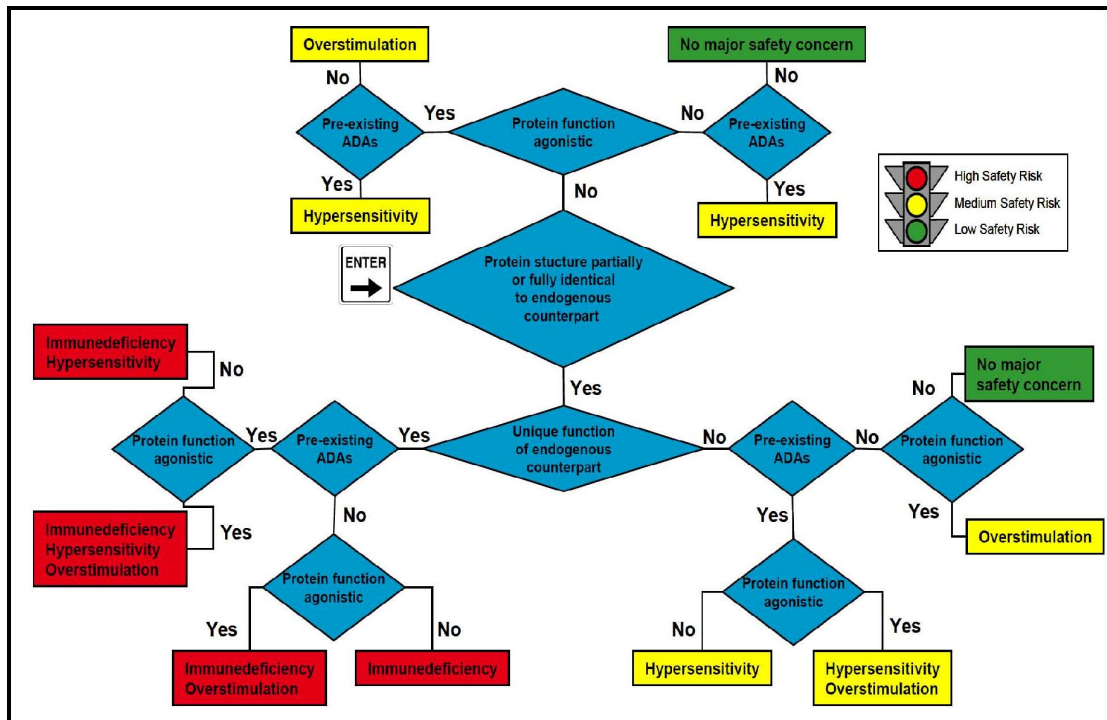


Fig. 6

An algorithm to identify “primary” risk factors of a given compound: Potential clinical consequences of immunogenicity



Instruction: Start at the Enter gateway and follow the pathway by answering the compound-related questions. Finally a prediction of potential immunogenicity-related side effects is provided:

- **Overstimulation:** Decreased clearance of agonistic drugs, which may lead to overstimulation of the affected signaling pathway.
- **Hypersensitivity:** Infusion reactions or anaphylaxis, especially in cases where pre-existing immune responses against therapeutic protein can be detected.
- **Immunodeficiency:** Neutralization of endogenous counterparts in cases they have a unique function.

Potential immunogenicity-related effects on efficacy are not addressed on this map !

According to Dr. B. Liedert, Oct. 2010

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## Fig. 7

“Secondary” disease- and product-related risk factors of a given compound: Probability of immunogenicity

### Disease-related risk factors

- Immune status of patients:  
immuno-suppressed (e.g cancer) < healthy < autoimmune disorders

### Product-related risk factors

- Sequence homology of therapeutic protein with human counterparts:  
fully human < de-immunized < humanized < chimeric < non-human
- Route of administration: i.v. < i.m. < s.c.
- Treatment regimen: single treatment < short-term treatment < long-term treatment
- Aggregates break B-cell tolerance
- Process-related impurities: e.g. host cell proteins or Protein A acting as adjuvants

According to Dr. B. Liedert, Oct. 2010

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