What are the line-of-sight rules?

Line-of-sight is necessary for all attacks (including every hex of an area attack) and all other abilities that specify a range (including looting, which technically has a range). Any non-attack ability that does not specify a range does not require line-of-sight.

Can I target empty hexes with an area attack?

While you are not technically "targeting" the empty hex, the hex of an area attack that is within the range specified by the attack can be empty. It can even be a wall, so long as there are enemies in the attack area that are in your line-of-sight.

Are there any line of sight or adjacency restrictions on what I can target with a melee area attack (area attack containing a grey hex)?

The only restriction, as above, is that you have to have line of sight on a figure to target it with an attack. Other than that, if the hex is in the configuration shown on the card, you can attack it.

If my area of effect for an attack is chiral (not equal to its mirror image) can I use the mirror image of the area instead?

Yes, in addition to applying any rotation to an area of effect, you can also use the mirror image of the area.

How does Add Target interact with area attacks?

Add Target always adds a single extra target within the range of your attack to the attack, and this target cannot be an enemy already targeted by the attack (a single attack ability cannot target the same enemy multiple times). So if you got an Add Target effect on an area attack, you could pick one enemy within range but outside of the area (because all enemies in the area are already getting attacked) to get hit by the attack as well. All conditions and other effects of the attack (other than effects that would add additional attack targets) would apply to the added target, as well. Each instance of the Add Target effect adds an additional target to the attack using the above guidelines. Note that if an attack ability targets everything within a specified range, Add Target would do nothing since you are already targeting everything in that range.

If I take one point of damage from an attack and have multiple abilities (from ability cards or items) which give me Shield when taking damage from an attack, do I have to use all of them?

No. You can choose which Shield bonus to apply in this case, and once the damage is reduced to zero, it is no longer a source of damage, so any other bonuses do not have to be used.

What exactly is considered using an item?

Any instance of you applying the effects of an item card to a situation is considered a use.

When exactly can I use an item? Can I use it in the middle of a movement or other ability?

You can use an item pretty much whenever you want, within the restrictions of what is written on the item card. So if it says "on your turn," use it any time you want on your turn, including during a movement or after you have taken all your actions. The only restriction is that if an item affects an attack (e.g. adds a bonus, adds an effect, adds advantage or disadvantage), it has to be used before an