDA approval

Wiley Rein LLP

Liability Of The Foreign Supplier Before Launch
Case Law as of 2003

YES

- *SmithKline Beecham Corp. v. Geneva Pharms., Inc.*, 287 F. Supp.2d 576 (E.D. Pa. 2002)
- *SmithKline Beecham Corp. v. Pentech Pharms., Inc.*, 2001 WL 184804 (N.D. Ill. Feb. 20, 2001)

NO

- *Ortho-McNeil Pharm., Inc. v. Mylan Labs, Inc.*, 267 F.Supp.2d 545 (N.D. W.Va. 2003)

Liability Of The Foreign Supplier Before Launch
The Mylan/Esteve Court's Ruling

"There is no doubt that Astra's proposed complaints sufficiently allege that [EQ and LDE] significantly and intentionally aided Mylan . . . in the preparation of [its] ANDA and would likely participate in the manufacture of the proposed product if approved."

BUT . . .

"[T]he appropriate question in an inducement inquiry brought under section 271(b) with respect to an ANDA filing is whether the drug, if approved, will induce infringement of the plaintiff's patents. Therefore, the Court finds that an action for inducement for aiding and abetting the filing of an ANDA is unavailable."

AstraZeneca AB v. Mylan Labs., 265 F.Supp.2d 213 (S.D.N.Y. 2003)

Liability Of The Foreign Supplier Before Launch
Federal Circuit 2007: *Forest Labs*

- District court permitted addition of foreign API supplier as a party; issued injunction against both ANDA applicant and supplier
- Majority: "Cipla has therefore actively induced the acts of Ivax that will constitute direct infringement upon approval of the ANDA, and it was thus not inappropriate for the district court to include Cipla within the scope of the injunction."

  Forest Labs, Inc. v. Ivax Pharms., Inc., 501 F.3d 1263 (Fed. Cir. 2007)
- Dissent (Schall, C.J.): Cipla's activities of contributing to the ANDA fell within the 271(e)(2) safe harbor and thus should have been immune from suit

Liability Of The Foreign Supplier Before Launch
Impact of *Forest Labs*

- Foreign suppliers less likely to avoid being brought into ANDA litigation
- Involvement in the ANDA submission triggers potential liability
- Scope of injunction against API supplier should be narrowly tailored
- U.S. subsidiary/affiliate of foreign supplier may be at risk if it was involved in the ANDA filing process or will be involved in importing, selling, manufacturing, or marketing of the future product

Liability Of The Foreign Supplier After Launch

- No safe harbor -- importation, sale, etc. are subject to liability
- Post-launch remedies include
  - pre-launch remedies (injunction/stay of FDA approval) -- 35 U.S.C. 271(e)(4)(A), (B)
  - monetary relief (*e.g.*, damages) -- 35 U.S.C. 271(e)(4)(C)
- Direct and indirect infringers are jointly and severally liable
- No less than a reasonable royalty -- 35 U.S.C. 284
- Lost Profits
- Enhanced damages for willfulness -- 35 U.S.C. 284
- Attorneys Fees for "Exceptional Case" -- 35 U.S.C. 285

Foreign Third-Party Discovery Generally

- U.S. discovery rules permit broad discovery of information within the "possession, custody and control" of parties and non-parties that are within the federal courts' jurisdiction
- Discovery from foreign third parties located outside the U.S. is governed by international treaty (*e.g.*, Hague Convention)
- Letter of Request limits permissible discovery, *e.g.*, requests for documents may be prohibited (as in Spain); deposition questions must be disclosed in advance

Some Discovery Considerations For The Non-Party Foreign Supplier

- Potential discovery under Hague Convention
- Consideration of voluntary compliance with discovery requests issued to ANDA applicant
- Potential inability of ANDA applicant to rely on incomplete information or information not produced during discovery (*e.g.*, underlying test data; partial test results produced)
- Potential that supplier will eventually be added as a party
- Potential requirement for expedited discovery to catch up in a consolidated action
- Potential that document production will lead to identification of additional witnesses for depositions

Discovery Issues For The Foreign Supplier As A Party

- Full discovery under the U.S. Federal Rules
  - Paper Documents/Samples/Site Inspections
  - Electronic Discovery
  - Depositions
  - Interrogatories
  - Requests for Admissions
- Discovery and use of information from prior litigations
- Privilege and immunity issues
  - Attorney-Client Privilege
  - Work Product Immunity
  - Joint Defense
  - Common Interest

Discovery Of Esteve In The Omeprazole Case

- Dec 2002: Astra seeks documents from Esteve's files from Mylan -- Esteve produces limited voluntary discovery through Mylan
- May 2003: Court denies Astra's motion to compel production
- May 2003: Court denies Astra's motion to add Esteve as party
- May 2003: Astra submits motion for Letter of Request to take depositions of Esteve witnesses in Spain – granted in June
- Jul 29, 2003: Esteve depositions in Court of First Instance 24 Barcelona
- Aug 4, 2003: Mylan launches product
- Aug 8, 2003: Astra files separate lawsuit against Esteve
- Dec 03 – Apr 04: Expedited discovery of Esteve in Spain and U.S.

Testing of Finished Product and Intermediates

- Hundreds of samples produced by Mylan/Esteve
- Finished Product (capsules) – Mylan
- Intermediates (pellets at each coating level) – LDE
- Raw Materials (API and 9 excipients) – EQ, LDE and Mylan

Some Samples Production Issues

- Chain of custody
- Complications of shipping samples overseas
  - Shipping/storage conditions
  - Customs issues
- Sufficient supply of materials for counter-testing
- Representativeness of samples
  - Expiration/Degradation
  - Changes in specifications or manufacturing process

Some Testing Issues In Mylan/Esteve's Case

- "Alkaline Reacting Compound" = (1) pharmaceutically acceptable alkaline compound that (2) stabilizes the omeprazole [in the formulation] by (3) reacting to create a "micro-pH" around the omeprazole particles of not less than 7
- Astra alleged that every component of Mylan/Esteve's omeprazole-containing layer met the "ARC" requirement
- At least four potential areas for testing
  - presence of alleged ARC
  - pH of alleged ARC
  - stabilization by alleged ARC
  - "micro-pH" around omeprazole
- Astra presented some test evidence purporting to establish each of the above but focused mainly on pH and "micro-pH"

Astra's Battery of "ARC" Testing

- pH Testing: talc, HPMC, omeprazole, mixtures
- "micro-pH" testing: active layer material from pellet intermediates
- "Acid Challenge" tests and pH titrations: talc, HPMC
- EDX and FTIR spectroscopy: carbonates in talc
- "Stability" tests: active layer coating suspensions
- GC/MS: carbonates in HPMC
- Selected Mylan/Esteve early R&D and regulatory data

How Mylan/Esteve Overcame Astra's Tests

- Introduced contradictory test results
  - Samples testing by Mylan/Esteve's pH expert
  - Data submitted in previous litigation against Esteve in Europe
- Introduced credible expert testimony of pH and organic chemistry experts who pointed out inconsistencies and unsupported assumptions in opposing expert testimony/test evidence
- Highlighted inconsistency in testing of co-defendant's formulated pellet for presence of impurity while failing to use the same test on Mylan/Esteve's pellet to test for the same alleged impurity (the "super sniffer")

How Mylan/Esteve Overcame Astra's Tests

- Highlighted prior rulings in "First Wave" case
- Attacked relevance of Astra's testing
  - Design around theme (deliberate avoidance of "ARCs")
  - Patent disclosures (HPMC and talc not "ARCs")
  - Prior admission in EPO counterpart (talc not an "ARC")
  - Use of tests predating change in specifications
- Used simple, yet effective, in-court demonstration by organic chemistry expert to attack trace impurity stabilization theory
- Presented stability data for talc-free versions of Mylan/Esteve formulation

How Mylan/Esteve Overcame Astra's Tests

- Highlighted selective reliance on tests that did not represent Mylan/Esteve product
  - Early stability data for non-US versions of Esteve's products having different structures and specifications
  - Esteve's early pH testing predating change to pH specification for HPMC for Mylan/Esteve product
- Presented credible fact testimony about Esteve's product development
- Attacked failures of proof on multiple levels: presence of alleged ARC in raw material, presence of ARC in final product, presence of stabilizing amount in final product

Sales "At Risk" Prior To Adjudication
Risk/Reward Balancing

- Value of early market entry

  Versus

- Potential for considerable damages exposure
  - Damages not less than a "reasonable royalty"
  - Potential lost profits (multi-billion dollar, high margin product)
  - Potential enhanced damages (up to 3x actual)
  - Potential attorneys fees in "exceptional case"
  - Even if prevail at trial, damages accrue while decision is on appeal
- Mylan/Esteve's omeprazole launch in 2003 is believed to be first generic at-risk launch prior to a favorable trial court decision

Sales "At Risk" Prior To Adjudication
Likely Trend: More At-Risk Launches

- Reduced risk of willfulness finding under recent Fed. Cir. case law
- Increasingly competitive market environment
- Waning number of blockbuster drugs
- Consolidation and growth of generic industry
- Increase in authorized generics
- Recent change in law regarding obviousness
- Previously feared doomsday scenario has not occurred

Some Concluding Points

- A good pre-litigation design-around story can have significant impact (*e.g.*, avoidance of ARCs)
- Changes in an accused product or process even after start of litigation can have significant impact (*e.g.*, HPMC specification)
- Counter testing, while not required, can tip the balance *(e.g.*, "micro-pH")
- Discovery of previous litigation positions and foreign counterpart prosecution histories can reveal critical admissions (*e.g.*, talc is not an ARC; Esteve's omeprazole is acidic)
- Avoiding discovery from non-party collaborator could prevent assertion of potential defenses (*e.g.*, talc-free stability studies)

Some Concluding Points

- Common issues in consolidated case may be a significant advantage or disadvantage (*e.g.*, the "super sniffer")
- Reliance on non-representative data and/or cherry-picking documents produced by the other side can damage credibility (outdated pH testing/inapplicable stability studies)
- Multiple level attacks can expose critical failures of proof (*e.g.*, presence of alleged ARC in raw material, presence of ARC in final product, presence of stabilizing amount in final product)
- Early involvement of both local counsel and U.S. counsel in projects likely to lead to litigation helps reduce litigation risks and provides an invaluable liaison to U.S. litigation counsel when litigation occurs